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As confidentially submitted to the Securities and Exchange Commission on May 10, 2019.
This draft registration statement has not been filed publicly with the Securities and Exchange Commission and all information contained herein remains confidential.

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1
REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

PLIANT THERAPEUTICS, INC.

(Exact name of Registrant as specified in its charter)

Delaware	**2834**	**47-4272481**
(State or other jurisdiction of incorporation or organization)	**(Primary Standard Industrial Classification Code Number)**	**(I.R.S. Employer Identification No.)**

260 Littlefield Avenue
South San Francisco, CA 94080
(650) 481-6770
(Address, including zip code and telephone number, including area code, of Registrant's principal executive offices)

Bernard Coulie, M.D., Ph.D.
President and Chief Executive Officer
Pliant Therapeutics, Inc.
260 Littlefield Avenue
South San Francisco, CA 94080
(650) 481-6770
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Sam Zucker **Deepa M. Rich** **James Xu** **Goodwin Procter LLP** **601 Marshall Street** **Redwood City, CA 94063** **(650) 752-3100**	**Keith Cummings** **Chief Financial Officer** **Pliant Therapeutics, Inc.** **260 Littlefield Avenue** **South San Francisco, CA 94080** **(650) 481-6770**	**Kristin VanderPas** **Sean Clayton** **David Peinsipp** **Charles S. Kim** **Cooley LLP** **101 California Street 5th Floor** **San Francisco, CA 94111** **(415) 693-2000**

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

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

Large accelerated filer	☐	Accelerated filer	☐
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 7(a)(2)(B) of the Securities Act. ☐

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	**Proposed Maximum Aggregate Offering Price(1)**	**Amount of Registration Fee(2)**
Common Stock, par value $0.0001 per share	**$**	**$**

(1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act. Includes the offering price of any additional shares that the underwriters have the option to purchase.
(2) Calculated pursuant to Rule 457(o) under the Securities Act based on an estimate of the proposed maximum aggregate offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any state or other jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED , 2019

PRELIMINARY PROSPECTUS

Shares

Pliant Therapeutics, Inc.

Common Stock

$ per share

This is the initial public offering of our common stock. We are selling shares of common stock. Prior to this offering there has been no public market for our shares. We currently expect the initial public offering price to be between $ and $ per share of common stock.

We have granted the underwriters an option to purchase up to additional shares of common stock. The underwriters can exercise this option at any time within 30 days after the date of this prospectus.

We intend to apply to list our common stock on The Nasdaq Global Market under the symbol "PLRX."

Investing in our common stock involves risks. See "Risk Factors" beginning on page 11.

We are an "emerging growth company" as defined in the Jumpstart Our Business Act of 2012 and, as such, we have elected to comply with certain reduced reporting requirements for this prospectus and may elect to do so in future filings.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public Offering Price	$	$
Underwriting Discounts and Commissions(1)	$	$
Proceeds to Pliant Therapeutics, Inc. (before expenses)	$	$

(1) See "Underwriting" for additional information regarding total underwriter compensation.

The underwriters expect to deliver the shares of common stock to purchasers on or about , 2019 through book-entry facilities of The Depository Trust Company.

Joint Book-Running Managers

Citigroup **Cowen** **Piper Jaffray**

Lead Manager

Needham & Company

, 2019

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We and the underwriters have not authorized anyone to provide any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside of the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes included elsewhere in this prospectus. You should also consider, among other things, the matters described in the sections entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Unless otherwise stated, all references to "us," "our," "Pliant," "we," the "Company" and similar designations refer to Pliant Therapeutics, Inc.

Overview

We are a clinical stage biopharmaceutical company focused on discovering and developing novel therapies for the treatment of fibrosis. Our initial focus is on treating fibrosis by inhibiting integrin-mediated activation of TGF-ß. Our lead product candidate, PLN-74809, is an oral small-molecule dual selective inhibitor of avß6 and avß1 integrins that we are developing for the treatment of idiopathic pulmonary fibrosis, or IPF, and primary sclerosing cholangitis, or PSC. We have completed a Phase 1a SAD/MAD trial and are currently conducting a Phase 1b proof-of-mechanism trial of PLN-74809 in IPF and expect to receive data in mid-2019. In the second half of 2019, we plan to initiate two Phase 2a trials in IPF. We also plan to submit an IND for PLN-74809 for the treatment of PSC in the second half of 2019, and plan to initiate a Phase 2a trial as soon as possible thereafter. Our second product candidate, PLN-1474, is an oral small-molecule selective inhibitor of avß1 for the treatment of stage F3/F4 liver fibrosis associated with NASH. We are currently conducting IND-enabling studies and plan to submit an IND application for PLN-1474 by the end of 2019. We have applied our deep understanding of fibrosis biology, along with our medicinal chemistry and translational medicine expertise to develop a set of proprietary tools designed to discover and de-risk product candidates quickly and efficiently. Our goal is to become a world-leading fibrosis company, developing and commercializing disease-modifying therapies across a spectrum of fibrotic diseases.

Fibrosis Background

Fibrosis refers to excessive scarring, often resulting from aberrant tissue repair processes. Fibrosis occurs when normal tissue repair pathways become dysregulated, causing excessive collagen deposition in the affected organs and ultimately impairing their physiological function. Fibrosis occurs in many organ systems throughout the body including the lungs, liver, kidneys, gastrointestinal tract, skin and muscles. While the exact pathologies for diseases in these organs vary, the development of fibrosis involves many common cell types and biochemical pathways including the transforming growth factor beta, or TGF-ß, signaling pathway.

TGF-ß and Integrins in Fibrosis

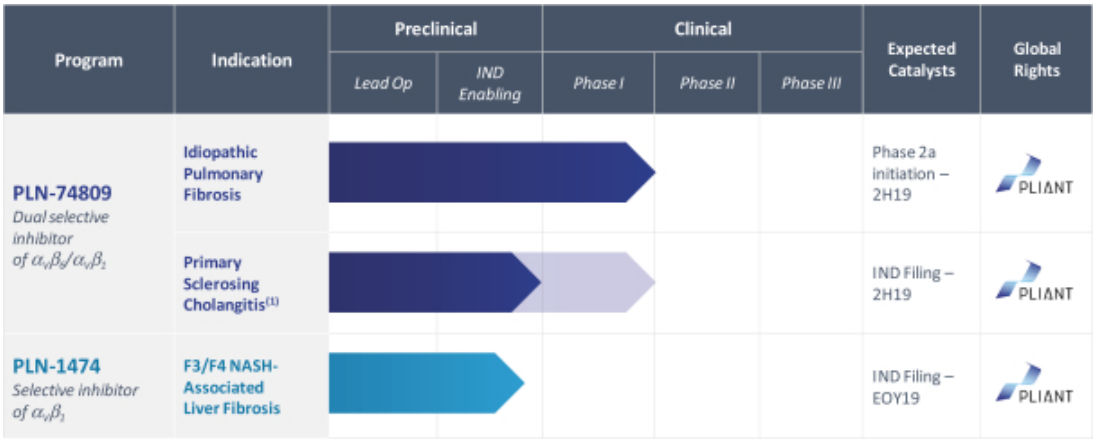
TGF-ß signaling is the central pathway by which fibrosis occurs. TGF-ß is a signaling molecule that is secreted by cells as an inactive complex and stored in the extra-cellular matrix. In healthy tissue, TGF-ß is transiently activated in response to tissue injury, resulting in collagen production and, ultimately, healing of the tissue. In fibrosis, however, TGF-ß becomes continuously activated, leading to excess collagen production in the absence of the initial tissue injury which leads to thickening and stiffening of tissues.

There have been a number of prior approaches to treating fibrosis through TGF-ß inhibition, including through antibodies to TGF-ß and its receptor. However, systemic blockade of TGF-ß signaling has shown significant toxicity due to effects on TGF-ß's normal physiologic functions.

TGF-ß can be activated by a class of cell surface proteins known as integrins. In certain fibrotic diseases such as IPF and PSC, the integrins avß6 and avß1, which are normally expressed at very low levels, have been

shown to be upregulated and to cause the continuous activation of TGF-ß. We believe that, by inhibiting fibrosis-specific TGF-ß activators such as avß6 and avß1, it may be possible to block abnormal TGF-ß activation in fibrotic tissues without affecting TGF-ß signaling in healthy tissues. Historically, integrin drug development has been hampered by the difficulty of developing integrin inhibitors that are both selective for specific integrins and orally bioavailable. We believe our pipeline of orally bioavailable, highly selective integrin inhibitors has the potential to address these challenges.

Our Pipeline



(1) We plan to submit an IND for PLN-74809 for the treatment of PSC in the second half of 2019 incorporating the data from the completed Phase 1a healthy volunteer trial and plan to initiate a Phase 2a clinical trial for PSC thereafter.

PLN-74809 in IPF and PSC

Our lead wholly owned product candidate, PLN-74809, is a small-molecule, dual-selective inhibitor of avß6 and avß1 that we are advancing in IPF and PSC. IPF is the most common and severe form of progressive pulmonary fibrosis, affecting approximately 140,000 patients in the United States. The average life expectancy for patients with confirmed IPF is between three and five years. There are currently two U.S. Food and Drug Administration, or FDA, approved therapies for IPF. Both have shown modest slowing of disease progression. However, both therapies have raised significant safety and tolerability concerns. PSC is a progressive liver disorder affecting approximately 30,000 to 45,000 patients in the United States. Patients have a median survival of 10 to 12 years without intervention and carry high lifetime risk of developing gastrointestinal malignancies. There are currently no FDA-approved therapies for PSC.

While expressed at very low levels in normal tissues, avß6 and avß1 are upregulated in the pulmonary tissues of IPF patients, and in the liver tissues of PSC patients. They both serve as activators of TGF-ß, leading to increased collagen production and fibrosis in these tissues. By blocking TGF-ß activation by both avß6 and avß1, we believe PLN-74809 may slow and potentially halt the progression of fibrosis in these patient populations. PLN-74809 has been granted orphan drug designation by the FDA for both IPF and PSC.

We have completed a Phase 1a single ascending dose, or SAD, multiple ascending dose, or MAD, and food effect clinical trial involving 85 healthy volunteers in which PLN-74809 was shown to be orally bioavailable and generally well tolerated with a half-life that may support once-daily dosing.

We are currently conducting a Phase 1b proof-of-mechanism trial in 16 healthy volunteers measuring pSMAD, a key biomarker for TGF-ß activation. This trial will evaluate safety, pharmacokinetics and

pharmacodynamics, or PK/PD, and inform dose selection for our Phase 2 program. We expect to receive data from our Phase 1b in mid-2019. In the second half of 2019, we plan to initiate two Phase 2a trials in IPF. We also plan to submit an IND for PLN-74809 for the treatment of PSC in the second half of 2019, and plan to initiate a Phase 2a trial as soon as possible thereafter.

PLN-1474 in F3/F4 Liver Fibrosis Associated with NASH

Our second wholly owned product candidate, PLN-1474, is an oral, small-molecule, selective inhibitor of avß1 in development for treatment of stage F3/F4 liver fibrosis associated with nonalcoholic steatohepatitis, or NASH. NASH is a more severe form of non-alcoholic fatty liver disease, or NAFLD. NASH is highly prevalent, affecting approximately 16.5 million adults in the United States, including approximately 3.3 million with stage F3/F4 fibrosis. The stage of fibrosis is the strongest predictor of liver-related morbidity and all-cause mortality in NASH. Patients with F3 and F4 fibrosis carry liver-related mortality risk that is 17 times and 42 times greater, respectively, than NASH patients without fibrosis. Therefore, we believe that treating F3/F4 liver fibrosis will have an impact on liver-related morbidity and all-cause mortality in NASH. There are currently no approved therapies for NASH and the candidates in development to date have shown only modest antifibrotic effects in published clinical trials.

avß1 serves as an activator of TGF-ß and its expression has been shown to be upregulated in activated hepatic stellate cells and correlated with severity of liver fibrosis. By inhibiting avß1, we believe PLN-1474 could have a potent direct antifibrotic effect in advanced liver fibrosis. We are currently completing investigational new drug, or IND, enabling studies of PLN-1474 and plan to submit an IND application by the end of 2019.

Our Approach and Capabilities

Our approach to drug development in fibrosis combines our deep knowledge of the biology of fibrosis with various cellular, tissue, and *in vivo* assays developed in house to uncover pathways and potential targets. We have developed and utilized a quantitative fibrosis target expression atlas to identify and validate novel fibrosis targets. We have built a library of over 4,500 integrin inhibitors that we test against these identified targets to select potential candidates. In addition to our integrin library, we have a non-integrin based library of over 70,000 compounds that we also screen against non-integrin targets. We evaluate potential candidates in a series of integrin selectivity assays, cell-based assays, precision cut tissue slices and animal models prior to advancing our product candidates into development.

A key component of our de-risking strategy is our live fibrotic human tissue program. We obtain live fibrotic human tissue post-transplant through our partners at the University of California, San Francisco and Stanford University and utilize proprietary protocols to maintain viability of these tissues for multiple days. We test our product candidates in this live tissue and measure multiple markers of antifibrotic activity, effectively bridging the gap between animal models and clinical proof-of-concept. We believe data from these live fibrotic human tissue experiments will increase our confidence that the tested product candidates will show anti-fibrotic effects in patients.

Once in the clinic, we continue to de-risk our programs by designing clinical trials that allow us to show proof-of-mechanism in advance of clinical efficacy data. We utilize pharmacodynamic biomarkers and advanced imaging techniques, including positron emission tomography, or PET, to evaluate target engagement of our product candidates over relatively short time periods and observe whether the product candidate is having its anticipated effect. We believe these collective capabilities uniquely allow us to (i) efficiently identify targets, (ii) optimize the potency and selectivity of candidates and (iii) de-risk product candidates in advance of clinical proof-of-concept.

Pliant was founded in 2015 by world-renowned researchers Dean Sheppard, Rik Derynck, Bill DeGrado and Hal Chapman from the University of California, San Francisco who bring broad experience in fibrosis biology and small-molecule chemistry among other related disciplines. In addition, we have built an executive team with highly relevant experience in drug discovery and clinical development. To date, Pliant has raised over $120 million from investors including Third Rock Ventures, Cowen Healthcare Investments, Eventide Asset Management, Schroder Adveq Management, Menlo Ventures, S-Cubed Capital and Agent Capital.

Our Strategy

Our goal is to become a world-leading fibrosis company, developing and commercializing disease-modifying therapies across a spectrum of fibrotic diseases. To achieve this, we are focused on the following key strategies:

- Rapidly advance PLN-74809 in IPF and PSC through clinical development and commercialization.
- Rapidly advance our second compound, PLN-1474, in NASH.
- Selectively evaluate partnerships in indications and geographies where we believe partners can add commercial and/or development capabilities.
- Explore opportunities for our pipeline assets in additional fibrotic indications.
- Leverage our industry leading tools and capabilities to advance our mission of becoming a leading fibrosis company.

Risks Associated with Our Business

Our business is subject to numerous risks that you should be aware of before making an investment decision. These risks are described more fully in the section entitled “Risk Factors.” These risks include, among others:

- We have a limited operating history, which may make it difficult to evaluate our prospects and likelihood of success.
- Our financial condition raises substantial doubt as to our ability to continue as a going concern.
- Our business is highly dependent on the success of our lead product candidate, PLN-74809, as well as any other product candidates that we advance into the clinic. All of our product candidates will require significant additional preclinical and clinical development before we may be able to seek regulatory approval for and launch a product commercially.
- Clinical development involves a lengthy, complex and expensive process, with an uncertain outcome.
- We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of PLN-74809 or any other product candidates.
- If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than us.
- If we lose key management personnel, or if we fail to recruit additional highly skilled personnel, our ability to develop current product candidates or identify and develop new product candidates will be impaired, could result in loss of markets or market share and could make us less competitive.

- Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.

Corporate History and Information

We were incorporated under the laws of the State of Delaware in June 2015. Our principal executive office is located at 260 Littlefield Avenue, South San Francisco, California 94080, and our telephone number is (650) 481-6770. Our website address is https://pliantrx.com. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus.

We use various trademarks and trade names in our business, including without limitation our corporate name and logo. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Implications of Being an Emerging Growth Company

We qualify as an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include, but are not limited to:

- being permitted to present only two years of audited financial statements in this prospectus and only two years of related "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our periodic reports and registration statements, including this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements, and registration statements, including in this prospectus; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these exemptions for up to five years from the date of effectiveness of this registration statement or such earlier time that we are no longer an emerging growth company. We will cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the last day of the fiscal year in which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth

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

THE OFFERING

Common stock offered by us	shares.
Option to purchase additional shares	We have granted the underwriters an option to purchase up to additional shares of common stock from us. The underwriters can exercise this option at any time within 30 days from the date of this prospectus.
Common stock to be outstanding immediately after this offering	shares (or shares if the underwriters exercise their option to purchase additional shares in full).
Use of proceeds	We estimate that we will receive net proceeds from the sale of our common stock in this offering of approximately $ million, or $ million if the underwriters exercise in full their option to purchase additional shares, assuming an initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to fund the clinical development of our lead product candidate, PLN-74809, the preclinical and clinical development of our second product candidate, PLN-1474, and for business development activities, working capital and other general corporate purposes. See the section entitled “Use of Proceeds” for additional information.
Risk factors	You should read carefully the section entitled “Risk Factors” and other information included in this prospectus for a discussion of factors that you should consider before deciding to invest in our common stock.
Proposed Nasdaq Global Market symbol	“PLRX”

The number of shares of our common stock to be outstanding after this offering is based on 120,608,203 shares of common stock (including our redeemable convertible preferred stock on an as-converted basis) outstanding as of December 31, 2018, and excludes:

- 841,800 shares of our common stock issuable upon the exercise of options outstanding as of December 31, 2018, under the 2015 Equity Incentive Plan, or the 2015 Plan, at a weighted-average exercise price of $0.29 per share, or pursuant to rights to purchase restricted stock at a weighted-average purchase price of $0.01 per share;
- 7,029,718 shares of our common stock reserved for future issuance under the 2015 Plan as of December 31, 2018;
- shares of our common stock reserved for future issuance under our 2019 Stock Option and Incentive Plan, or the 2019 Plan, which will become available for issuance upon the effectiveness of the registration statement of which this prospectus is a part; and
- shares of our common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan, or the 2019 ESPP, which will become available for issuance upon the effectiveness of the registration statement of which this prospectus is a part.

Unless otherwise indicated, this prospectus reflects and assumes the following:

- a 1-for- reverse stock split of our common stock to be effected on , 2019;
- the automatic conversion of all outstanding shares of our redeemable convertible preferred stock as of December 31, 2018 into an aggregate of 105,501,221 shares of our common stock immediately prior to the completion of this offering;
- no exercise of the outstanding options or purchase rights described above;
- no exercise by the underwriters of their option to purchase up to additional shares of our common stock in this offering; and
- the filing and effectiveness of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws, which will occur immediately prior the completion of this offering.

Unless otherwise indicated, the number of shares of common stock outstanding includes 5,361,529 unvested restricted shares of common stock subject to repurchase as of December 31, 2018.

Summary Financial Data

The following tables present summary financial data for our business. We have derived the summary statements of operations data for the years ended December 31, 2017 and 2018 and the summary balance sheets data as of December 31, 2018 from our audited financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future. You should read this data together with our financial statements and related notes appearing elsewhere in this prospectus and the information in the sections entitled "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

(In thousands, except share and per share amounts)	Years Ended December 31, 2017	2018
Statements of Operations Data:		
Operating expenses:		
Research and development	$ 14,526	$ 24,415
General and administrative	3,823	6,500
Total operating expenses	18,349	30,915
Loss from operations	(18,349)	(30,915)
Interest income	16	688
Other income (expense), net	—	(49)
Net loss	$ (18,333)	$ (30,276)
Accretion to redemption value and cumulative dividends on redeemable convertible preferred stock	(2,289)	(4,876)
Net loss attributable to common stockholders	$ (20,622)	$ (35,152)
Net loss per share attributable to common stockholders, basic and diluted(1)	$ (3.59)	$ (4.22)
Weighted-average shares used in computing net loss per share attributable to common stockholders, basic and diluted(1)	5,745,000	8,333,000
Pro forma net loss per share attributable to common stockholders, basic and diluted(1)		$
Weighted-average shares outstanding used in computing pro forma net loss per share attributable to common stockholders, basic and diluted(1)		

(1) See Notes 3 and 16 to our financial statements included elsewhere in the prospectus for an explanation of the calculations of our basic and diluted net loss per share, pro forma net loss per share and the weighted-average number of shares used in the computation of the per share amounts.

(In thousands)	As of December 31, 2018		
	Actual	Pro Forma(1)	Pro Forma As Adjusted(2)(4)
Balance Sheets Data:			
Cash and cash equivalents	$ 60,949		$
Working capital(3)	56,649		
Total assets	66,529		
Redeemable convertible preferred stock	132,103		
Accumulated deficit	(71,470)		
Total stockholders' (deficit) equity	(71,469)		

(1) The pro forma column in the balance sheet data table above gives effect to (i) the automatic conversion of all outstanding shares of our redeemable convertible preferred stock as of December 31, 2018 into an aggregate of 105,501,221 shares of our common stock immediately prior to the completion of this offering as if such conversion had occurred on December 31, 2018; and (ii) the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the completion of this offering.

(2) The pro forma as adjusted column in the balance sheet data table above gives effect to (i) the pro forma adjustments set forth in footnote (1) above; and (ii) the issuance and sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

(3) We define working capital as current assets less current liabilities. See our financial statements and related notes appearing elsewhere in this prospectus for details regarding our current assets and current liabilities.

(4) Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, the amount of each of cash and cash equivalents, working capital, total assets and total stockholders' (deficit) equity by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase or decrease of 1.0 million shares in the number of shares we are offering would increase or decrease, as applicable, the amount of each of cash and cash equivalents, working capital, total assets and total stockholders' (deficit) equity by approximately $ million, based on the assumed initial public offering price per share, the midpoint of the price range as set forth on the cover page of this prospectus, remains the same. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus, including our financial statements and related notes appearing elsewhere in this prospectus and in the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant net losses since inception and we expect to continue to incur significant net losses for the foreseeable future.

We have incurred significant net losses in each reporting period since our inception, have not generated any revenue to date and have financed our operations principally through equity financing. If our product candidates are not successfully developed and approved, we may never generate any revenue. We continue to incur significant research and development and other expenses related to our ongoing operations. For the years ended December 31, 2017 and 2018, we reported a net loss of $18.3 million and $30.3 million, respectively. As of December 31, 2018, we had an accumulated deficit of $71.5 million. We have devoted substantially all of our resources and efforts to research and development and we expect that it will be several years, if ever, before we generate revenue from product sales. Even if we receive marketing approval for and commercialize one or more of our product candidates, we expect that we will continue to incur substantial research and development and other expenses in order to develop and market additional potential product candidates.

We expect to continue to incur significant losses for the foreseeable future, and we anticipate that our expenses will increase substantially if, and as, we:

- advance the development of our lead product candidate, PLN-74809, and our other product candidates through clinical development, and, if successful, later-stage clinical trials;
- discover and develop new product candidates;
- advance our preclinical development programs, including PLN-1474, into clinical development;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- commercialize PLN-74809, our other product candidates and any future product candidates, if approved;
- increase the amount of research and development activities to identify and develop product candidates;
- hire additional clinical development, quality control, scientific and management personnel;
- expand our operational, financial and management systems and increase personnel, including personnel to support our clinical development and manufacturing efforts and our operations as a public company;
- establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any products for which we may obtain marketing approval and intend to commercialize on our own or jointly with third parties;
- maintain, expand and protect our intellectual property portfolio; and
- invest in or in-license other technologies or product candidates.

To become and remain profitable, we must develop and eventually commercialize products with significant market potential. This will require us to be successful in a range of challenging activities, including completing

preclinical studies and clinical trials, obtaining marketing approval for product candidates, manufacturing, marketing and selling products for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenue that is significant enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would 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.

Even if this offering is successful, we will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs, future commercialization efforts or other operations.

Developing biopharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct our planned clinical trials of PLN-74809, continue research and development to initiate clinical trials of PLN-1474 and any future product candidates that we may develop, seek regulatory approvals for our product candidates and to launch and commercialize any products for which we receive regulatory approval. Following this offering, we also expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in order to maintain our continuing operations. If we are unable to raise capital when needed or on acceptable terms, we may be forced to delay, reduce or eliminate one or more of our research and drug development programs or future commercialization efforts.

As of December 31, 2018, we had approximately $60.9 million in cash and cash equivalents. Based on our current operating plan, we believe that the net proceeds from this offering, together with existing cash and cash equivalents, will be sufficient to fund our operating expenses and capital expenditure requirements through . However, our future capital requirements and the period for which our existing resources will support our operations may vary significantly from what we expect, and we will in any event require additional capital in order to complete clinical development of any of our current programs. Our monthly spending levels will vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development, marketing and commercialization activities. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the initiation, progress, timing, costs and results of preclinical studies and clinical trials for our product candidates;
- the clinical development plans we establish for these product candidates;
- the number and characteristics of product candidates that we develop;
- the outcome, timing and cost of meeting regulatory requirements established by the U.S. Food and Drug Administration, or FDA, and other comparable foreign regulatory authorities;
- whether we are able to enter into collaboration agreements and the terms of any such agreements;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates;
- the effect of competing technological and market developments;
- the cost and timing of completion of commercial-scale outsourced manufacturing activities; and

- the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own.

We do not have any committed external source of funds or other support for our development efforts and we cannot be certain that additional funding will be available on acceptable terms, or at all. Until we can generate sufficient revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements. If we raise additional funds through public or private equity offerings, the terms of these securities may include liquidation or other preferences that adversely the rights of our common stockholders. Further, to the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, your ownership interest will be diluted. In addition, any debt financing may subject us to fixed payment obligations and covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable intellectual property or other rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. We also may be required to seek collaborators for any of our product candidates at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates or one or more of our other research and development initiatives. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

The amount of our future losses is uncertain and our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

Our quarterly and annual operating results may fluctuate significantly in the future due to a variety of factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and success or failure of clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- our ability to successfully recruit and retain subjects for clinical trials, and any delays caused by difficulties in such efforts;
- our ability to obtain marketing approval for our product candidates, and the timing and scope of any such approvals we may receive;
- the timing and cost of, and level of investment in, research and development activities relating to our product candidates, which may change from time to time;
- the cost of manufacturing our product candidates, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- our ability to attract, hire and retain qualified personnel;
- expenditures that we will or may incur to develop additional product candidates;
- the level of demand for our product candidates should they receive approval, which may vary significantly;

- the risk/benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future therapeutics that compete with our product candidates;
- the changing and volatile U.S. and global economic environments; and
- future accounting pronouncements or changes in our accounting policies.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. 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.

Our financial condition raises substantial doubt as to our ability to continue as a going concern.

Our financial statements have been prepared assuming that we will continue to operate as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. However, based on our current forecast, we do not have sufficient resources for at least the next year following the date that the financial statements appearing elsewhere in this prospectus were issued. These conditions raise substantial doubt about our ability to continue as a going concern. Additionally, our independent registered public accounting firm has included in its audit opinion for the year ended December 31, 2018 an explanatory paragraph that there is substantial doubt as to our ability to continue as a going concern. Our ability to continue as a going concern will require us to obtain additional financing or enter into strategic transactions. The reaction of investors to the inclusion of a going concern statement by our auditors and our potential inability to continue as a going concern may materially adversely affect our share price and our ability to raise new capital or enter into strategic alliances. If we become unable to continue as a going concern, we may have to liquidate our assets and the values we receive for our assets in liquidation or dissolution could be significantly lower than the values reflected in our financial statements.

Risks Related to Research and Development and the Biopharmaceutical Industry

We have a limited operating history, which may make it difficult to evaluate our prospects and likelihood of success.

We are a clinical-stage biopharmaceutical company with a limited operating history. We were incorporated in 2015, have no products approved for commercial sale and have not generated any revenue. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and performing research and development of our product candidates and our technology related to transforming growth factor beta, or TGF-ß, signaling and integrin biology, medicinal chemistry, translational screening technologies, and clinical insights to discover and develop novel therapies for the treatment of fibrosis. Our approach to the discovery and development of product candidates is unproven, and we do not know whether we will be able to develop any products of commercial value. In addition, our lead product candidate, PLN-74809, is in early clinical development for the treatment of IPF and preclinical development for the treatment of PSC, while our second product candidate, PLN-1474, is in the preclinical stage. Both programs will require substantial additional development and clinical research time and resources before we would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. We have not yet demonstrated the ability to progress any product candidate through clinical trials. We are still in preclinical and early clinical development and may be unable to obtain regulatory approval, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Investment in biopharmaceutical product

development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval and become commercially viable. In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields. Consequently, we have no meaningful history of operations upon which to evaluate our business, and predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing drug products.

Our business is highly dependent on the success of our lead product candidate, PLN-74809, as well as any other product candidates that we advance into the clinic. All of our product candidates will require significant additional preclinical and clinical development before we may be able to seek regulatory approval for and launch a product commercially.

We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We are very early in our development efforts and have only one product candidate, PLN-74809, in early clinical development. Because PLN-74809 is our lead product candidate, if PLN-74809 encounters safety or efficacy problems, development delays, regulatory issues or other problems, our development plans and business would be significantly harmed. We have completed a Phase 1a SAD/MAD trial and are currently conducting a Phase 1b proof-of-mechanism trial of PLN-74809 in IPF and expect to receive data in the second quarter of 2019. In the second half of 2019, we plan to initiate two Phase 2a trials in idiopathic pulmonary fibrosis, or IPF. We also plan to submit an IND for PLN-74809 for the treatment of primary sclerosing cholangitis, or PSC, in the second half of 2019, and plan to initiate a Phase 2a trial thereafter. We are also developing PLN-1474 for liver fibrosis associated with nonalcoholic steatohepatitis, or NASH, but have not yet advanced this candidate into the clinic. We are currently conducting investigational new drug, or IND-enabling activities for PLN-1474 and plan to submit an IND application by the end of 2019.

Before we can generate any revenue from sales of our lead product candidate, PLN-74809, or any of our other product candidates, we must undergo additional preclinical and clinical development, regulatory review and approval in one or more jurisdictions. In addition, if one or more of our product candidates are approved, we must ensure access to sufficient commercial manufacturing capacity and conduct significant marketing efforts in connection with any commercial launch. These efforts will require substantial investment, and we may not have the financial resources to continue development of our product candidates.

We may experience setbacks that could delay or prevent regulatory approval of, or our ability to commercialize, our product candidates, including:

- negative or inconclusive results from our preclinical studies or clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- product-related side effects experienced by subjects in our clinical trials or by individuals using drugs or therapeutics similar to our product candidates;
- delays in submitting INDs or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- delays in enrolling subjects in clinical trials;
- high drop-out rates of subjects from clinical trials; inadequate supply or quality of product candidates or other materials necessary for the conduct of our clinical trials;

- greater than anticipated clinical trial costs;
- inability to compete with other therapies;
- poor efficacy of our product candidates during clinical trials;
- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or
- varying interpretations of data by the FDA and similar foreign regulatory agencies.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and our manufacturing, marketing, distribution and sales efforts or that of any future collaborator.

Our approach to drug discovery and development in the area of fibrotic diseases, with an initial focus on tissue-specific integrin modulation and TGF-ß signaling inhibition, is unproven and may not result in marketable products.

Our approach is designed to discover and develop targeted treatments for fibrosis with an initial focus on the antagonism of tissue-specific TGF-ß signaling through the inhibition of integrins known to mediate the release of activated TGF-ß in fibrotic tissue. However, although multiple studies are currently underway, to date, this mechanism has not been definitively proven to successfully treat fibrosis. Targeting integrins to treat fibrosis is a novel approach in a rapidly developing field, and there can be no assurance that we will not experience currently unknown problems or delays in developing our product candidates, that such problems or delays will not result in unanticipated costs, or that any such development problems can be solved. We have only tested our lead product candidate, PLN-74809, in healthy volunteers. Therefore, we may ultimately discover that our approach and any product candidates resulting therefrom do not possess properties required for therapeutic effectiveness. As a result, we may never succeed in developing a marketable product.

In addition, while we have developed an extensive panel of cell assays and precision cut tissue assays and have utilized animal models to uncover biological pathways, understood gene expression changes and optimized the potency and selectivity of our potential product candidates, there can be no assurance that our technology will yield their intended benefits. While we believe our assays represent a differentiator in our approach to drug development, our approach has not yet been clinically proven to yield results. Our practice of evaluating our product candidates in live human fibrotic tissue samples before advancing them into the clinic is intended to serve as a bridge between animal models and clinical proof-of-concept. However, there can be no assurance that positive results observed from preclinical animal testing and human fibrotic tissue models will be replicated when a program is advanced into clinical development. In addition, our practice of utilizing live human fibrotic tissue as part of our development efforts may become more widespread in the future, and this approach may be adopted and replicated by others, including our competitors.

Studies involving human tissue samples may also be subject to institutional and government human subject privacy policies that may vary by territory. We or our partners who provide us with human tissue samples, or conduct tissue and/or animal studies on our behalf, may be found to be in violation of one or more of these regulations or policies and may be subject to closure, censure or other penalties. In some cases, these penalties could materially impact the performance, availability, or validity of studies conducted by us on our behalf. Even in the absence of violations resulting in penalties, regulatory and other authorities may refuse to authorize the conduct or to accept the results of studies for regulatory or ethical reasons.

Clinical development involves a lengthy, complex and expensive process, with an uncertain outcome.

To obtain the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. In particular, the general approach for FDA approval of a new drug is dispositive data from two well-controlled, Phase 3 clinical trials of the relevant drug in the relevant patient population. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and take years to complete. A product candidate can fail at any stage of testing, even after observing promising signals of activity in earlier preclinical studies or clinical trials. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence clinical trials are never approved as products and there can be no assurance that any of our future clinical trials will ultimately be successful or support further clinical development of PLN-74809 or any of our other product candidates. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons, including:

- preclinical studies or clinical trials may show the product candidates to be less effective than expected (e.g., a clinical trial could fail to meet its primary endpoint(s)) or to have unacceptable side effects or toxicities;
- failure to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful;
- failure to receive the necessary regulatory approvals;
- manufacturing costs, formulation issues, pricing or reimbursement issues, or other factors that make a product candidate uneconomical; and
- the proprietary rights of others and their competing products and technologies that may prevent one of our product candidates from being commercialized.

In addition, differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products. Additionally, some of our trials may be open-label studies, where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Therefore, it is possible that positive results observed in open-label trials will not be replicated in later placebo-controlled trials.

In addition, the standards that the FDA and comparable foreign regulatory authorities use when regulating us require judgment and can change, which makes it difficult to predict with certainty how they will be applied. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also

encounter unexpected delays or increased costs due to new government regulations. Examples of such regulations include future legislation or administrative action, or changes in FDA policy during the period of product development and FDA regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any product candidates that we develop.

If we seek to conduct clinical trials in foreign countries or pursue marketing approvals in foreign jurisdictions, we must comply with numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the United States and vice versa.

Successful completion of clinical trials is a prerequisite to submitting a marketing application to the FDA and similar marketing applications to comparable foreign regulatory authorities, for each product candidate and, consequently, the ultimate approval and commercial marketing of any product candidates. We may experience negative or inconclusive results, which may result in our deciding, or our being required by regulators, to conduct additional clinical studies or trials or abandon some or all of our product development programs, which could have a material adverse effect on our business.

We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of PLN-74809 or any other product candidates.

We may experience delays in initiating or completing clinical trials. We also may experience numerous unforeseen events during, or as a result of, any future clinical trials that could delay or prevent our ability to receive marketing approval or commercialize PLN-74809 or any other product candidates, including:

- regulators or institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- the FDA or other comparable regulatory authorities may disagree with our clinical trial design, including with respect to dosing levels administered in our planned clinical trials, which may delay or prevent us from initiating our clinical trials with our originally intended trial design;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- the number of subjects required for clinical trials of any product candidates may be larger than we anticipate or subjects may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- 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, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs, Data Safety Monitoring Boards, or DSMBs, or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

- we may not have the financial resources available to begin and complete the planned trials, or the cost of clinical trials of any product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate to initiate or complete a given clinical trial; and
- the FDA or other comparable foreign regulatory authorities may require us to submit additional data such as long-term toxicology studies, or impose other requirements before permitting us to initiate a clinical trial.

Our product development costs will increase if we experience delays in clinical testing or in obtaining marketing approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. If we do not achieve our product development goals in the time frames we announce and expect, the approval and commercialization of our product candidates may be delayed or prevented entirely. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations. Any delays in our clinical development programs may harm our business, financial condition and results of operations significantly.

Our ongoing and future clinical trials may reveal significant adverse events or unexpected drug-drug interactions not seen in our preclinical studies and may result in a safety profile that could delay or prevent regulatory approval or market acceptance of any of our product candidates.

We completed our Phase 1a clinical trial of our lead product candidate PLN-74809 in healthy volunteers, and, with the exception of a number of reported minor adverse events, the product candidate was observed to be well-tolerated across all doses in 71 trial participants. However, if significant adverse events or other side effects are observed in any of our ongoing or future clinical trials, we may have difficulty recruiting patients to our clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts altogether. In addition, in our planned Phase 2a clinical trials, we expect to evaluate PLN-74809 administered with approved IPF agents. As a result, we may encounter unexpected drug-drug interactions in our planned trials, and may be required to further test these candidates, including in drug-drug interaction studies, which may be expensive, time-consuming and result in delays to our programs. Some potential therapeutics developed in the biopharmaceutical industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance of the approved product due to its tolerability versus other therapies.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. The enrollment of patients depends on many factors, including:

- the patient eligibility and exclusion criteria defined in the protocol;
- the size of the patient population required for analysis of the trial’s primary endpoints and the process for identifying patients;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;

- clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- the availability of competing commercially available therapies and other competing drug candidates' clinical trials;
- our ability to obtain and maintain patient informed consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

For example, we are initially developing PLN-74809 for the treatment of IPF and PSC, each of which is an orphan indication. In the United States, IPF is estimated to affect approximately 140,000 patients, while PSC is estimated to affect approximately 30,000 to 45,000 patients. As a result, we may encounter difficulties enrolling subjects in our clinical trials of PLN-74809 due, in part, to the small size of these patient populations. In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. Certain of our planned clinical trials may also involve invasive procedures such as bronchoscopy and broncho-alveolar lavage, or BAL, procedure, which may lead some patients to drop out of trials to avoid these follow-up procedures.

The design or execution of our ongoing and future clinical trials may not support marketing approval.

The design or execution of a clinical trial can determine whether its results will support marketing approval, and flaws in the design or execution of a clinical trial may not become apparent until the clinical trial is well advanced. For example, we plan to initiate our second Phase 2a randomized, double-blind, placebo-controlled IPF trial in the second half of 2019 evaluating up to three doses of our lead product candidate, PLN-74809, enrolling approximately 40 IPF patients. This trial is planned to be initiated as a 4-week trial in a limited number of patients and will then be amended into a 12-week trial once non-clinical data support longer term dosing. However, it is possible that the non-clinical data fail to support such longer dosing, which may prevent our ability to transition into such 12-week trial. Further, it is possible that amending our clinical trial, which would require us to resubmit our clinical trial protocols to IRBs for reexamination, may impact the costs, timing or successful completion of such clinical trial. In addition, we may desire to test PLN-74809 at doses exceeding those evaluated in the Phase 1a trial, and may not be able to do so.

Additionally, in some instances, there can be significant variability in safety or efficacy results between different trials with the same product candidate due to numerous factors, including differences in trial protocols, size and type of the patient populations, variable adherence to the dosing regimen or other protocol requirements and the rate of dropout among clinical trial participants. We do not know whether any clinical trials we conduct will demonstrate consistent or adequate efficacy and safety to obtain marketing approval to market our product candidates.

Further, the FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and in determining when or whether marketing approval will be obtained for any of our product candidates. Our product candidates may not be approved even if they achieve their primary endpoints in future Phase 3 clinical trials or registrational trials. The FDA or comparable foreign regulatory authorities may disagree with our trial designs and our interpretation of data from preclinical studies or clinical trials. In addition, any of these regulatory authorities may change requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal Phase 3 or registrational clinical trial. In addition, any of these regulatory authorities may also approve a product candidate for fewer or more limited

indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. The FDA or comparable foreign regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our product candidates, if approved.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our future clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

Although we have received US orphan drug designation for PLN-74809 for IPF and PSC indications, we may be unable to obtain and maintain orphan drug designation for our other product candidates and, even if we obtain such designation, we may not be able to realize the benefits of such designation, including potential marketing exclusivity of our product candidates, if approved.

Regulatory authorities in some jurisdictions, including the United States and other major markets, may designate drugs intended to treat conditions or diseases affecting relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States.

Although we have received U.S. orphan drug designation for PLN-74809 for IPF and PSC indications, the designation of any of our product candidates as an orphan drug does not mean that any regulatory agency will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of any regulatory agency to grant orphan drug designation to product candidates of other companies that treat the same indications as our product candidates.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or foreign regulatory authorities from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances. The applicable period is seven years in the United States. Orphan drug exclusivity may be revoked if any regulatory agency determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition in the United States. Even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates progress through preclinical to late stage clinical 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. Any of these changes could cause our product 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 product candidates and jeopardize our ability to commercialize our product candidates and generate revenue.

In addition, there are risks associated with large scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with good manufacturing practices, lot consistency and timely availability of raw materials. Even if we obtain marketing approval for any of our product candidates, there is no assurance that our manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential commercial launch of the product or to meet potential future demand. If our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

We may not be successful in our efforts to identify or discover additional product candidates in the future.

Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- our inability to design such product candidates with the pharmacological properties that we desire or attractive pharmacokinetics; or
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be medicines that will receive marketing approval and achieve market acceptance.

Research programs to identify new product candidates require substantial technical, financial and human resources. If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

Due to our limited resources and access to capital, we must make decisions on the allocation of resources to certain programs and product candidates; these decisions may prove to be wrong and may adversely affect our business.

We have limited financial and human resources and intend to initially focus on research programs and product candidates for a limited set of indications. As a result, we may forgo or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. In addition, we seek to accelerate our development timelines, including by initiating certain clinical trials of our product candidates before earlier-stage studies have been completed. This approach may cause us to commit significant resources to prepare for and conduct later-stage trials for one or more product candidates that subsequently fail earlier-stage clinical testing. Therefore, our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities, or expend resources on product candidates that are not viable.

There can be no assurance that we will ever be able to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential product candidates or other potential programs that ultimately prove to be unsuccessful.

If product liability lawsuits are brought against us, we may incur substantial financial or other liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of testing PLN-74809 and any of our other product candidates in clinical trials, and will face an even greater risk if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- inability to bring a product candidate to the market;
- decreased demand for our products;
- injury to our reputation;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- fines, injunctions or criminal penalties;
- costs to defend the related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to trial participants;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate, if approved; and
- decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We need to obtain additional insurance for clinical trials as our lead product candidate, PLN-74809, continues its clinical development and as additional product candidates enter the clinic. However, we may be unable to obtain, or may obtain on unfavorable terms, clinical trial insurance in amounts adequate to cover any liabilities from any of our clinical trials. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

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

The development and commercialization of new drug products is highly competitive. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from

major biopharmaceutical companies, specialty biopharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large biopharmaceutical and biotechnology companies that are currently pursuing the development of products for the treatment of fibrosis. Companies that we are aware of that are targeting the treatment of various fibrosis indications through inhibiting various parts of the TGF-ß pathway include large companies with significant financial resources such as Biogen, Inc., AbbVie Inc., Gilead Sciences, Inc., Indalo Therapeutics, Inc., FibroGen, Inc., Galapagos NV, Bristol Myers Squibb Co., and Novartis AG. However, we know of no other companies currently in clinical development with an orally bioavailable small-molecule, selective integrin inhibitor. For additional information regarding our competition, see "Business—Competition."

Many of our current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do.

Mergers and acquisitions in the biopharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, more convenient, or less expensive than any products that we may develop. Furthermore, products currently approved for other indications could be discovered to be effective treatments of fibrosis as well, which could give such products significant regulatory and market timing advantages over PLN-74809 or other product candidates that we may identify. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours and may do, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete and we may not be successful in marketing any product candidates we may develop against competitors. The availability of competitive products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

Risks Related to Marketing, Reimbursement, Healthcare Regulations and Ongoing Regulatory Compliance

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

Even if PLN-74809 or any other product candidate we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, such as Medicare and Medicaid programs and managed care organizations, and others in the medical community. In addition, the availability of coverage by third-party payors may be affected by existing and future health care reform measures designed to reduce the cost of health care. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable.

The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;

- the ability to offer our products, if approved, for sale at competitive prices;
- 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 recommendations with respect to our product candidates in guidelines published by various scientific organizations applicable to us and our product candidates;
- the strength of marketing and distribution support;
- the ability to obtain sufficient third-party coverage and adequate reimbursement; and
- the prevalence and severity of any side effects.

If government and other third-party payors do not provide coverage and adequate reimbursement levels for any products we commercialize, market acceptance and commercial success would be reduced.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, if approved, which could make it difficult for us to sell any product candidates profitably.

The success of our product candidates, if approved, depends on the availability of coverage and adequate reimbursement from third-party payors. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor’s determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of product candidates, once approved. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. There is significant

uncertainty related to insurance coverage and reimbursement of newly approved products. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates, if approved.

For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, also called the Medicare Modernization Act, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug and biologic benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs and biologics. Unlike Medicare Parts A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs and biologics, and each drug plan can develop its own formulary that identifies which drugs and biologics it will cover, and at what tier or level. However, Part D prescription drug formularies must include products within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs and biologics in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs and biologics may increase demand for products for which we obtain marketing approval. Any negotiated prices for any of our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug or biologic product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the average manufacturer price, or AMP, and Medicaid rebate amounts reported by the manufacturer. As of 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, expanded the types of entities eligible to receive discounted 340B pricing, although under the current state of the law these newly eligible entities (with the exception of children's hospitals) will not be eligible to receive discounted 340B pricing on orphan drugs. As 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase. Further, on December 27, 2018, the District Court for the District of Columbia invalidated a recent reimbursement formula change instituted by the Centers for Medicare and Medicaid Services, or CMS, under the 340B program. It is unclear how this decision could affect covered hospitals who might purchase our products in the future, and affect the rates we may charge such facilities for our approved products.

Changes to these current laws and state and federal healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes.

At the federal level, the Trump administration's budget for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 legislative session 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. 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 are increasingly passing legislation and implementing regulations designed to control biopharmaceutical and biologic 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.

On May 10, 2019, the Centers for Medicare and Medicaid Services announced a new pricing transparency rule, which goes into effect on July 9, 2019. This final rule requires direct-to-consumer television advertisements for prescription drugs and biological products for which reimbursement is available, directly or indirectly, through or under Medicare or Medicaid to include the list price of that product, except for a prescription drug or biological product that has a list price of less than $35 per month for a 30-day supply or typical course of treatment. The pricing transparency rule could have a negative effect on our business.

Even if we obtain FDA approval of any of our product 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 product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

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

We have no internal sales, marketing or distribution capabilities, nor have we commercialized a product. If any of our product candidates ultimately receives regulatory approval, we expect to establish a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in major markets, which will be expensive and time consuming. We have no prior experience as a company in the marketing, sale and distribution of pharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the

development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may also choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenues and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are not successful in commercializing our products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

Our relationships with healthcare providers and physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of biopharmaceutical products. Arrangements with third-party payors and customers can expose biopharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute biopharmaceutical products. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. The applicable federal, state and foreign healthcare laws and regulations laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity can be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. In addition, a claim submitted for payment to any federal health care program that includes items or services that were made as a result of a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA. The Anti-Kickback Statute has been interpreted to apply to arrangements between biopharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers, among others, on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution;
- the federal civil and criminal false claims laws and civil monetary penalty laws, including the FCA, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal healthcare programs, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or an obligation to pay or transmit money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the federal government. 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. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose, among other things, requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as their respective business associates, independent contractors that perform services for covered entities them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of 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 federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- the federal Physician Payments Sunshine Act, created under the ACA, and its implementing regulations, which require some manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and may be broader in scope than their federal equivalents; state and foreign laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing; state and local laws that require the registration of biopharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The distribution of biopharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of biopharmaceutical products.

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. For

example, on January 31, 2019, the Department of Health and Human Services, or HHS, and HHS Office of Inspector General, or OIG, proposed an amendment to one of the existing federal Anti-Kickback Statute safe harbors (42 C.F.R. 1001.952(h)) which would prohibit certain biopharmaceutical manufacturers from offering rebates to pharmacy benefit managers, or PBMs, in the Medicare Part D and Medicaid managed care programs. The proposed amendment would remove protection for "discounts" from federal Anti-Kickback Statute enforcement action, and would include criminal and civil penalties for knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or reward the referral of business reimbursable under federal health care programs. At the same time, HHS also proposed to create a new safe harbor to protect point-of-sale discounts that drug manufacturers provide directly to patients, and adds another safe harbor to protect certain administrative fees paid by manufacturers to PBMs. If this proposal is adopted, in whole or in part, it could affect the pricing and reimbursement for any products for which we receive approval in the future. 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. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business.

It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and 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 civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, possible exclusion from participation in federal and state funded healthcare programs, contractual damages and the curtailment or restricting of our operations, as well as 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. Further, 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. Any action for violation of these laws, even if successfully defended, could cause a biopharmaceutical manufacturer to incur significant legal expenses and divert management's attention from the operation of the business. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way.

Even if we receive regulatory approval of any product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-approval.

Manufacturers and their facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any marketing application, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a risk evaluation and mitigation strategies, or REMS, program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA may impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. However companies may share truthful and not misleading information that is not inconsistent with the labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability. The policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

Ongoing healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ACA was passed, which substantially changed the way health

care is financed by both governmental and private insurers, and significantly impacted the U.S. biopharmaceutical industry. The ACA, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must 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.

Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges, as well as efforts by the Trump administration to repeal or replace certain aspects of the ACA. For example, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed repeal legislation, the Tax Reform Act includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." As a result of the individual mandate repeal, subsequent litigation challenged the validity of the ACA. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. It is unclear how this decision and any subsequent appeals and other efforts to repeal and replace the ACA will impact the ACA and our business.

Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Further, the Trump administration has concluded that cost-sharing reduction, or CSR, payments to insurance companies required under the ACA have not received necessary appropriations from Congress and announced that it will discontinue these payments immediately until those appropriations are made. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. Bipartisan bills to appropriate funds for CSR payments were proposed in 2017 and 2018, but the proposals have not been enacted into law. Multiple state Attorneys General filed suit to stop the administration from terminating the subsidies, but their case was dismissed by a federal judge in California on July 18, 2018. Furthermore, on June 14, 2018, the U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and the potential effect on our business, are not yet known.

Additionally, CMS has recently proposed regulations that would 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 ACA for plans sold through such marketplaces. The Bipartisan Budget Act of 2018, or BBA, also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Moreover, in July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare

Advantage plans to use pre authorization (PA) and step therapy (ST) for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" while a definition of "price concession" in the regulations. Litigation and legislative efforts to change or repeal the ACA are likely to continue, with unpredictable and uncertain results.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. The Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs, including aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 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. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers.

These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, upon completion of this offering and in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

EU drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for our products in the European member states.

We intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of drugs is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of

adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future health care reform measures.

Much like the federal Anti-Kickback Statute prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

In addition, in most foreign countries, including the European Economic Area, or EEA, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be required to conduct a clinical study or other studies that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales and the potential profitability of any of our product candidates in those countries would be negatively affected.

We may incur substantial costs in our efforts to comply with evolving global data protection laws and regulations, and any failure or perceived failure by us to comply with such laws and regulations may harm our business and operations.

The global data protection landscape is rapidly evolving, and we may be or become subject to or affected by numerous federal, state and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, transfer, security and processing of personal data, such as information that we collect about participants and healthcare providers in connection with clinical trials. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, which may create uncertainty in our business, affect our or our service providers' ability to operate in certain jurisdictions or to collect, store, transfer use and share personal data, result in liability or impose additional compliance or other costs on us. Any failure or perceived failure by us to comply with federal, state, or foreign laws or self-regulatory standards could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others. Recently, California passed the California Data Privacy Protection Act, which goes into effect in January 2020 and provides broad rights to California consumers with respect to the collection and use of their information by businesses. The new California law further expands the privacy and process enhancements and commitment of resources in support of compliance with California's regulatory requirements and may lead to similar laws in other U.S. states or at a national level.

In addition to our operations in the United States, which may be subject to healthcare and other laws relating to the privacy and security of health information and other personal information, may seek to conduct clinical trials in EEA and may become subject to additional European data privacy laws, regulations and guidelines. The General Data Protection Regulation, (EU) 2016/679, or GDPR, became effective on May 25, 2018, and deals with the processing of personal data and on the free movement of such data. The GDPR imposes a broad range of strict requirements on companies subject to the GDPR, including requirements relating to having legal bases for processing personal information relating to identifiable individuals and transferring such information outside the EEA, including to the United States, providing details to those individuals regarding the processing of their personal information, keeping personal information secure, having data processing agreements with third parties who process personal information, responding to individuals' requests to exercise their rights in respect of their personal information, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments, and record-keeping. The GDPR increases substantially the penalties to which we could be subject in the event of any non-compliance, including fines of up to 10,000,000 Euros or up to 2% of our total worldwide annual turnover for certain comparatively minor offenses, or up to 20,000,000 Euros or up to 4% of our total worldwide annual turnover for more serious offenses. Given the limited enforcement of the GDPR to date, we face uncertainty as to the exact interpretation of the new requirements on our trials and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the new law.

In particular, national laws of member states of the EU are in the process of being adapted to the requirements under the GDPR, thereby implementing national laws which may partially deviate from the GDPR and impose different obligations from country to country, so that we do not expect to operate in a uniform legal landscape in the EEA. Also, as it relates to processing and transfer of genetic data, the GDPR specifically allows national laws to impose additional and more specific requirements or restrictions, and European laws have historically differed quite substantially in this field, leading to additional uncertainty. Further, the impact of the impending "Brexit", (whereby the United Kingdom is planning to leave the EEA in October of 2019), either with or without a "deal" is uncertain and cannot be predicted at this time.

In the event we commence clinical trials in the EEA, we must also ensure that we maintain adequate safeguards to enable the transfer of personal data outside of the EEA, in particular to the United States, in compliance with European data protection laws. We expect that we will continue to face uncertainty as to whether our efforts to comply with any obligations under European privacy laws will be sufficient. If we are investigated by a European data protection authority, we may face fines and other penalties. Any such investigation or charges by European data protection authorities could have a negative effect on our existing business and on our ability to attract and retain new clients or biopharmaceutical partners. We may also experience hesitancy, reluctance, or refusal by European or multi-national clients or biopharmaceutical partners to continue to use our products and solutions due to the potential risk exposure as a result of the current (and, in particular, future) data protection obligations imposed on them by certain data protection authorities in interpretation of current law, including the GDPR. Such clients or biopharmaceutical partners may also view any alternative approaches to compliance as being too costly, too burdensome, too legally uncertain, or otherwise objectionable and therefore decide not to do business with us. Any of the forgoing could materially harm our business, prospects, financial condition and results of operations.

Additional laws and regulations governing international operations could negatively impact or restrict our operations.

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The FCPA prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The

U.S. Foreign Corrupt Practices Act, or the FCPA, also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

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

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

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

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.

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit 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 in time. We plan to engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals and 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.

Risks Related to Our Intellectual Property

Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.

Our business will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, their respective components, synthetic intermediates, formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities and whether a court would issue an injunctive remedy. If we are unable to secure and maintain patent protection

for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop may be adversely affected.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue, obtain, or maintain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees.

The strength of patents in the biotechnology and biopharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our technology, including our product candidates, or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced.

We cannot be certain that we were the first to file any patent application related to our technology, including our product candidates, and, if we were not, may be precluded from obtaining patent protection for our technology, including our product candidates.

We cannot be certain that we are the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. Furthermore, for United States applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the United States patent office, or USPTO, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Similarly, for United States applications in which at least one claim is not entitled to a priority date before March 16, 2013, derivation proceedings can be instituted to determine whether the subject matter of a patent claim was derived from a prior inventor’s disclosure.

We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent or patent application claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, would adequately protect our product candidates, or would be found by a court to be infringed by a competitor’s technology or product. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidates or our activities infringing such claims. The possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights, or will design around the claims of patents that we have had issued that cover our products.

Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Under the enacted Leahy-Smith America Invents Act, or America Invents Act, enacted in 2013, the United States moved from a "first to invent" to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear as the USPTO only recently developed new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the "first-to-file" provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds that are similar to the compositions of our product candidates but that are not covered by the claims of our patents;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;
- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;

- we have engaged in scientific collaborations in the past, and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on our business.

We may enter into license or other collaboration agreements in the future that may impose certain obligations on us. If we fail to comply with our obligations under such future agreements with third parties, we could lose license rights that may be important to our future business.

In connection with our efforts to expand our pipeline of product candidates, we may enter into certain licenses or other collaboration agreements in the future pertaining to the in-license of rights to additional candidates. Such agreements may impose various diligence, milestone payment, royalty, insurance or other obligations on us. If we fail to comply with these obligations, our licensor or collaboration partners may have the right to terminate the relevant agreement, in which event we would not be able to develop or market the products covered by such licensed intellectual property.

Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our product candidates, technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

In addition, we may have limited control over the maintenance and prosecution of these in-licensed patents and patent applications, or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by any future licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to patent protection, we rely heavily upon know-how and trade secret protection, as well as non-disclosure agreements and invention assignment agreements with our employees, consultants and third-parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not, for example, in the case of misappropriation of a trade secret by an employee or third-party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, trade secrets may be independently developed by others in a manner that could prevent legal recourse by us. For example, our clinical development strategy includes the testing of live tissue samples, and our techniques for preserving and testing these samples are proprietary and confidential. If one or more third parties obtain or are otherwise able to replicate these techniques, an important feature and differentiator of our clinical development strategy will become available to potential competitors. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed.

In addition, courts outside the United States are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third-party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology.

Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties. We have also adopted policies and conduct training that provides guidance on our expectations, and our advice for best practices, in protecting our trade secrets.

Third-party claims of intellectual property infringement may prevent or delay our product discovery and development efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and biopharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that

our product candidates and/or proprietary technologies infringe their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and biopharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

If a third-party claims that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;
- substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third-party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third-party licenses its product rights to us, which it is not required to do;
- if a license is available from a third-party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products and any license that is available may be non-exclusive, which could result in our competitors gaining access to the same intellectual property; and
- redesigning our product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure.

Our collaborators may assert ownership or commercial rights to inventions they develop from research we support or that we develop from our use of the tissue samples or other biological materials, which they provide to us, or otherwise arising from the collaboration.

We collaborate with several institutions, universities, medical centers, physicians and researchers in scientific matters and expect to continue to enter into additional collaboration agreements. In certain cases, we do not have written agreements with these collaborators, or the written agreements we have do not cover intellectual property rights. Also, we rely on numerous third parties to provide us with tissue samples and biological materials that we use to conduct our research activities and develop our product candidates. If we cannot successfully negotiate sufficient ownership and commercial rights to any inventions that result from our use of a third-party collaborator's materials, or if disputes arise with respect to the intellectual property developed with the use of a collaborator's samples, or data developed in a collaborator's study, we may be limited in our ability to capitalize on the market potential of these inventions or developments.

Third parties may assert that we are employing their proprietary technology without authorization.

There may be third-party patents of which we are currently unaware with claims to compositions of matter, materials, formulations, methods of manufacture or methods for treatment that encompass the composition, use or manufacture of our product candidates. There may be currently pending patent applications of which we are currently unaware which may later result in issued patents that our product candidates or their use or manufacture may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patent were held by a court of competent jurisdiction to cover our product candidates, intermediates used in the manufacture of our product candidates or our materials generally, aspects of our formulations or methods of use, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly.

Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.

As is common in the biotechnology and biopharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, and although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract 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 price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development 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

substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

We may not be successful in obtaining or maintaining necessary rights to develop any future product candidates on acceptable terms.

Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights.

Our product candidates may also require specific formulations to work effectively and efficiently and these rights may be held by others. We may develop products containing our compounds and pre-existing biopharmaceutical compounds. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

Additionally, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our current or future licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question or for other reasons. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

We may choose to challenge the patentability of claims in a third-party's U.S. patent by requesting that the USPTO review the patent claims in an *ex-parte* re-exam, *inter partes* review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third-party's patent in patent opposition proceedings in the European Patent Office, or EPO, or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third-party alleging that the patent may be infringed by our product candidates or proprietary technologies.

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our owned and in-licensed patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to those owned by or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the United States. If we or one of our licensors is a party to an interference proceeding involving a U.S. patent application on inventions owned by or in-licensed to us, we may incur substantial costs, divert management's time and expend other resources, even if we are successful.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Litigation or interference proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process and following the issuance of a patent. 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. Noncompliance events that could result in

abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In certain circumstances, even inadvertent noncompliance events may permanently and irrevocably jeopardize patent rights. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO.

If we or one of our licensors initiate legal proceedings against a third-party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third-party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, inter partes review, post grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

Likewise, our current licensed patents covering our companion technologies, licensed from UCSF are expected to expire in 2036, without taking into account any possible patent term adjustments or extensions. Our earliest patents may expire before, or soon after, our first product achieves marketing approval in the United States or foreign jurisdictions. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on our business, results of operations, financial condition and prospects. We own pending patent applications covering our proprietary technologies or our product candidates that if issued as patents are expected to expire from 2037 through 2040, without taking into account any possible patent term adjustments or extensions. However, we cannot be assured that the USPTO or relevant foreign patent offices will grant any of these patent applications.

Changes in patent law in the U.S. and in foreign jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were

the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. 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. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of biopharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.

We have limited intellectual property rights outside the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, 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. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of, and may require a compulsory license to, patents, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally. The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing

and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions such as patent term adjustments and/or extensions, may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984 Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct certain aspects of our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates.

We depend upon third parties to conduct certain aspects of our preclinical studies and clinical trials, under agreements with universities, medical institutions, CROs, strategic collaborators and others. We expect to have to negotiate budgets and contracts with such third parties, which may result in delays to our development timelines and increased costs.

We will rely especially heavily on third parties over the course of our clinical trials, and, as a result, will have limited control over the clinical investigators and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP requirements.

Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting aspects of our preclinical studies or clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our preclinical studies and clinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the preclinical or clinical data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements or for other reasons, our development timelines, including clinical development timelines, may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms.

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

We rely on third parties for tissue samples and other materials required for our research and development activities, and if we are unable to reach agreements with these third parties our research and development activities would be delayed.

We rely on third parties, primarily hospitals, health clinics and academic institutions, for the provision of tissue samples and other materials required in our research and development activities. Obtaining these materials requires various approvals as well as reaching a commercial agreement on acceptable terms with the hospital or other provider of the materials. While we currently have agreements in place with the institutions from which we receive our tissue samples, we do not have any exclusive arrangements with such sources and there is no guarantee that we will be able to maintain or renew such agreements on commercially reasonable terms, if at all. If we were unable to maintain or renew such agreements we would be forced to seek new arrangements with new hospitals, clinics or health institutions. If so, we may not be able to reach agreements with alternative partners or do so on terms acceptable to us. If we are unable to enter into such agreements, our research and development activities will be delayed and our ability to implement a key part of our development strategy will be compromised.

Because we rely on third-party manufacturing and supply vendors, our supply of research and development, preclinical and clinical development materials may become limited or interrupted or may not be of satisfactory quantity or quality.

We rely on third-party contract manufacturers to manufacture our product candidates for preclinical studies and clinical trials. We do not own manufacturing facilities for producing any clinical trial product supplies. There can be no assurance that our preclinical and clinical development product supplies will not be limited, interrupted, or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of our manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMPs. 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 reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty 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 product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for PLN-74809 or any other product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third-party's failure to execute on our manufacturing requirements and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;

- delay in submitting regulatory applications, or receiving regulatory approvals, for product 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;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

We rely on a sole supplier for the manufacture of PLN-74809. If this sole supplier is unable to supply to us in the quantities we require, or at all, or otherwise defaults on its supply obligations to us, we may not be able to obtain alternative supplies from other suppliers on acceptable terms, in a timely manner, or at all. We also do not have long-term supply agreements with any of our suppliers. Our current contracts with certain suppliers may be canceled or not extended by such suppliers and, therefore, do not afford us with protection against a reduction or interruption in supplies. Moreover, in the event any of these suppliers breach their contracts with us, our legal remedies associated with such a breach may be insufficient to compensate us for any damages we may suffer.

In addition, we contract with fill and finishing providers with the appropriate expertise, facilities and scale to meet our needs. Failure to maintain cGMP can result in a contractor receiving FDA sanctions, which can impact our ability to operate or lead to delays in any clinical development programs. We believe that our current fill and finish contractor is operating in accordance with cGMP, but we can give no assurance that FDA or other regulatory agencies will not conclude that a lack of compliance exists. In addition, any delay in contracting for fill and finish services, or failure of the contract manufacturer to perform the services as needed, may delay any clinical trials, registration and launches, which could negatively affect our business.

Future collaborations will be important to our business. If we are unable to enter into new collaborations, or if these collaborations are not successful, our business could be adversely affected.

A part of our strategy is to selectively evaluate partnerships in indications and geographies where we believe partners can add significant commercial and/or development capabilities. Further, we have limited capabilities for product development and do not yet have any capability for commercialization. Accordingly, we may enter into collaborations with other companies to provide us with important technologies and funding for our programs and technology.

Our existing collaborations and any future collaborations we enter into may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs or license arrangements based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- collaborators may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- collaborators with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not provide us with timely and accurate information regarding development progress and activity under any future license agreement, which could adversely impact our ability to report progress to our investors and otherwise plan development of our product candidates;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us; and
- collaborations may be terminated by the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our collaborations do not result in the successful discovery, development and commercialization of product candidates or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under such collaboration. All of the risks relating to product development, regulatory approval and commercialization described in this prospectus also apply to the activities of our therapeutic collaborators.

Additionally, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

We face significant competition in seeking appropriate collaborators for our product candidates, and the negotiation process is time-consuming and complex. In order for us to successfully establish a collaboration for one or more of our product candidates, potential collaborators must view these product candidates as economically valuable in markets they determine to be attractive in light of the terms that we are seeking and other available products for licensing by other companies. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large biopharmaceutical companies that have resulted in a reduced number of potential future collaborators. 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. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the

development of a product 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 sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms, or at all. If we fail to enter into collaborations or do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates, bring them to market and generate revenue from sales of drugs or continue to develop our technology, and our business may be materially and adversely affected. Even if we are successful in our efforts to establish new strategic collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic collaborations if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing. Any delay in entering into new strategic collaboration agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

Risks Related to Managing Our Business and Operations

We may encounter difficulties in managing our growth, which could adversely affect our operations.

As of March 31, 2019, we had 48 full-time employees. As our clinical development and commercialization plans and strategies develop, and as we transition into operating as a public company, we will need to expand our managerial, clinical, regulatory, sales, marketing, financial, development, manufacturing and legal capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, suppliers and other third parties. Our future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our development and commercialization efforts effectively, including the clinical and FDA review process for PLN-74809 and any other product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our ability to continue to develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert 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.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including contract manufacturers and companies focused on research and development and discovery activities. There can be no assurance that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality, accuracy or quantity of the services provided is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain, or may be substantially delayed in obtaining, regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize PLN-74809 or any other product candidates and, accordingly, may not achieve our research, development and commercialization goals.

We may acquire additional technology and complementary businesses in the future. Acquisitions involve many risks, any of which could materially harm our business, including the diversion of management's attention from core business concerns, failure to effectively exploit acquired technologies, failure to successfully integrate the acquired business or realize expected synergies or the loss of key employees from either our business or the acquired businesses.

If we lose key management personnel, or if we fail to recruit additional highly skilled personnel, our ability to develop current product candidates or identify and develop new product candidates will be impaired, could result in loss of markets or market share and could make us less competitive.

Our ability to compete in the highly competitive biotechnology and biopharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel, including Bernard Coulie, M.D., Ph.D., our Chief Executive Officer and President, Keith Cummings, M.D., our Chief Financial Officer, Johannes (Hans) Hull, J.D., our Chief Business Officer and Éric Lefebvre, M.D., our Chief Medical Officer. The loss of the services of any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements could result in delays in product development and harm our business.

We conduct our operations at our facility in South San Francisco, California. This region is headquarters to many other biopharmaceutical companies, biotechnology companies and research institutions. Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided restricted stock awards and stock options that vest over time. The value to employees of restricted stock awards and stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Our key employees are at-will employees, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain "key person" insurance policies on the lives of these individuals or the lives of any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior scientific and medical personnel.

Our internal computer systems, or those used by our contract research organizations, or other contractors, service providers, partners or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our future CROs, and other contractors, service providers, partners and consultants may be vulnerable to damage or interruption from system malfunction or failure, service interruptions, cyberattacks (including but not limited to tradition "hacking", computer viruses, malware, ransomware, denial-of-service attacks, phishing scams and other social engineering attacks), security breaches, computer theft and other types of incidents, which could include inadvertent or intentional actions by our employees, contractors, consultants, business partners and/or other third parties. While we have not experienced any material system failures or material security breaches to date. We cannot guarantee that such failures or breaches will not occur. If such actual or perceived events were to occur and cause interruptions in our operations, they could result in a material disruption of our development programs and our business operations. For example, the loss of preclinical or clinical data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we may rely on third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any actual or perceived disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

Our current operations are concentrated in one location, and we or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our current operations are located in our facilities in South San Francisco, California. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our third-party contract manufacturers, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. Earthquakes or other natural disasters could further disrupt our operations, and have a material and adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third-party contract manufacturers, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Portions of our future clinical trials may be conducted outside of the United States and unfavorable economic conditions resulting in the weakening of the U.S. dollar would make those clinical trials more costly to operate. Furthermore, the most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn could result in a variety of risks to our business, including a reduced ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or international trade disputes could also strain our suppliers, some of which are located outside of the United States, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

The estimates of market opportunity and forecasts of market growth included in this prospectus may prove to be inaccurate, and even if the markets in which we compete achieve the forecasted growth, our business may not grow at similar rates, or at all.

Market opportunity estimates and growth forecasts included in this prospectus are subject to significant uncertainty and are based on assumptions and estimates which may not prove to be accurate. The estimates and forecasts included in this prospectus relating to size and expected growth of our target market may prove to be inaccurate. Even if the markets in which we compete meet the size estimates and growth forecasts included in this prospectus, our business may not grow at similar rates, or at all. Our growth is subject to many factors, including our success in implementing our business strategy, which is subject to many risks and uncertainties.

Our employees, independent contractors, consultants, commercial partners, collaborators and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners, collaborators and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to comply with the laws of the FDA and other similar foreign regulatory bodies, provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies, comply with manufacturing standards we have established, comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws, or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws will also increase. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. In connection with this offering, we will adopt a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by our employees, independent contractors, consultants, commercial partners and vendors, 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 actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in the imposition of civil, criminal and administrative penalties, damages, monetary fines, imprisonment, disgorgement, possible exclusion from participation in government healthcare programs, 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, contractual damages, reputational harm, diminished profits and future earnings and the curtailment of our operations.

We use and generate materials that may expose us to material liability.

Our research programs involve the use of hazardous materials and chemicals, which are currently only handled by third parties. We are subject to foreign, federal, state and local environmental and health and safety laws and regulations governing, among other matters, the use, manufacture, handling, storage and disposal of hazardous materials and waste products such as human tissue samples that may have the potential to transmit diseases. We may incur significant costs to comply with these current or future environmental and health and safety laws and regulations. In addition, we cannot completely eliminate the risk of contamination or injury from hazardous materials and may incur material liability as a result of such contamination or injury. In the event of an accident, an injured party may seek to hold us liable for any damages that result. Any liability could exceed the limits or fall outside the coverage of our workers' compensation, property and business interruption insurance and we may not be able to maintain insurance on acceptable terms, if at all. We currently carry no insurance specifically covering environmental claims.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our research and development activities involve the use of biological and hazardous materials and produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we

believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological waste or hazardous waste insurance coverage, workers compensation or property and casualty and general liability insurance policies that include coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

Compliance with governmental regulations regarding the treatment of animals used in research could increase our operating costs, which would adversely affect the commercialization of our products.

The Animal Welfare Act, or AWA, is the federal law that covers the treatment of certain animals used in research. Currently, the AWA imposes a wide variety of specific regulations that govern the humane handling, care, treatment and transportation of certain animals by producers and users of research animals, most notably relating to personnel, facilities, sanitation, cage size, and feeding, watering and shipping conditions. Third parties with whom we contract are subject to registration, inspections and reporting requirements under the AWA. Furthermore, some states have their own regulations, including general anti-cruelty legislation, which establish certain standards in handling animals. Comparable rules, regulations, and or obligations exist in many foreign jurisdictions. If we or our contractors fail to comply with regulations concerning the treatment of animals used in research, we may be subject to fines and penalties and adverse publicity, and our operations could be adversely affected.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act, or the TCJA, that significantly reforms the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from 34.0% to a flat rate of 21.0%, limitation of the tax deduction for interest expense to 30.0% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80.0% of annual taxable income and elimination of net operating loss carrybacks and modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as "orphan drugs"). We urge investors to consult with their legal and tax advisers regarding the implications of the TCJA on an investment in our common stock.

Our ability to use our net operating loss carryforwards and certain tax credit carryforwards may be subject to limitation.

As of December 31, 2018, we had net operating loss carryforwards for federal and state income tax purposes of $29.9 million and $59.6 million, respectively, which will begin to expire in 2035. As of December 31, 2018, we also had available tax credit carryforwards for federal income tax purposes of $2.3 million, which begin to

expire in 2036, and state income tax purposes of $2.1 million. Under Section 382 of the Code, changes in our ownership may limit the amount of our net operating loss carryforwards and tax credit carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and tax credit carryforwards before they expire. Private placements and other transactions that have occurred since our inception, as well as this offering, may trigger such an ownership change pursuant to Section 382. Any such limitation, whether as the result of this offering, prior private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us, could have a material adverse effect on our results of operations in future years. The reduction of the corporate tax rate under TCJA may cause a reduction in the economic benefit of our net operating loss carryforwards and other deferred tax assets available to us. Under the TCJA, net operating losses generated after December 31, 2017 will not be subject to expiration.

Risks Related to Our Common Stock and this Offering

There has been no prior public market for our common stock, the stock price of our common stock may be volatile or may decline regardless of our operating performance and you may not be able to resell your shares at or above the initial public offering price.

Prior to this offering there has been no public market for shares of our common stock. You may not be able to sell your shares quickly or at the market price if trading in shares of our common stock is not active. The initial public offering price for our common stock will be determined through negotiations with the underwriters, and the negotiated price may not be indicative of the market price of the common stock after the offering. An active or liquid market in our common stock may not develop upon the completion of this offering or, if it does develop, it may not be sustainable. As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the initial public offering price.

Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies or products by using our shares of common stock as consideration.

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

The trading price of our common stock following this offering is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this “Risk Factors” section and elsewhere in this prospectus, these factors include:

- the results from our ongoing Phase 1b clinical trial of PLN-74809, as well as the commencement, enrollment or results of our planned Phase 2a clinical trials of PLN-74809;
- any delay in identifying and advancing a clinical candidate for our other development programs;
- any delay in our regulatory filings for PLN-74809 or our other product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority’s review of such filings, including without limitation the FDA’s issuance of a “refusal to file” letter or a request for additional information;
- adverse results or delays in future clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval of PLN-74809 or any other product candidate;
- changes in laws or regulations applicable to PLN-74809 or any other product candidate, including but not limited to clinical trial requirements for approvals;

- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- our inability to establish collaborations, if needed;
- our failure to commercialize our product candidates, if approved;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of PLN-74809 or any other product candidate;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or product candidates in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- changes in the structure of the healthcare payment systems;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the market for biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. If the market price of our common stock after this offering does not exceed the initial public offering price, you may not realize any return on your investment in us and may lose some or all of your investment. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Furthermore, future debt or other financing arrangements may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock.

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

Immediately following the completion of this offering, our executive officers, directors and their affiliates will beneficially hold, in the aggregate, approximately % of our outstanding voting stock. These stockholders, acting together, would be able to significantly influence all matters requiring stockholder approval. For example, these stockholders would be able to significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

The initial public offering price will be substantially higher than the pro forma as adjusted net tangible book value per share of our common stock after this offering. Investors purchasing common stock in this offering will pay a price per share that substantially exceeds the pro forma as adjusted net tangible book value per share after this offering. As a result, investors purchasing common stock in this offering will incur immediate dilution of $ per share, based on an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, representing the difference between our pro forma as adjusted net tangible book value per share after giving effect to this offering and the assumed initial public offering price. Further, investors purchasing common stock in this offering will contribute approximately % of the total amount invested by stockholders since our inception, but will own only approximately % of the shares of common stock outstanding after this offering.

This dilution is due to our investors who purchased shares prior to this offering having paid substantially less when they purchased their shares than the price offered to the public in this offering. To the extent outstanding options are exercised, there will be further dilution to new investors. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. For a further description of the dilution that you will experience immediately after this offering, see the section entitled “Dilution.”

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, or EGC, as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be

an emerging growth company for up to five years following the year in which we complete this offering, although circumstances could cause us to lose that status earlier. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (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 requires the market value of our common stock that is held by non-affiliates to exceed $700.0 million as of the prior June 30th, and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens in this prospectus. In particular, we have not included all of the executive compensation information that would be required if we were not an EGC. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of 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.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies, which may make our financial statements less comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

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

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. We will be subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, which will require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and the Nasdaq Global Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial reporting controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as “say on pay” and proxy access. Recent legislation permits emerging growth companies to implement many of these requirements over a longer period and up to five years from the pricing of this offering. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have an adverse effect on our business. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an EGC, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an EGC for up to five years. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to restatements of our financial statements and require us to incur the expense of remediation.

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

Upon completion of this offering, we will become subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Substantial amounts of our outstanding shares may be sold into the market when lock-up or market standoff periods end. If there are substantial sales of shares of our common stock, the price of our common stock could decline.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the trading price of our common stock could decline. Based on shares of common stock outstanding as of December 31, 2018, upon the completion of this offering we will have outstanding a total of shares of common stock. Of these shares, only the shares of common stock sold in this offering by us, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable without restriction in the public market immediately following this offering.

The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus, subject to earlier release of all or a portion of the shares subject to such agreements by the representatives of the

underwriters in this offering in their sole discretion. After the lock-up agreements expire, based upon the number of shares of common stock, on an as-converted basis, outstanding as of December 31, 2018, up to an additional shares of common stock will be eligible for sale in the public market. Approximately % of these additional shares are beneficially held by directors, executive officers and their affiliates and will be subject to certain limitations of Rule 144 under the Securities Act of 1933, as amended, or the Securities Act.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our existing equity compensation plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline. Additionally, the number of shares of our common stock reserved for issuance under 2019 Stock Option and Incentive Plan will automatically increase on January 1 of each year, beginning on January 1, 2020, by % of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by our board of directors or compensation committee. Moreover, the number of shares of our common stock reserved for issuance under 2019 Employee Stock Purchase Plan will automatically increase on January 1 of each year, beginning on January 1, 2020, by % of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by our board of directors or compensation committee. Unless our board of directors elects not to increase the number of shares available for future grant each year, our stockholders may experience additional dilution.

After this offering, the holders of shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act as provided under the terms of an investors' rights agreement between us and the holders of our convertible preferred stock, subject to the 180-day lock-up agreements described above. See "Description of Capital Stock — Registration Rights." Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

We have broad discretion in the use of our existing cash and cash equivalents and the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of our existing cash and cash equivalents and the net proceeds from this offering, other than the payment required to be made to UCSF pursuant to our license agreement with them upon the closing of this offering, including for any of the purposes described in the section entitled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether such proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of our existing cash and cash equivalents and the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply our existing cash and cash equivalents and the net proceeds from this offering in ways that ultimately increase the value of your investment. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws, which are to become effective upon the completion of this offering, contain provisions that could delay or prevent a change of

control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the lead director of the board of directors, the chief executive officer, or by a majority of the total number of authorized directors;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue convertible preferred stock on terms determined by the board of directors without stockholder approval and which convertible preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws 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 the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

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. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company, the trading price for our stock would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Our amended and restated by-laws will designate the Court of Chancery of the State of Delaware as the exclusive forum for certain state law litigation that may be initiated by our stockholders, which could limit our stockholders' ability to litigate disputes with us in a different judicial forum.

Pursuant to our amended and restated by-laws, as will be in effect upon the completion of this offering, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of

Delaware will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (iii) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware, our amended and restated certificate of incorporation or our amended and restated by-laws; (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or by-laws; or (v) any action asserting a claim governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein. This exclusive forum provision will not apply to any causes of action arising under the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. The forum selection clause in our amended and restated by-laws may limit our stockholders' ability to litigate disputes with us in a different judicial forum.

Our issuance of additional capital stock in connection with financings, acquisitions, investments, our stock incentive plans or otherwise will dilute all other stockholders.

We expect to issue additional capital stock in the future that will result in dilution to all other stockholders. We expect to grant equity awards to employees, directors, and consultants under our stock incentive plans. We may also raise capital through equity financings in the future. As part of our business strategy, we may acquire or make investments in complementary companies, products, or technologies and issue equity securities to pay for any such acquisition or investment. Any such issuances of additional capital stock may cause stockholders to experience significant dilution of their ownership interests and the per share value of our common stock to decline.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the sections entitled “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business,” contains forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition that are based on our management’s belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the success, cost and timing of our product development activities and clinical trials of our lead product candidate, PLN-74809, including the progress of, and results from, our ongoing Phase 1b clinical trial, and future clinical trials of this and our other product candidates;
- the success, cost and timing of completing IND-enabling studies of PLN-74809 in uses for PSC, and the timing of our planned Investigational New Drug Application, or IND, submissions for PLN-74809 in uses for PSC;
- our plans to initiate, recruit and enroll patients in, and conduct our clinical trials at the pace that we project;
- our plans and strategy to obtain and maintain regulatory approvals of our product candidates;
- our plans and strategy to obtain funding for our operations, including funding necessary to complete further development and, upon successful development, if approved, commercialize any of our product candidates;
- the potential benefit of orphan drug designations for PLN-74809;
- the success, cost and timing of completing IND-enabling studies of our second product candidate, PLN-1474, and the timing of our planned IND submissions for PLN-1474;
- our ability to compete with companies currently marketing or engaged in the development of treatments for fibrosis;
- our plans and strategy regarding obtaining and maintaining intellectual property protection for our product candidates and the duration of such protection;
- our plans and strategy regarding the manufacture of our product candidates for clinical trials and for commercial use, if approved;
- our plans and strategy regarding the commercialization of any products that are approved for marketing;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets, either alone or in combination with others;
- our expectations regarding government and third-party payor coverage and reimbursement; and
- our expected use of the proceeds from this offering.

In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue” or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed in the section entitled “Risk factors” and elsewhere in this prospectus. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to rely unduly upon these statements.

MARKET AND INDUSTRY DATA AND FORECASTS

We obtained the industry, market and competitive position data used throughout this prospectus from our own internal estimates and research, as well as from independent market research, industry and general publications and surveys, governmental agencies and publicly available information in addition to research, surveys and studies conducted by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires. In addition, while we believe the industry, market and competitive position data included in this prospectus is reliable and based on reasonable assumptions, such data involve risks and uncertainties and are subject to change based on various factors, including those discussed in the section entitled “Risk Factors.” These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties or by us.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of shares of our common stock in this offering will be approximately $ million, or approximately $ million if the underwriters exercise in full their option to purchase additional shares, assuming an initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, the net proceeds to us from this offering by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase or decrease of 1.0 million shares in the number of shares we are offering would increase or decrease, as applicable, the net proceeds to us from this offering by approximately $ million, assuming the assumed initial public offering price to the public remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We do not expect that a change in the initial price to the public or the number of shares by these amounts would have a material effect on the uses of the proceeds from this offering, although it may accelerate the time at which we will need to seek additional capital.

The principal purposes of this offering are to increase our financial flexibility, create a public market for our common stock and facilitate our future access to capital markets.

We currently expect to use the net proceeds from this offering as follows:

- approximately $ million to fund the clinical development of our lead product candidate, PLN-74809, including for conducting our planned Phase 2a clinical trials in IPF and PSC;
- approximately $ million to fund the preclinical and clinical development of our second product candidate, PLN-1474; and
- the remainder, if any, for business development activities, working capital and other general corporate purposes, including early stage research and development activities.

Based on our current plans, we believe our existing cash and cash equivalents, together with the net proceeds from this offering, will be sufficient to fund our operating expenses and capital expenditure requirements through .

We may also use a portion of the net proceeds to in-license, acquire or invest in new businesses, technology or assets. Although we have no current agreements, commitments or understandings with respect to any such in-license or acquisition, we evaluate such opportunities and engage in related discussions with third parties from time to time.

The expected use of net proceeds from this offering represents our intentions based upon our present plans and business conditions. We cannot specify with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering. Due to uncertainties inherent in the product development process, it is difficult to estimate the exact amounts of the net proceeds that will be used for any particular purpose. We may use our existing cash and cash equivalents and the future payments, if any, generated from any future collaboration agreements to fund our operations, either of which may alter the amount of net proceeds used for a particular purpose. In addition, the amount, allocation and timing of our actual expenditures will depend upon

numerous factors, including the results of our research and development efforts, the timing and success of clinical trials and the timing of regulatory submissions. Accordingly, we will have broad discretion in using these proceeds.

Pending the uses described above, we plan to invest the net proceeds of this offering in short- and immediate- term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We do not anticipate paying any dividends on our capital stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. Any future determination to declare dividends will be subject to the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects and any other factors deemed relevant by our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividends.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of December 31, 2018:

- on an actual basis;
- on a pro forma basis to give effect to (i) the automatic conversion of all outstanding shares of our redeemable convertible preferred stock as of December 31, 2018 into an aggregate of 105,501,221 shares of our common stock as if such conversion had occurred on December 31, 2018, and (ii) the filing and effectiveness of our amended and restated certificate of incorporation immediately prior to the completion of this offering; and
- on a pro forma as adjusted basis to give effect to (i) the pro forma adjustments described above, and (ii) the issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information together with our financial statements and related notes appearing elsewhere in this prospectus and the information set forth in the sections entitled "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	As of December 31, 2018		
	Actual	Pro Forma	Pro Forma As Adjusted(1)
	(in thousands, except share and per share data)		
Cash and cash equivalents	$ 60,949	$	$
Redeemable convertible preferred stock, par value $0.0001 per share; 114,109,973 shares authorized, 105,501,221 issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	$ 132,103	$	
Stockholders' (deficit) equity:			
Common stock, par value $0.0001 per share; 147,682,655 shares authorized, 9,745,453 shares issued and outstanding, actual; shares authorized, 115,246,674 shares issued and outstanding, pro forma; shares authorized, shares issued and outstanding, pro forma as adjusted(2)	1		
Preferred stock, $0.0001 par value per share; no shares authorized, issued or outstanding, actual; shares authorized, no shares issued or outstanding, pro forma and pro forma as adjusted	—		—
Additional paid-in capital	—		
Accumulated deficit	(71,470)		
Total stockholders' (deficit) equity	(71,469)		
Total capitalization	$ 60,634	$	$

(1) Each $1.00 increase or decrease in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, each of pro forma as adjusted cash and cash equivalents, additional paid-in capital, total stockholders' (deficit) equity, and total capitalization by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. We may also increase or decrease the number of shares we are offering. Each increase or decrease of 1.0 million shares in the number of shares we are offering would increase or decrease, as applicable, each of pro forma as adjusted cash and cash equivalents, additional paid-in capital, total stockholders' (deficit) equity, and total capitalization by approximately $ million, assuming the assumed initial public offering price per share, as set forth on the cover page of this prospectus, remains the same. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

(2) Shares issued and outstanding, actual, pro forma and pro forma as adjusted excludes 5,361,529 unvested restricted shares subject to repurchase.

The number of shares of common stock issued and outstanding pro forma and pro forma as adjusted in the table above is based on 115,246,674 shares of common stock (including our redeemable convertible preferred stock on an as-converted basis) outstanding as of December 31, 2018, and excludes:

- 841,800 shares of common stock issuable upon exercise of outstanding options issued as of December 31, 2018 under our 2015 Plan, at a weighted-average exercise price of $0.29 per share, or pursuant to rights to purchase restricted stock at a weighted average purchase price of $0.01 per share;
- 7,029,718 shares of common stock reserved for future issuance under our 2015 Plan as of December 31, 2018;
- 5,361,529 shares of unvested restricted common stock issued under the 2015 Plan and shares issued to our founders as of December 31, 2018 and subject to our right to repurchase;
- shares of our common stock reserved for future issuance under our 2019 Plan, which will become available for issuance upon the effectiveness of the registration statement of which this prospectus is a part; and
- shares of our common stock reserved for future issuance under our 2019 ESPP, which will become available for issuance upon the effectiveness of the registration statement of which this prospectus is a part.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book (deficit) value per share of our common stock immediately after this offering.

Our historical net tangible book (deficit) value per share as of December 31, 2018 is determined by dividing our total tangible assets less our total liabilities and redeemable convertible preferred stock, which are not included within stockholders' deficit, by the number of shares of common stock outstanding as of such date. Our historical net tangible book value (deficit) was $(71.5) million, or $(4.73) per share as of December 31, 2018.

Our pro forma net tangible book value (deficit) as of December 31, 2018 was $ million, or $ per share. Our pro forma net tangible book value (deficit) per share represents the amount of our total tangible assets reduced by the amount of our total liabilities and divided by the total number of shares of our common stock outstanding as of December 31, 2018, assuming the automatic conversion of all outstanding shares of our redeemable convertible preferred stock as of December 31, 2018 into an aggregate of 105,501,221 shares of common stock, which conversion will occur immediately prior to the completion of this offering.

Our pro forma as adjusted net tangible book value (deficit) represents our pro forma net tangible book (deficit) value, plus the effect of the sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Net tangible book value dilution per share to new investors represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the pro forma as adjusted net tangible book value per share of common stock immediately after completion of this offering. After giving effect to our sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2018 would have been $ million, or $ per share. This represents an immediate increase in net tangible book value of $ per share to existing stockholders and an immediate dilution in net tangible book value of $ per share to purchasers of common stock in this offering, as illustrated in the following table:

Assumed initial public offering price per share		$
Historical net tangible book value (deficit) per share as of December 31, 2018	$(4.73)	
Pro forma increase in net tangible book value (deficit) per share as of December 31, 2018		
Pro forma net tangible book value (deficit) per share as of December 31, 2018		
Increase in pro forma net tangible book value per share attributable to new investors participating in this offering		
Pro forma as adjusted net tangible book value (deficit) per share after this offering		
Dilution per share to new investors participating in this offering		$

If the underwriters' option to purchase additional shares from us is exercised in full, the pro forma as adjusted net tangible book value per share after this offering would be $ per share, the increase in pro forma as adjusted net tangible book value per share to existing stockholders would be $ per share and the dilution to new investors purchasing shares in this offering would be $ per share.

Each $1.00 increase or decrease in the assumed public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease, as applicable, our pro

forma as adjusted net tangible book value by $ million, or $ per share, and dilution per share to investors in this offering by $ per share, assuming that the number of shares offered by us, as set forth on the cover of this prospectus, remains the same and after deducting underwriting discounts and commissions, and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase or decrease of 1.0 million shares in the number of shares we are offering would increase or decrease, as applicable, our pro forma as adjusted net tangible book value by approximately $ million, or approximately $ per share and would increase or decrease, as applicable, dilution per share to investors in this offering by approximately $ per share, assuming the assumed initial public offering price per share remains the same and after deducting underwriting discounts and commissions, and estimated offering expenses payable by us.

If the underwriters' option to purchase additional shares from us is exercised in full, the pro forma as adjusted net tangible book value per share after this offering would be $ per share, the increase in pro forma as adjusted net tangible book value per share to existing stockholders would be $ per share and the dilution to new investors purchasing shares in this offering would be $ per share.

The following table shows, as of December 31, 2018, on a pro forma as adjusted basis (but before deducting underwriting discounts and commissions and estimated offering expenses payable by us), the differences between the existing stockholders and the purchasers of shares in this offering with respect to the number of shares purchased from us, the total consideration paid, which includes net proceeds received from the issuance of common and redeemable convertible preferred stock, cash received from the exercise of stock options, and the value of any stock issued for services and the average price paid per share (in thousands, except per share amounts and percentages):

	Shares Purchased		Total Consideration		Weighted-Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders before this offering		%	$	%	$
New investors participating in this offering					$
Totals		100%	$	100%	

The foregoing tables and calculations (other than the historical net tangible book value calculations) are based on 120,608,203 shares of common stock (including our redeemable convertible preferred stock on an as-converted basis) outstanding as of December 31, 2018 and excludes:

- 841,800 shares of common stock issuable upon exercise of outstanding options issued as of December 31, 2018 under our 2015 Plan, at a weighted-average exercise price of $0.29 per share, or pursuant to rights to purchase restricted stock at a weighted average price of $0.01 per share;
- 7,029,718 shares of common stock reserved for future issuance under our 2015 Plan as of December 31, 2018;
- shares of our common stock reserved for future issuance under our 2019 Plan, which will become available for issuance upon the effectiveness of the registration statement of which this prospectus is a part; and
- shares of our common stock reserved for future issuance under our 2019 ESPP, which will become available for issuance upon the effectiveness of the registration statement of which this prospectus is a part.

To the extent that any outstanding options are exercised, new options are issued under our stock-based compensation plans or we issue additional shares of common stock or convertible debt in the future, there will be further dilution to investors participating in this offering.

SELECTED FINANCIAL DATA

The following tables present selected financial data for our business. We have derived the selected statements of operations data for the years ended December 31, 2017 and 2018 and the selected balance sheet data as of December 31, 2017 and 2018 from our audited financial statements appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future. You should read this data together with our financial statements and related notes appearing elsewhere in this prospectus and the information in the section entitled "Management Discussion and Analysis of Financial Condition and Results of Operations."

(In thousands, except share and per share amounts)	Years Ended December 31, 2017	2018
Statements of Operations Data:		
Operating expenses:		
Research and development	$ 14,526	$ 24,415
General and administrative	3,823	6,500
Total operating expenses	18,349	30,915
Loss from operations	(18,349)	(30,915)
Interest income	16	688
Other expense, net	—	(49)
Net loss	$ (18,333)	$ (30,276)
Accretion to redemption value and cumulative dividends on redeemable convertible preferred stock	$ (2,289)	$ (4,876)
Net loss attributable to common stockholders	$ (20,622)	$ (35,152)
Net loss per share attributable to common stockholders, basic and diluted(1)	$ (3.59)	$ (4.22)
Weighted-average shares used in computing net loss per share attributable to common stockholders, basic and diluted(1)	5,745,000	8,333,000
Pro forma net loss per share attributable to common stockholders, basic and diluted(1)		$
Weighted-average shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted(1)		

(1) See Notes 3 and 16 to our audited financial statements included elsewhere in the prospectus for an explanation of the calculations of our basic and diluted net loss per share, pro forma net loss per share and the weighted-average number of shares used in the computation of the per share amounts.

(In thousands)	As of December 31, 2017	2018
Balance Sheets Data:		
Cash and cash equivalents	$ 4,251	$ 60,949
Working capital(1)	1,519	56,649
Total assets	6,553	66,529
Redeemable convertible preferred stock	39,910	132,103
Accumulated deficit	(36,566)	(71,470)
Total stockholders' deficit	(36,565)	(71,469)

(1) We define working capital as current assets less current liabilities. See our financial statements and related notes appearing elsewhere in this prospectus for details regarding our current assets and current liabilities.

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 the section entitled "Selected Financial Data" and our financial statements and related notes appearing elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risks and uncertainties, such as our plans, objectives, expectations, intentions and beliefs. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those discussed in the section entitled "Risk Factors."

Overview

We are a clinical stage biopharmaceutical company focused on discovering and developing novel therapies for the treatment of fibrosis. Our initial focus is on treating fibrosis by inhibiting integrin-mediated activation of TGF-ß. Our lead product candidate, PLN-74809, is an oral small-molecule dual selective inhibitor of avß6 and avß1 integrins that we are developing for the treatment of idiopathic pulmonary fibrosis, or IPF, and primary sclerosing cholangitis, or PSC. We have completed a Phase 1a SAD/MAD trial and are currently conducting a Phase 1b proof-of-mechanism trial of PLN-74809 in IPF and expect to receive data in mid-2019. In the second half of 2019, we plan to initiate two Phase 2a trials in IPF. We also plan to submit an IND application for PLN-74809 for the treatment of PSC in the second half of 2019, and plan to initiate a Phase 2a trial as soon as possible thereafter. Our second product candidate, PLN-1474, in an oral small-molecule selective inhibitor of avß1 for the treatment of stage F3/F4 liver fibrosis associated with NASH. We are currently conducting IND-enabling studies and plan to submit an IND application for PLN-1474 by the end of 2019. We have applied our deep understanding of fibrosis biology, along with our medicinal chemistry and translational medicine expertise to develop a set of proprietary tools designed to discover and de-risk product candidates quickly and efficiently. Our goal is to become a world-leading fibrosis company, developing and commercializing disease-modifying therapies across a spectrum of fibrotic diseases.

Since our inception in 2015, our operations have been limited to organizing and hiring personnel for our company, business planning, raising capital, establishing our intellectual property portfolio and performing research and development of TGF-ß signaling and integrin biology, medicinal chemistry, translational screening technologies, and clinical insights to create tissue-specific inhibitors of fibrotic diseases. We do not have any products approved for commercial sale and have not generated any revenues. To date, we have funded our operations primarily through private placements of our redeemable convertible preferred stock.

Since our inception, we have incurred significant operating losses. Our net loss was $30.3 million for the year ended December 31, 2018. As of December 31, 2018, we had an accumulated deficit of $71.5 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future. In addition, we anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- advance the development of our lead product candidate, PLN-74809, through clinical development, and, if successful, later-stage clinical trials;
- advance our other preclinical development programs, including PLN-1474, into clinical development;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- increase the amount of research and development activities to identify and develop product candidates;
- hire additional clinical, quality control and scientific personnel;
- expand our operational, financial and management systems and increase personnel, including personnel to support our clinical development, manufacturing and commercialization efforts and our operations as a public company;
- maintain, expand and protect our intellectual property portfolio;

- establish a sales, marketing, medical affairs and distribution infrastructure to commercialize any products for which we may obtain marketing approval and intend to commercialize on our own or jointly with third parties; and
- invest in or in-license other technologies or product candidates.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for PLN-74809 or any of our other product candidates. In addition, if we obtain regulatory approval for PLN-74809 or any of our other product candidates and do not enter into one or more collaborations with third-parties for commercialization, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing and distribution activities.

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

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or magnitude of expenses. Even if we can generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2018, we had cash and cash equivalents of $60.9 million. We expect to continue to incur losses for the foreseeable future and will require additional financial resources to continue to advance our products and intellectual property. Based on our current forecast we do not have sufficient cash and cash equivalents for at least the next year following the date that the financial statements appearing elsewhere in this prospectus were issued. These circumstances raise substantial doubt about our ability to continue as a going concern. We will need to obtain additional financing to sustain our operations. However, we may be unable to obtain sufficient financing at acceptable terms, if at all, and the failure to do so, when needed, could have a material adverse effect on our business, results of operations and financial condition. Our financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Financial Operations Overview

Operating Expenses

Research and Development

Our research and development expenses consist of expenses incurred in connection with the development of our product candidates. Research and development expenses include:

- employee-related expenses, which include salaries, benefits and stock-based compensation for our research and development personnel;
- expenses incurred under agreements with third-party contract organizations, investigative clinical trial sites and consultants that conduct research and development activities on our behalf;
- costs associated with preclinical studies and clinical trials;
- depreciation of laboratory equipment and costs of supplies;

- costs associated with technology and intellectual property licenses; and
- facilities and other allocated expenses, which include expenses for rent and other facility related costs and other supplies.

We expense all research and development costs in the periods in which they are incurred. We do not allocate our costs by product candidates or by preclinical programs as these are in early stages of clinical trials or development, and our internal expenses are not allocated between candidates and programs. Although external third-party costs are allocable between candidates and programs, we do not perform this allocation.

We are eligible for a research and development tax credit. The tax incentive is available to us based on research and development activity within the United States and California. These research and development tax incentives are recognized as a contra to FICA payroll tax expense when the right to receive has been attained and funds are collectible and is capped at $250,000 per year. For additional information, see Note 3 to our audited financial statements included elsewhere in this prospectus.

We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates and our preclinical programs and as they advance into later stages of development. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

General and Administrative

Our general and administrative expenses consist primarily of personnel costs, allocated facilities costs and other expenses for outside professional services, including legal, marketing, investor relations, human resource and accounting services. Personnel costs consist of salaries, benefits and stock-based compensation for our general and administrative personnel. We expect to incur additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC, The Nasdaq Global Market, additional insurance expenses, investor relations activities and other administrative and professional services. We also expect to increase the size of our administrative function to support the growth of our business. In addition, if we obtain regulatory approval for any of our product candidates and do not enter into a third-party commercialization collaboration, we expect to incur significant expenses related to building a sales and marketing team to support product sales, marketing and distribution activities.

Interest Income

Our interest income consists of interest income earned on cash and money market funds.

Results of Operations

Comparison of the Years Ended December 31, 2017 and 2018

(In thousands, except percentages)	Years Ended December 31, 2017	2018	$ Change	% Change
Operating expenses:				
Research and development	$ 14,526	$ 24,415	$ 9,889	68.1%
General and administrative	3,823	6,500	2,677	70.0%
Total operating expenses	18,349	30,915	12,566	68.5%
Loss from operations	(18,349)	(30,915)	(12,566)	(68.5)%
Interest income	16	688	672	NM
Other expense, net	—	(49)	(49)	NM
Net loss	$ (18,333)	$ (30,276)	$ (11,943)	(65.1)%

NM: Results not meaningful

Research and Development Expenses

Research and development expenses increased by $9.9 million, or 68.1%, for the year ended December 31, 2018, compared to the year ended December 31, 2017. The increase was primarily due to $4.8 million of increased consulting and outside services costs, $2.2 million of increased compensation costs, $2.1 million of increased laboratory supply costs, $0.6 million of increased rent expense, $0.3 million increase in depreciation expense, $0.1 million increase in miscellaneous and other expenses and $0.1 million increase in stock-based compensation expense, partially offset by a $0.3 million reduction in sponsored research expenses. Consulting and outside services and laboratory and equipment supplies costs increased due to increased PLN-74809 and PLN-1474 development activities. Compensation costs increased as a result of headcount increases. Rent expense increased due to the move to new office space in South San Francisco in mid-2018. Depreciation expense increased due to increased leasehold improvements installed at the South San Francisco office. The decrease in sponsored research was due to a decrease in spending for sponsored research activities with universities in 2018, compared to the 2017 period.

General and Administrative Expenses

General and administrative expenses increased by $2.7 million, or 70.0%, for the year ended December 31, 2018, compared to the year ended December 31, 2017. The increase was primarily due to $1.0 million of increased professional and consulting costs, $0.5 million of increased compensation costs, $0.5 million increase in charitable contributions, $0.2 million increase in travel related expenses, $0.3 million increase in miscellaneous and other expenses and $0.1 million increase in stock-based compensation expense. Professional and consulting costs increased primarily as a result of increased legal, marketing, investor relations and accounting fees. Compensation costs increased as a result of increased headcount. Travel related expenses increased due to increased executive travel related to equity raising activities.

Interest Income

Interest income increased by $0.7 million for the year ended December 31, 2018, compared to the year ended December 31, 2017. The increase was attributable to interest income earned on an increased cash and cash equivalents balance from increased convertible preferred stock issuances in 2018 when compared to 2017.

Liquidity and Capital Resources

Overview

Since inception and through December 31, 2018, we have funded our operations primarily by net proceeds of $123.8 million from the sale of our redeemable convertible preferred stock. At December 31, 2018, we had available cash and cash equivalents of $60.9 million.

We have incurred operating losses and experienced negative operating cash flows since our inception, we will continue to incur losses for the foreseeable future and will require additional financial resources to continue to advance our products and intellectual property. Our net loss was $30.3 million for the year ended December 31, 2018, and, as of December 31, 2018, we had an accumulated deficit of $71.5 million. Based on our current forecast we do not have sufficient cash and cash equivalents for at least the next year following the date that the financial statements appearing elsewhere in this prospectus were issued. These circumstances raise substantial doubt about our ability to continue as a going concern. We will need to obtain additional financing to sustain our operations. However, we may be unable to obtain sufficient financing at acceptable terms, if any at all, and the failure to do so, when needed, could have a material adverse effect on our business, results of operations and financial condition. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Funding Requirements

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

Our future funding requirements will depend on many factors, including the following:

- the initiation, progress, timing, costs and results of preclinical studies and clinical trials for our product candidates;
- the clinical development plans we establish for these product candidates;
- the number and characteristics of product candidates that we develop;
- the outcome, timing and cost of meeting regulatory requirements established by the U.S. Food and Drug Administration, or FDA, and other comparable foreign regulatory authorities;
- whether we enter into any collaboration agreements and the terms of any such agreements;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties against us or our product candidates;
- the effect of competing technological and market developments;
- the cost and timing of completion of commercial-scale outsourced manufacturing activities; and
- the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval in regions where we choose to commercialize our products on our own.

Further, our operating plan may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development expenditures.

If we need to raise additional capital to fund our operations, funding may not be available to us on acceptable terms, or at all. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of or suspend one or more of our preclinical studies, clinical trials, research and development programs or commercialization efforts. We may seek to raise any necessary additional capital through a combination of public or private equity offerings, debt financings, collaborations and other licensing arrangements. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional capital through marketing and distribution arrangements or other

collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us.

Cash Flows

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

	Years Ended December 31,	
	2017	2018
Cash used in operating activities	$(16,924)	$(28,328)
Cash used in investing activities	(1,405)	(2,323)
Cash provided by financing activities	20,006	87,349
Net increase in cash and cash equivalents	$ 1,677	$ 56,698

Cash Used in Operating Activities

Net cash used in operating activities was $28.3 million for the year ended December 31, 2018 and $16.9 million for the year ended December 31, 2017.

Cash used in operating activities in the year ended December 31, 2018, was primarily due to our net loss for the year of $30.3 million adjusted by non-cash charges of $0.9 million and a net change of $1.1 million in our net operating assets and liabilities. The non-cash charges consisted of $0.7 million of depreciation expense and $0.2 million of stock-based compensation expense. The changes in our net operating assets and liabilities were primarily due to an increase of $1.5 million in accounts payable and accrued expenses and $0.4 million increase in deferred rent, partially offset by a decrease of $0.8 million in other non-current assets, prepayments and tax credit receivable.

Cash used in operating activities in the year ended December 31, 2017 was primarily due to our net loss for the year of $18.3 million adjusted by non-cash charges of $0.3 million and net change of $1.1 million in our net operating assets and liabilities. The non-cash charges consisted primarily of $0.3 million for depreciation expense. The changes in our net operating assets and liabilities were primarily due to an increase of $1.3 million in accounts payable and accrued expenses and $0.1 million in other non-current assets, partially offset by a decrease of $0.3 million in prepayments and tax credit receivable.

Cash Used in Investing Activities

During the years ended December 31, 2017 and 2018, cash used in investing activities was $1.4 million and $2.3 million, respectively, primarily resulting from the purchase of laboratory equipment and leasehold improvements.

Cash Provided by Financing Activities

During the year ended December 31, 2017, cash provided by financing activities was $20.0 million from the issuance of shares of Series A redeemable convertible preferred stock.

During the year ended December 31, 2018, cash provided by financing activities was $87.3 million of proceeds from the issuance of shares of Series A and Series B redeemable convertible preferred stock.

Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations and other commitments as of December 31, 2018 (in thousands):

	Payments Due by Period				
	Less than 1 Year	1 to 3 Years	3 to 5 Years	More Than 5 Years	Total
Operating lease	$ 1,892	$3,986	$4,269	$ 3,391	$13,538
Total obligations	$ 1,892	$3,986	$4,269	$ 3,391	$13,538

We enter into contracts in the normal course of business with third-party contract organizations for clinical trials, non-clinical studies and testing, manufacturing and other services and products. These contracts generally provide for termination following a certain period after notice and therefore we believe that our cancelable obligations under these agreements are not material and they are not included in the table above.

We have not included milestone or royalty payments or other contractual payment obligations in the table above if the timing and amount of such obligations are unknown or uncertain.

Off-Balance Sheet Arrangements

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements or holdings in any variable interest entities.

Quantitative and Qualitative Disclosures about Market Risk

The primary objectives of our investment activities are to ensure liquidity and to preserve capital. We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. We had cash and cash equivalents of $4.3 million and $60.9 million as of December 31, 2017 and 2018, respectively, which consisted of bank deposits and highly liquid money market funds. Historical fluctuations in interest rates have not been significant for us. We had no outstanding debt as of December 31, 2017, and 2018. Due to the short-term maturities of our cash equivalents, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents. To minimize the risk in the future, we intend to maintain our portfolio of cash equivalents in institutional market funds that are composed of U.S. Treasury and U.S. Treasury-backed repurchase agreements or short-term U.S. Treasury securities. We do not believe that inflation, interest rate changes, or exchange rate fluctuations had a significant impact on our results of operations for any periods presented herein.

Critical Accounting Polices and 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 United States generally accepted accounting principles. The preparation of these 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.

While our significant accounting policies are described in more detail in Note 3 to our financial statements appearing elsewhere in this prospectus, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Accrued Research and Development Costs

We record accrued expenses for estimated costs of our research and development activities conducted by third-party service providers, which include the conduct of clinical studies and preclinical studies. We record the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced and include these costs in accrued liabilities in the balance sheets and within research and development expense in the statement of operations. These costs are a significant component of our research and development expenses. We record accrued expenses for these costs based on factors such as estimates of the work completed and in accordance with agreements established with these third-party service providers. Any payments made in advance of services provided are recorded as prepaid assets, which are expensed as the contracted services are performed.

We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed, the number of patients enrolled and the rate of patient enrollment may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from clinical research organizations and other third-party service providers. For the periods presented, we have experienced no material differences between our accrued expenses and actual expenses.

Stock-Based Compensation

We recognize compensation costs related to stock awards and stock options granted to employees, nonemployees and directors based on the estimated fair value of the awards on the date of grant. We estimate the grant date fair value and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The grant date fair value of the stock-based awards is recognized on a straight-line basis over the requisite service periods, which are generally the vesting period of the respective awards. Forfeitures are accounted for as they occur.

The Black-Scholes option-pricing model requires the use of subjective assumptions which determine the fair value of stock-based awards, including the expected term and the price volatility of the underlying stock. These assumptions include:

- *Fair value of common stock*—See “Determination of the Fair Value of Our Common Stock” below.
- *Expected term*—The expected term represents the period that the stock-based awards are expected to be outstanding. The expected term for our stock options was calculated based on the weighted-average vesting term of the awards and the contract period, or simplified method, as allowed by the SEC.
- *Expected volatility*—Since we are not yet a public company and do not have any trading history for our common stock, the expected volatility was estimated based on the average historical volatilities of common stock of comparable publicly traded entities over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their size, stage in the life cycle or area of specialty. We will continue to apply this process until enough historical information regarding the volatility of our own stock price becomes available.
- *Risk-free interest rate*—The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the expected term of the awards.
- *Expected dividend*—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

Determination of the Fair Value of Our Common Stock

As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors as of the date of each option grant, with input from management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*.

For our stock awards granted during 2017, our common stock valuations were developed primarily based on the Current Value Method, or CVM, and the Probability Weighted Expected Return Method, or PWERM. The primary considerations were the liquidation and going concern scenario and to a lesser degree, a merger and acquisition and IPO scenarios. For the liquidation scenario, we considered application of the CVM to value the Company and for the going concern scenario, the PWERM was considered.

The CVM is based on an allocation theory that shareholders with senior stock rights would attempt to maximize the value of their holdings based solely on the senior interest's underlying liquidation preference, participation rights and conversion rights, as well as an imminent liquidity event. This approach determines the value of the enterprise at the valuation date, distributes that value through the existing capital structure and then applies discounts or premiums as may be appropriate to the varying securities classes. It does not consider optionality or upside payoffs for those securities that may not receive value at the current valuation.

Under the PWERM, the value of a Company's equity class is estimated based upon an analysis of future values for the entire enterprise assuming various future outcomes. Share value is based upon the probability-weighted present value of these expected outcomes, as well as the rights of each class of preferred and common stock.

For stock awards and options granted in 2018, we considered the use of the Income and Market approaches. Under the income approach, the cash generating ability of the company is valued. This approach focuses on determining a forecast benefit stream that is reflective of the subject company's most likely future performance. The forecast benefit stream is then discounted to present value based on the appropriate risk-adjusted discount rate or capitalization rate.

Under the Market approach, we referenced actual transactions involving our company or similar assets and/or enterprises. The Market approach generally consists of two primary methodologies: The Guideline Comparables Method, or GCM and the Guideline Transaction Method, or GTM. The GCM involves identifying and selecting publicly traded companies or guideline public companies, or Guideline Public Companies, with financial and operating characteristics like the subject being valued, and subsequently deriving multiples and other metrics from such Guideline Public Companies to apply to the subject being valued.

Taking the stage of our development into consideration and expected liquidity events into account, we elected not to rely upon a pure application of the Income or Market valuation approaches. We determined that the PWERM was more appropriate to value our equity classes as the approach is based upon an analysis of future values for the entire enterprise assuming various future outcomes. We did consider elements of the Income and Market approaches for gauging the appropriateness of certain PWERM inputs and assumptions.

In addition to considering the results of these third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, which may be as a date later than the most recent third-party valuation date, including:

- the prices at which we sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to our common stock at the time of each grant;

- the progress of our research and development programs, including the status of pre-clinical and planned clinical trials for our product candidates;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the biotechnology industry, and trends within the biotechnology industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or a sale of our company considering prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

For financial reporting purposes, we considered the amount of time between the valuation date and the grant date of our stock awards and options to determine whether to use the latest common stock valuation or an interpolated fair value between the two valuation dates. This determination included an evaluation of whether the subsequent valuation indicated that any significant change in valuation had occurred between the previous valuation and the grant date.

The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation expense could be materially different. Following the closing of this offering, the fair value of our common stock will be determined based on the quoted market price of our common stock.

As of December 31, 2018, we had $0.7 million and $0.4 million of unrecognized stock-based compensation expense that is expected to be recognized over the weighted-average periods of 2.2 years and 3.7 years related to restricted stock awards and stock options, respectively. Based upon the assumed initial public offering price of $, the midpoint of the price range set forth on the cover page of this prospectus, the aggregate intrinsic value of options outstanding as of December 31, 2018 was $ million, $ million of which related to unvested options.

Recent Accounting Pronouncements

See Note 3 to our financial statements appearing elsewhere in this prospectus for more information.

Emerging Growth Company Status and JOBS Act Accounting Election

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have elected to avail ourselves of this exemption and adopt ASU No. 2016-02 *(Topic 842*), Leases when the standard is effective for private companies which is for fiscal years beginning after December 15, 2019. 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.

In addition, we intend to rely on the other exemptions and reduced reporting requirements provided by the JOBS Act. Subject to certain conditions set forth in the JOBS Act, if as an "emerging growth company" we intend to rely on such exemptions, we are not required to, among other things, (i) provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-

Oxley Act of 2002, (ii) provide all of the compensation disclosure that may be required of non-emerging growth public companies under the Dodd-Frank Wall Street Reform and Consumer Protection Act, (iii) 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 (auditor discussion and analysis) and (iv) disclose certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the Chief Executive Officer's compensation to median employee compensation. These exemptions will apply for a period of five years following the completion of this offering or until we no longer meet the requirements of being an emerging growth company, whichever is earlier.

Business

Overview

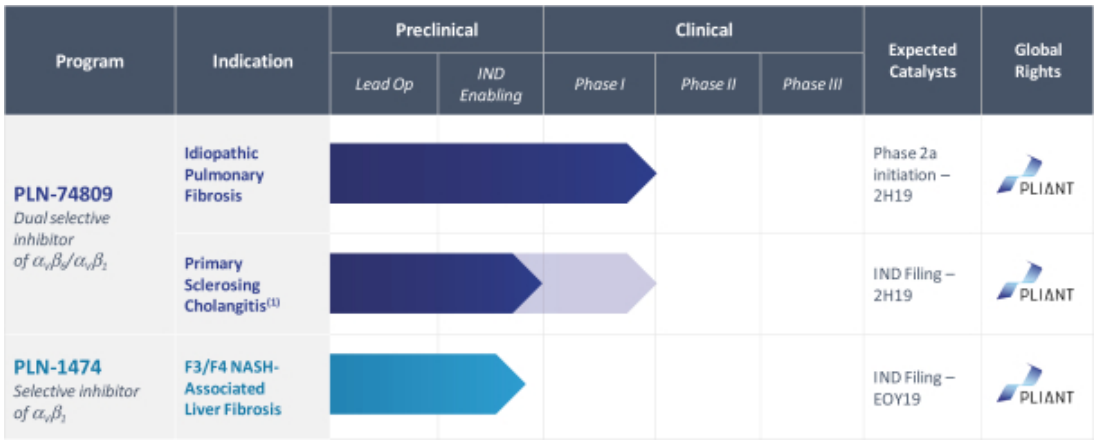
We are a clinical stage biopharmaceutical company focused on discovering and developing novel therapies for the treatment of fibrosis. Our initial focus is on treating fibrosis by inhibiting integrin-mediated activation of TGF-ß. Our lead product candidate, PLN-74809, is an oral small-molecule dual selective inhibitor of avß6 and avß1 integrins that we are developing for the treatment of idiopathic pulmonary fibrosis, or IPF, and primary sclerosing cholangitis, or PSC. We have completed a Phase 1a SAD/MAD trial and are currently conducting a Phase 1b proof-of-mechanism trial of PLN-74809 in IPF and expect to receive data in mid-2019. In the second half of 2019, we plan to initiate two Phase 2a trials in IPF. We also plan to submit an IND for PLN-74809 for the treatment of PSC in the second half of 2019, and plan to initiate a Phase 2a trial as soon as possible thereafter. Our second product candidate, PLN-1474, is an oral small-molecule selective inhibitor of avß1 for the treatment of stage F3/F4 liver fibrosis associated with NASH. We are currently conducting IND-enabling studies and plan to submit an IND application for PLN-1474 by the end of 2019. We have applied our deep understanding of fibrosis biology, along with our medicinal chemistry and translational medicine expertise to develop a set of proprietary tools designed to discover and de-risk product candidates quickly and efficiently. Our goal is to become a world-leading fibrosis company, developing and commercializing disease-modifying therapies across a spectrum of fibrotic diseases.

Fibrosis refers to the abnormal thickening and scarring of connective tissue due to the production and deposition of excess collagen in the extra-cellular matrix. Fibrosis can occur in many different tissues including lung, liver, kidney, muscle, skin and the gastrointestinal tract, and often causes severe and debilitating disease potentially leading to organ failure and death. Fibrosis has historically proven difficult to treat, which we believe is due to the complexity of the disease biology and the challenge of targeting fibrotic tissues selectively without affecting healthy tissues.

We believe that tissue-specific inhibition of TGF-ß may hold the key to successfully treating fibrosis. In normal tissues TGF-ß is activated in response to tissue injury which initiates a cascade that results in collagen production and, ultimately, scar formation to heal the tissue. In fibrosis, however, TGF-ß signaling becomes dysregulated, with TGF-ß being continuously activated, leading to excess collagen deposition, even in the absence of acute tissue injury. TGF-ß, while implicated in fibrosis pathophysiology, is expressed and intermittently activated across all tissue types and plays important, context-specific roles in tissue homeostasis. Therefore, TGF-ß cannot be blocked systemically without disrupting these homeostatic functions and causing significant toxicities. To more precisely treat fibrosis in specific tissues, we believe it is crucial to discover and treat the underlying mechanism causing excess TGF-ß activation.

Our scientific founders are pioneers in elucidating the role of specific extracellular receptors known as integrins as a key element in the activation of TGF-ß. While the role of integrins in TGF-ß activation has been well-characterized over the past 10 years, integrins have historically been difficult to target therapeutically using small-molecules due to the difficulty of engineering molecules with high receptor selectivity and oral bioavailability. We believe that we have addressed these challenges with our platform. We have built a library of compounds that includes orally bioavailable, selective and potent inhibitors of multiple integrins that may be used to target a range of fibrotic diseases across different tissues.

Our Pipeline



(1) We plan to submit an IND for PLN-74809 for the treatment of PSC in the second half of 2019 incorporating the data from the completed Phase 1a healthy volunteer trial and plan to initiate a Phase 2a clinical trial for PSC thereafter.

Our lead wholly owned product candidate, PLN-74809, is a small-molecule, dual-selective inhibitor of avß6 and avß1 that we are advancing in IPF and PSC. While expressed at very low levels in normal tissues, avß6 and avß1 are upregulated in the pulmonary tissues of IPF patients, and in the liver tissues of PSC patients. They both serve as activators of TGF-ß, leading to increased collagen production and fibrosis in these tissues. By blocking TGF-ß activation by both avß6 and avß1, we believe PLN-74809 may slow and potentially halt the progression of fibrosis in these patient populations. PLN-74809 has been granted orphan drug designation by the U.S. Food and Drug Administration, or FDA, for both IPF and PSC.

IPF is the most common and severe form of progressive pulmonary fibrosis, affecting approximately 140,000 patients in the United States. While the underlying cause of IPF is unknown, the course of the disease is well documented, with progressive scarring that destroys the structure and function of the lungs over time. The average life expectancy for patients with confirmed IPF is between three and five years. There are currently two FDA-approved therapies for IPF. Both have shown modest slowing of disease progression. However, both therapies have raised significant safety and tolerability concerns.

PSC is a progressive liver disorder affecting approximately 30,000 to 45,000 patients in the United States. The disease is characterized by fibrosis originating in the bile ducts that ultimately results in bile flow obstruction, or cholestasis, causing liver damage and progressive fibrosis of the liver. Patients have a median survival of 10 to 12 years without intervention and carry high lifetime risk of developing gastrointestinal malignancies. There are currently no FDA-approved therapies for PSC.

In our live human tissue assay, PLN-74809 showed a greater than 50 percent decrease in the expression of pro-fibrotic genes, such as collagen type I alpha1 chain, or *COL1A1*, and collagen type 3 alpha1 chain, or *COL3A1*, that are responsible for collagen production in human IPF and PSC tissues. Additionally, we have completed a study in non-human primates in which we showed that inhibition of avß6 and avß1 reduced TGF-ß activation by greater than 75% in cells isolated from the lungs after seven days of treatment.

We have completed a Phase 1a single ascending dose, or SAD, multiple ascending dose, or MAD, and food effect clinical trial in which PLN-74809 was shown to be orally bioavailable and generally well tolerated with a half-life that may support once-daily dosing.

We are currently conducting a Phase 1b proof-of-mechanism trial in healthy volunteers that is similar in design to our previously completed non-human primate study. We will measure PLN-74809's ability to inhibit

TGF-ß activation as measured through pSMAD2/3 activation levels in certain types of pulmonary cells. pSMADs act as signaling molecules directly downstream from the TGF-ß receptor, and therefore pSMAD2/3 activation is used as a reliable biomarker for TGF-ß activation. We expect to receive data from this trial in mid-2019.

In the second half of 2019, we plan to initiate two Phase 2a trials of PLN-74809 in IPF. In the first of these trials, we plan to enroll 18 IPF patients and utilize a positron emission tomography, or PET, ligand to measure avß6 target engagement by PLN-74809 in the lungs post-treatment. The second trial is expected to be a 12-week double blind placebo-controlled trial involving approximately 40 IPF patients across four cohorts consisting of three doses of PLN-74809 and one placebo and will evaluate safety, tolerability and pharmacokinetics, or PK. We also plan to employ exploratory efficacy endpoints including biomarkers and pulmonary function. We plan to file an IND application for PLN-74809 in PSC in the second half of 2019 and initiate a Phase 2a trial as soon as possible thereafter. This trial is expected to be a 12-week double blind placebo-controlled trial involving approximately 40 PSC patients across four cohorts consisting of three doses of PLN-74809 and one placebo and will evaluate safety, tolerability and PK. We also plan to employ exploratory efficacy endpoints including biomarkers and evaluation of liver-stiffness.

Our second wholly owned product candidate, PLN-1474, is an oral, small-molecule, selective inhibitor of TGF-ß activation by the integrin avß1, in development for treatment of stage F3/F4 NASH. avß1 serves as an activator of TGF-ß and its expression has been shown to be upregulated in hepatic stellate cells in stage F3 and F4 NASH-associated liver fibrosis.

NASH is a severe form of non-alcoholic fatty liver disease, or NAFLD, that is associated with the development of liver fibrosis and potentially life-threatening liver dysfunction. NASH is highly prevalent, affecting approximately 16.5 million adults in the United States, including approximately 3.3 million with stage F3/F4 fibrosis. Over time, NASH-related liver fibrosis may progress to cirrhosis, resulting in impaired liver function and increased risk of liver-related complications and mortality. There are currently no approved therapies for NASH, and to date investigational NASH therapies have only shown modest anti-fibrotic benefits in clinical trials.

We have shown through our assays of live human fibrotic liver tissue that PLN-1474 is able to decrease the expression of pro-fibrotic genes such as *COL1A1*, the gene associated with the production of the most abundant type of collagen produced in fibrosis. We have also shown in multiple animal models of NASH that PLN-1474 has a potent anti-fibrotic effect. We are currently completing IND-enabling studies of PLN-1474 and plan to submit an IND application by the end of 2019.

Pliant was formed to build upon our scientific founders' pioneering work elucidating the biology of fibrosis and its underlying causes. Our mission is to advance the understanding of fibrosis by building a biology-, chemistry- and screening-based engine to drive drug development across the spectrum of fibrotic diseases. We have established what we believe is a leading capability to both identify relevant fibrosis targets across different tissue types and address those targets with product candidates that have been optimized for potency and selectivity. We have established collaborations with top medical research institutions such as Stanford University and the University of California, San Francisco that provide us access to human fibrotic tissue from patients undergoing transplant to use in evaluation of our product candidates and share insights with thought leaders to further engage them in our mission. By refining the development of biology-driven product candidates in our laboratories through testing in freshly obtained human fibrotic tissue, we believe that we may be able to increase the efficiency of our development process and maximize the probability of success.

We have assembled an executive team with highly relevant experience in fibrosis, small-molecule drug discovery and clinical development. Bernard Coulie, M.D., Ph.D., our CEO, has 20 years of experience in drug development, previously serving as CEO and CMO of ActoGeniX, as well as holding senior roles at Johnson & Johnson. Éric Lefebvre, M.D., our Chief Medical Officer, brings deep experience in clinical development in liver disease. He previously served as head of clinical research and development for NASH at Allergan. Prior to

Allergan, Dr. Lefebvre led HIV and HCV development at Janssen and later served as CMO at Tobira. Eduard Gorina, M.D., our Vice President of Clinical Development, brings extensive experience in fibrotic disease. Prior to Pliant, Dr. Gorina served as executive director of clinical development at FibroGen where he led clinical programs in IPF and Duchenne muscular dystrophy. He also held senior director roles at InterMune, where he played a key role in the development of pirfenidone, the first therapy approved for IPF. We were founded by world-renowned researchers Dean Sheppard, Rik Derynck, Bill DeGrado and Hal Chapman from the University of California, San Francisco, who bring broad experience in fibrosis biology and small-molecule chemistry among other related disciplines.

To date, we have raised over $120 million from investors including Third Rock Ventures, Cowen Healthcare Investments, Eventide Asset Management, Schroder Adveq Management, Menlo Ventures, S-Cubed Capital and Agent Capital**.**

Our Strategy

Our goal is to become a world-leading fibrosis company, developing and commercializing disease-modifying therapies across a spectrum of fibrotic diseases. To achieve this, we are focused on the following key strategies:

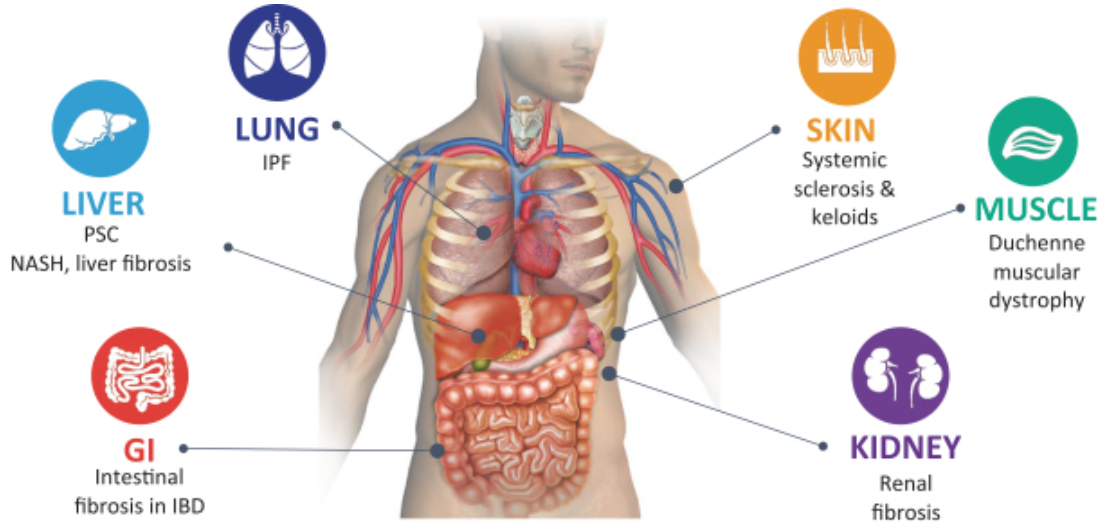
- **Rapidly advance PLN-74809 in IPF and PSC through clinical development and commercialization**. We are developing our lead oral small-molecule inhibitor of avß6 and avß1 as a potential best-in-class treatment for both IPF and PSC, each areas of high unmet medical need. Both IPF and PSC are orphan indications that we believe we can commercialize on our own in key geographies using targeted sales forces.
- **Rapidly advance our second compound, PLN-1474, in NASH**. PLN-1474 is an oral small-molecule selective inhibitor of avß1 in development for the treatment of stage F3/F4 liver fibrosis associated with NASH, an area of high unmet medical need with no currently FDA-approved treatments. PLN-1474 is currently in IND-enabling studies and we expect to submit an IND for this product candidate by the end of 2019.
- **Selectively evaluate partnerships in indications and geographies where we believe partners can add significant commercial and/or development capabilities.** Fibrotic diseases represent a broad set of disease indications to pursue. Our focus is to commercialize our assets in orphan fibrosis indications and to selectively work with partners in larger fibrosis indications and in geographies outside of North America. Furthermore, we believe our platform is capable of generating product candidates in indications outside of fibrosis, which we will evaluate and potentially choose to partner.
- **Explore opportunities for our pipeline assets in additional fibrotic indications.** We are evaluating the potential benefit of our product candidates outside of their lead indications. Our product candidates have shown anti-fibrotic activity in multiple animal models as well as human tissue in indications outside of IPF, PSC and NASH. We will continue to evaluate additional indications to maximize the potential of our pipeline.
- **Leverage our industry leading tools and capabilities to advance our mission of becoming a leading fibrosis company.** Since our founding we have endeavored to advance the understanding of fibrosis biology, uncover new targets and advance novel product candidates. Currently, our proprietary capabilities include a target expression atlas, an expansive library of over 4,500 integrin inhibitor molecules, integrin screening assay platform, live fibrotic human tissue program, PET-ligand imaging program, and biomarker assays. We continue to expand our integrin inhibitor library and develop tools such as additional PET-ligands as well as novel disease biomarkers. In addition, we have over 70,000 compound library for non-integrin targets. We intend to leverage these tools and capabilities in a target- and modality-agnostic manner to expand our pipeline with a mission to become a leading fibrosis company.

Fibrosis: A Condition of Uncontrolled Scarring

Fibrosis refers to excessive scarring often resulting from aberrant tissue repair processes. In normal tissues, fibrotic pathways represent a repair mechanism by which the tissues heal themselves in response to injury or disease. These pathways are normally deactivated upon completion of tissue repair. However, when they become dysregulated and remain activated, excess collagen deposition can cause tissues to thicken and become stiff, ultimately impairing their physiological function.

Fibrosis is a disease of connective tissue. Normal connective tissue forms a supportive network between cells, lending structure and integrity to tissues built up of many cell types. Connective tissue is composed of collagenous and elastic fibers, as well as a number of supporting cells such as fibroblasts and white blood cells. These supporting cells are embedded in a gel-like matrix made up of proteins known as the extra-cellular matrix. The most important protein in this matrix is collagen, which takes the form of elongated, fine fibers, providing flexible support to the surrounding cells. In fibrotic tissues, initial insults such as tissue damage or inflammation spur the deposition of excess collagen. Normally such responses are balanced in finely controlled feedback loops, but in fibrotic disease these feedback loops are dysregulated, resulting in progressive scarring, thickening, and loss of function.

Fibrosis occurs in many organ systems throughout the body including the lungs, liver, kidneys, gastrointestinal tract, skin and muscles. While the exact pathologies of diseases in these organs vary, the development of fibrosis involves many common cell types and biochemical pathways, including the TGF-ß signaling pathway. The ultimate result is similar across many tissues: secretion and extracellular activation of growth factors that stimulate fibroblasts to secrete excess collagen, leading to runaway growth of scar tissue.



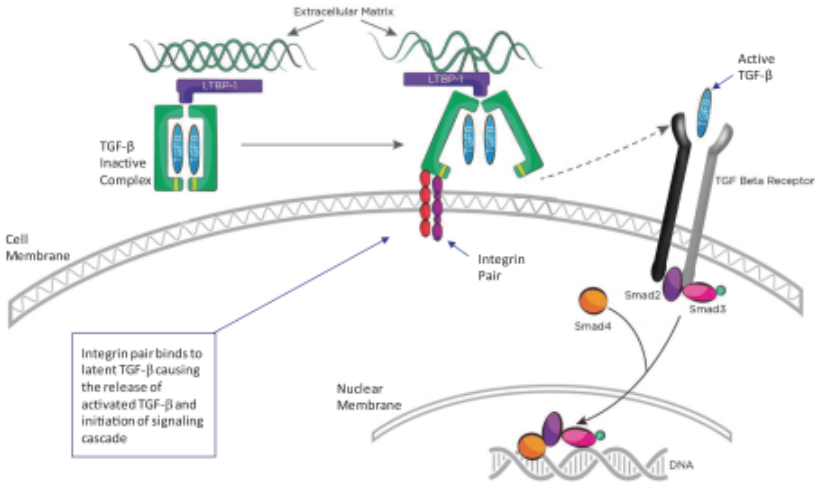
Role of TGF-ß Signaling in Fibrosis

We believe that selectively inhibiting TGF-ß activation holds the key to successfully treating fibrosis across multiple tissues and organs. TGF-ß is secreted by nearly all cells and organs in mammals and stored in large amounts outside of cells, in the extra-cellular matrix, as part of an inactive complex. In healthy tissues, TGF-ß is transiently activated in response to tissue injury which initiates a cascade that results in collagen production and, ultimately, healing of the tissue. In fibrosis, however TGF-ß signaling becomes dysregulated and perpetuated, with TGF-ß being continuously activated, leading to excess collagen deposition in the absence of acute tissue injury. Moreover, induced activation of TGF-ß alone in animal models has been shown to be sufficient to induce fibrosis, and inhibition of TGF-ß activation has been shown to prevent or attenuate fibrosis.

TGF-ß can be activated in multiple ways in response to specific tissue injury. One important class of cell-surface proteins that activate TGF-ß in fibrosis are integrins. Integrins have a variety of functions, including signaling inside the cells, providing tissue structure and stability through adhesion between cells. Integrins are heterodimeric proteins, meaning they are composed of two different protein subunits paired together. These subunits are known as a and ß subunits. In humans, there are eighteen distinct a subunits and eight distinct ß subunits, which combine to form 24 known and functional integrin pairs.

Certain integrins bind the inactive TGF-ß complex. In response to tissue injury, the cells expressing these integrins are induced to contract, exerting physical force on the bound TGF-ß complex. This mechanical force changes the shape of the complex, releasing active TGF-ß. This activation triggers a biological cascade which results in collagen production, and when dysregulated leads to fibrosis. As depicted in the figure below, this cascade involves (i) binding of active TGF-ß to its receptor, the TGF-ß type I receptor kinase also known as ALK5; (ii) phosphorylation of immediate downstream signaling proteins known as SMAD2 and SMAD3; (iii) formation of a transcription initiation complex by pSMAD2, pSMAD3 and SMAD4; and (iv) subsequent transcription of target genes that encode fibrotic proteins such as collagen. Importantly, whereas certain TGF-ß-activating integrins are expressed at very low levels in healthy tissues, the TGF-ß cascade can lead to the upregulation of the these integrins resulting in a TGF-ß-driven positive feed-forward loop which further increases TGF-ß activation. Furthermore, as fibrosis progresses and the fibrotic organ gets stiffer, it becomes progressively easier for contracting cells to activate integrin-bound TGF-ß. It is because of this continued, tissue-specific upregulation of integrins and their key roles in continued TGF-ß-activation that we believe that integrins provide an avenue to selectively inhibit TGF-ß activation in fibrotic tissue without affecting TGF-ß's important physiological roles in healthy tissues.

a_V Integrins promote fibrosis through activation of TGF-ß



Model of integrin regulation of TGF-ß signaling

Historical Challenges to Drug Development in Fibrosis

Fibrosis has historically been a difficult therapeutic area to target pharmaceutically. The biology and underlying causes of fibrosis are complex and, in many diseases, poorly understood. In the past, many patients with fibrotic disease were treated with anti-inflammatory agents such as steroids. While steroids may have a mild anti-fibrotic effect in some forms of fibrosis, they can exacerbate others, such as IPF. Additionally, the negative effects of chronic steroid exposure make it difficult to treat patients with these agents for long term periods.

More recently, it has become well understood that regardless of the underlying cause, TGF-ß activation is at the heart of several key processes that drive fibrosis, including collagen formation, deposition of extracellular matrix proteins and activation and proliferation of fibroblast cells. As such, much of the historic drug development efforts to treat fibrosis have been aimed at systemically inhibiting or disrupting the TGF-ß signaling pathway by either (i) blocking TGF-ß binding to the TGF-ß receptors with an antibody or (ii) preventing the type I TGF-ß receptor, also known as ALK5, from activating the SMADs using a small-molecule kinase inhibitor. However, because of TGF-ß's role in normal physiology, these approaches cause substantial toxicity and dysregulation of normal functions. In fact, documented toxicities that arise from systemic inhibition of TGF-ß signaling include cardiac toxicity, inflammation, and focal epithelial hyperplasia.

A potentially safer approach to fibrosis therapy is to inhibit specific pro-fibrotic signaling molecules, such as connective tissue growth factor and autotaxin, which operate downstream of TGF-ß activation, thereby mitigating the tolerability issues associated with systemic TGF-ß inhibition. While tolerability has been shown to improve with this approach, the efficacy shown to date has been modest, likely because TGF-ß activates multiple pro-fibrotic signaling pathways in addition to those targeted by these approaches.

Another recent approach is to prevent TGF-ß activation by stabilizing TGF-ß in its inactive form. However, it is not known whether latent TGF-ß stabilization can be accomplished in a tissue specific manner.

In addition to the historical difficulty in targeting TGF-ß, clinical development for the treatment of fibrosis has also been limited by the lack of tools to understand this complex multicellular process. Only certain parts of this process can be modeled using cellular assays. More complete representations of fibrosis can be generated in animal models, but these models tend to be acute in nature and do not accurately represent disease pathology in humans which, in most cases, develops over decades.

Integrin Inhibitors as a Potential Treatment for Fibrosis

An ideal approach to fibrosis treatment would be one that inhibits TGF-ß activation in only those tissues where fibrosis is occurring. One potential way to accomplish this is to inhibit the integrin proteins that are known to be overexpressed in specific fibrotic tissue and cause the abnormal activation of TGF-ß. In several forms of fibrosis, namely IPF and PSC, TGF-ß activating integrins such as avß6 and avß1 are over-expressed. These integrins are normally expressed at low levels in healthy tissue. Therefore, we would not expect off-target toxicity effects by selectively inhibiting avß6 and avß1. By inhibiting fibrosis-specific TGF-ß activators such as these specific integrins, it is possible to block abnormal TGF-ß activation in the specific tissues where fibrosis occurs, without affecting TGF-ß signaling in healthy tissues. However, integrin drug development has historically been challenging due to the difficulty of developing integrin inhibitors that are both selective for specific integrins and orally bioavailable. We believe our pipeline of orally bioavailable highly selective integrin inhibitors has the potential to address these challenges.

Recently, large biopharmaceutical companies have begun to recognize the potential of anti-integrin approaches to treat fibrosis and made large investments in the space. Biogen is currently developing a subcutaneous antibody against avß6 for treatment of IPF. In preclinical trials, Biogen presented results showing its avß6 antibody reduced pSMAD2 levels, a key biomarker for TGF-ß activation, in alveolar macrophages of non-human primates. In a Phase 2a study presented in 2018, Biogen's antibody was shown to have a similar effect in IPF patients. Biogen is currently conducting a 290 patient Phase 2b trial with their antibody candidate. In addition, AbbVie recently in-licensed a set of preclinical integrin inhibitors for the treatment of fibrosis including an avß6 inhibitor targeting IPF. The Biogen and AbbVie product candidates are all single selective inhibitors of avß6; however, it has been shown that the expression of both avß6 and avß1 is upregulated in IPF. We believe that our dual-selective avß6/avß1 inhibitor approach has the potential to provide a more potent anti-fibrotic effect than a single selective avß6 inhibitor.

We believe that recent developments in the field of integrin inhibitors validate our initial focus on integrin inhibitors as a treatment for fibrosis. Utilizing our proprietary discovery and development capabilities, we believe

that we have overcome key historical challenges to the development of integrin inhibitors, including potency, selectivity and oral bioavailability. We have identified two orally bioavailable and highly potent and selective integrin inhibitors. Our lead product candidate, PLN-74809, has completed Phase 1a trials and has demonstrated potential for a once daily oral dosing profile.

Our Capability and Approach to Fibrosis Drug Discovery and Development

Our approach to drug development in fibrosis combines our deep knowledge of the biology of fibrosis with various cellular, tissue, and *in vivo* assays developed in house to interrogate the biology of fibrosis and uncover pathways and potential targets. We developed an extensive panel of cell assays, precision cut tissue assays and animal models covering various types of fibrotic diseases. These assays allow us to evaluate target expression in fibrotic tissues as well as the anti-fibrotic activity of our candidates after treatment and begin to establish proof-of-biological-mechanism in both animal models and human tissue prior to initiating clinical trials. We believe these collective capabilities uniquely allow us to (i) efficiently identify targets, (ii) optimize the potency and selectivity of candidates and (iii) de-risk product candidates in advance of human proof-of-concept.

The first tool we use in our discovery process is our target expression atlas. Utilizing samples from normal and fibrotic human tissue, we developed a quantitative atlas of gene and protein expression across multiple fibrotic diseases. This database represents a wealth of data that we use to quantify expression of tissue specific targets for potential therapeutics. The atlas is continuously expanding through acquisition of additional samples as well as additional analyses. To date, we have advanced multiple potential targets to our early discovery pipeline.

The second important tool in our discovery process is our compound library that we screen for activity against targets identified through our target atlas. While we are agnostic to treatment modality, our initial targeted chemistry effort has been focused on integrin inhibitors, and our medicinal chemistry team has developed a proprietary library of over 4,500 potential integrin inhibitors. The goal of the library is to maximize structural diversity while targeting optimal absorption, distribution, metabolism and excretion, or ADME, properties. We expect that the library will continue to grow as we investigate new structures. We have designed the library based on in silico known X-ray structures/homology models, structure-activity relationships of structural motifs of known integrin inhibitors, and de novo molecular design. In addition to our proprietary integrin inhibitor library, we have a non-integrin compound library of over 70,000 compounds that we screen against non-integrin targets.

Once we have identified a potential target through our target expression atlas, we screen our library of compounds against the target. We have developed screening assays for 20 of the 24 known integrins and use these assays to evaluate the potency and selectivity of binding for our potential drug candidates prior to preclinical studies. Given the selectivity and potency challenges that have hampered integrin drug development, we believe our integrin assay panel represents a major step forward in integrin-based drug development.

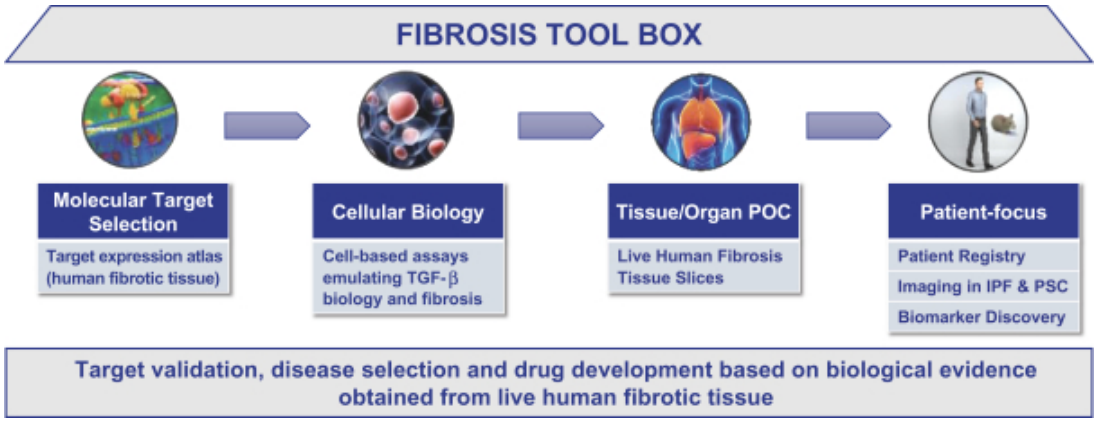
We believe a key advantage of our development strategy is our ability to test our product candidates in live human fibrotic tissue, which helps us to bridge the gap between animal models and clinical proof-of-concept. We have developed proprietary protocols that extend the viability of live human explant tissue samples which allow us to reproducibly perform multiday experiments. We also maintain an on-call, around the clock team that obtains tissue samples following transplant procedures and transports those tissues to our lab within hours of explant, in a highly coordinated process. Our access to these live tissue samples allows us to evaluate the effects of our product candidates on multiple markers of anti-fibrotic activity. The data from these experiments increase our confidence that the tested product candidates will show anti-fibrotic effects in patients. In this way, our human tissue program serves to further de-risk product candidates and increase their likelihood of success in the clinic.

Once in clinical development, we continue to de-risk our programs by designing clinical trials that allow us to show proof-of-mechanism in advance of clinical efficacy data. Because fibrosis is a chronic disease, proof-of-

efficacy in human trials is expensive and takes years to complete. We utilize pharmacodynamic biomarkers and advanced imaging techniques, including PET, to evaluate target engagement by our product candidates over relatively short time periods and observe whether the product candidate is having the anticipated effect. We believe obtaining these clinical data points in an efficient manner will allow us to optimize our clinical development strategy and resource allocation.

We and our partners also proactively conduct observational, natural history trials in target diseases to better understand disease pathophysiology and progression and develop new molecular biomarkers. Through these trials, we have gone on to develop patient registries and establish relationships with clinicians at leading medical research institutions dedicated to bringing novel fibrosis therapies to their patients.

We are developing an extensive biomarker discovery and validation program. We are seeking to develop biomarkers to (i) identify patients at high risk of rapid disease progression, (ii) identify patients more likely to respond to treatment and (iii) monitor early treatment responses. We are conducting clinical studies and other research with leading academic centers to track disease progression and collect biological samples such as blood, urine, and tissue biopsies which we can use to discover and validate novel biomarkers.



Our systematic approach to identifying and targeting integrins in fibrosis

Selective inhibition of TGF-ß activation in fibrotic tissues could potentially be the safest and most effective approach to treating fibrosis. One way to accomplish this is to inhibit the integrin receptors that drive excessive activation of TGF-ß. Given the importance of integrins in regulating the initial steps in fibrosis, we have focused our initial drug discovery efforts on a dual approach. This approach includes both biological profiling to identify which integrins are important in various diseased tissues and chemical profiling of libraries containing proprietary integrin inhibitors to help determine their selectivity and potency for individual integrins.

Utilizing our extensive in-house medicinal chemistry expertise, we have created a library of over 4,500 integrin-inhibitors. We screen this library against the integrin targets that we identify through our expression atlas and or biological profiling process. To our knowledge, this type of industrial-scale, systematic biological and chemical profiling, seeking selective inhibitors of one or more integrins, has not previously been carried out. We believe this combination makes our approach distinctive.

Central to our integrin inhibitor discovery process are our integrin assay panels. A key challenge in integrin inhibition, historically, has been selectivity for specific integrins. To address this challenge, we have developed assays against the 20 most relevant known integrins. We use these screening assays to measure potency and selectivity of potential candidates against these integrins. This allows us to quickly optimize the integrin binding profiles of potential development candidates in an iterative process.

Integrins can undergo conformational change. This results in different binding affinities. We believe an ideal integrin inhibitor should potently bind across the spectrum of conformations. Through the use of specific assays, we can measure the potency of our product candidates against multiple integrin conformations and seek to optimize for candidates that are able to potently bind to all conformations.

In addition to our deep understanding of integrin biology, we have gained significant insight in structure-activity relationships that determine integrin selectivity and optimal PK profiles. Utilizing this knowledge, we are now able to precisely engineer orally bioavailable integrin inhibitors with high potency and desired selectivity.

Our integrin inhibitor profiling capability has enabled us to quickly identify inhibitors that target individual integrins such as PLN-1474, which selectively inhibits avß1, as well as dual inhibitors such PLN-74809 which selectively targets both avß6 and avß1. Combining the data from our biological profiling and chemical profiling sets has enabled us to identify compounds that we believe have the highest potential for therapeutic activity in specific fibrotic diseases. Our iterative drug discovery effort focuses on drug-like properties of compounds early in the testing process. Compounds are screened for *in vitro* potency/selectivity and ADME/PK properties. This enables us to move from compound optimization to *in vivo* testing in a matter of months.

In addition to PLN-1474 and PLN-74809, we continue to evaluate our broad proprietary library of integrin inhibitors to identify additional product candidates to treat fibrotic diseases. Furthermore, our approach allows us to use our discovery and development capabilities to develop non-integrin therapeutic modalities to treat fibrotic diseases. Our rich library also provides a deep series of potential backup molecules with structurally unique chemotypes that we believe can enhance the probability of clinical success.

As with all of our development efforts, a key approach to pre-clinically de-risking our integrin inhibitor candidates is evaluation of the candidates in live human fibrotic tissue obtained following transplant procedures. The ability to observe effects of our product candidates on gene expression in human tissues prior to entering the clinic provides a bridge from animal models to clinical proof-of-concept and helps give us additional confidence as we move toward human trials. Similarly, if our *ex vivo* live human tissue studies show little or no effect on the target genes, we can quickly reallocate resources, saving time and money, and minimizing unnecessary patient exposure.

A second important de-risking strategy involves biomarker measurement in both preclinical and early stage clinical studies. By utilizing specific biomarkers such as pSMAD2/3 that operate immediately downstream from TGF-ß, we are able to measure the effects of our drugs on TGF-ß activation. We believe understanding the ability of our drug candidates to reduce TGF-ß activation is crucial to gaining confidence in the anti-fibrotic activity of our product candidates as we move forward in the clinic.

Once in Phase 2 clinical trials, we plan to use an advanced imaging technique to generate mechanistic data and de-risk the development of our candidates. Fibrosis is a chronic process and it can take 6 months to a year to see a clinical benefit with a drug candidate. We intend to utilize PET imaging to evaluate target engagement in patients and to determine if our candidates are having an effect in the tissues. We have an ongoing collaboration with Stanford pursuant to which we are evaluating Stanford's avß6 PET ligand in IPF patients. We plan to use this ligand to evaluate the level of avß6 expression in the lungs of IPF patients, as well as to measure our product candidate's ability to bind avß6. Over time, we believe this imaging modality will be able to detect changes in expression levels of avß6 and confirm whether our candidate is having its intended biological effect. In addition to the avß6 PET ligand, we are internally developing PET ligands to other integrins that we will use to evaluate subsequent product candidates.

Our product candidates

PLN-74809 for the treatment of IPF and PSC

Our lead product candidate, PLN-74809, is an oral small-molecule, dual-selective inhibitor of avß6 and avß1 integrins which we are developing for the treatment of IPF and PSC. We have received orphan drug

designation for PLN-74809 in both IPF and PSC. We completed a Phase 1a trial of PLN-74809 in healthy volunteers and are currently conducting a Phase 1b trial in which we will assess target engagement and proof-of-mechanism in healthy volunteers by examining the inhibition of TGF-ß activation in alveolar macrophages. We anticipate results from this trial to be available in mid-2019.

Idiopathic pulmonary fibrosis background

IPF is a debilitating, age-related lung disease of unknown causes that has few treatment options. It is a form of progressive pulmonary fibrosis that leads to thickening and stiffening of the lung tissue resulting in the loss of lung function. As tissue scarring progresses, the lungs' ability to transfer oxygen into the bloodstream becomes increasingly impaired. Average life expectancy at the time of confirmatory diagnosis of IPF is estimated to be between three and four years. Approximately 60 to 80 percent of patients die within five years of diagnosis. These survival rates are worse than those of many late stage cancers, such as stage 3 breast cancer.

Patients with IPF experience debilitating symptoms, including shortness of breath and difficulty performing routine functions, such as walking and talking. Other symptoms include a chronic, dry, hacking cough; fatigue; weakness; discomfort in the chest; loss of appetite; and weight loss. IPF is a rare disease that affects approximately 140,000 people in the United States. There are an estimated 30,000 to 40,000 new cases diagnosed each year.

Currently, there is no pharmacological cure for IPF and only a small proportion of late-stage IPF patients may be eligible for a lung transplant. The current non-transplant standard of care aims to slow the disease progression and improve the quality of life. Two therapies to treat IPF have recently been approved by the FDA: Esbriet (pirfenidone), marketed by Genentech, and OFEV (nintedanib), marketed by Boehringer Ingelheim. After decades during which the FDA approved no new treatments for IPF, the approvals of pirfenidone and nintedanib represented a major breakthrough for IPF patients. However, while these therapies slow the decline of lung function, neither drug has been shown to stop the progression of IPF.

Despite its mechanism of action being unknown, pirfenidone has been shown to have a modest effect on slowing the progression of IPF as measured by forced vital capacity, or FVC, in approximately fifteen percent of patients. Recent studies suggest that pirfenidone may have a small impact on survival compared to placebo, but these results have not been confirmed.

Nintedanib is an inhibitor of multiple tyrosine kinases that are receptors for growth factors such as platelet-derived growth factor, or PDGF, fibroblast growth factor, or FGF, and vascular endothelial growth factor or VEGF. Nintedanib reduced the rate of decline of pulmonary function in multiple trials by approximately half and led to significant delays in the time to acute disease exacerbation. While treatment was associated with a trend towards increased survival in registration trials, it has not been shown conclusively to have a survival benefit. Recent exploratory analyses from pooled data from six clinical trials of nintedanib suggest that nintedanib may extend life expectancy in patients with IPF.

In addition to only showing modest clinical efficacy, we believe the commercial adoption of these therapies has been limited by safety and tolerability. In the Phase 3 trials for pirfenidone and nintedanib, discontinuation rates for adverse events, or AEs, were approximately 15 percent and 21 percent, respectively. The primary reason for discontinuing treatment was tolerability, involving AEs such as diarrhea, nausea and decreased appetite with nintedanib and nausea and rash with pirfenidone. Elevated liver enzymes have been observed with both of these drugs, requiring monitoring of liver tests and potentially temporary dose reduction and discontinuation. Cases of drug-induced liver injury, including one fatal outcome, have been reported in patients treated with nintedanib. Real world evidence suggests that discontinuation rates may be higher than those observed in the registrational trials. Despite this limited efficacy and tolerability profile, combined sales of pirfenidone and nintedanib in 2018 were over $2 billion. IPF remains a major cause of morbidity and mortality and an area of high unmet medical need.

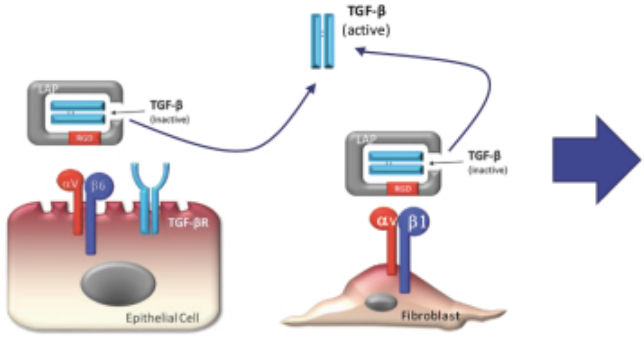
Primary sclerosing cholangitis background

PSC is a progressive liver disorder characterized by inflammation and fibrosis of the bile ducts which transport bile from the liver to the intestines. This type of fibrosis often results in obstruction or interruption of bile flow from the liver, a condition known as cholestasis, leading to liver fibrosis. Cirrhosis eventually develops and many individuals ultimately require a liver transplant. PSC patients are also at a higher risk of developing hepatobiliary cancers, including a 5 to 20 percent lifetime chance of developing cholangiocarcinoma, a typically rare form of cancer with an especially poor prognosis. The exact cause of PSC is unknown. PSC is normally diagnosed at middle age, with a median age at diagnosis of approximately 40 years old. The prevalence of PSC in the United States is estimated to be between 30,000 and 45,000 patients.

In the absence of liver transplant, median survival of PSC patients is 10 to 12 years following diagnosis without intervention. There are currently no approved pharmacological treatments for PSC. A number of immunosuppressive and anti-inflammatory agents have been studied in patients with PSC, but none has been conclusively proven to slow progression. Liver transplantation is the only available treatment for PSC patients; however, disease has been shown to recur in up to 20 percent of patients following transplantation.

Our solution, PLN-74809

PLN-74809 is a small-molecule that selectively inhibits both avß6 and avß1 integrins that we are developing as a potential once daily oral therapy for IPF and PSC. We have determined that TGF-ß activation in fibrosis associated with IPF and PSC involves both avß6 and avß1 integrins. It has been shown that expression of both avß6 on epithelial cells and avß1 on fibroblasts can lead to excessive activation of TGF-ß in fibrosis. Epithelial tissue includes any tissue that lines the surfaces of the body such as alveoli, bile ducts, urinary tract, skin, and gastrointestinal tract. Each of these tissues contains multiple cell types including epithelial cells and fibroblasts. An important secondary effect of the TGF-ß cascade is that it promotes upregulation of avß6 on epithelial cells. The increased expression of these integrins on the cell surface contributes in turn to further TGF-ß activation in a TGF-ß-driven positive feed-forward loop.

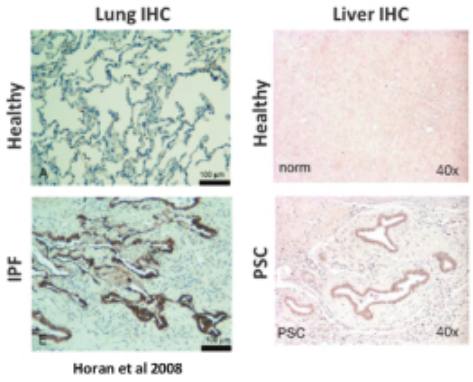


Activation of TGF-ß by $a_vß_6$ and $a_vß_1$ leads to:

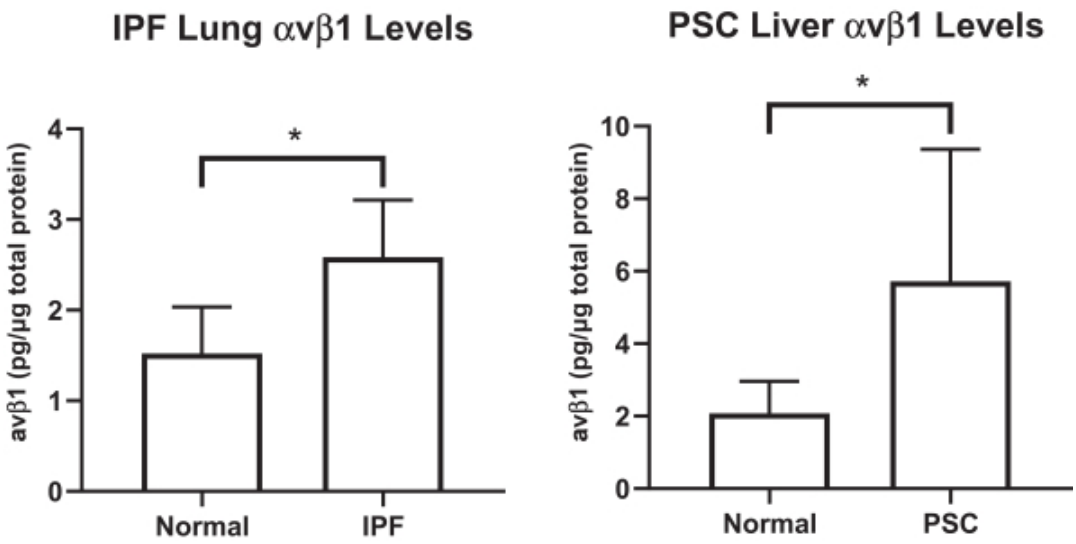
- Activation of TGF-ß signaling pathways
- Expression of pro-fibrotic genes including *COL1A1*
- Subsequent collagen production and deposition
- Additional upregulation of $a_vß_6$

Epithelial tissue fibrosis is driven by two types of integrins

Data from our lab, as well as scientific literature, have shown that avß6 and avß1 proteins are overexpressed in at least two different fibrosis indications: IPF and PSC. In lung tissue from IPF patients we and others have shown that alveolar epithelial cells have elevated avß6 expression, and that the level of over-expression correlates with disease severity. We have also shown that in these patients, avß1 expression is upregulated. In liver tissue from PSC patients, we have shown that avß6 is upregulated in cholangiocytes, the epithelial cells that line the bile ducts, and that avß1 is upregulated in whole fibrotic liver tissue. avß6 and avß1 are normally expressed at very low levels in healthy tissue making them ideal targets for selectively inhibiting TGF-ß activation in IPF and PSC.



avß6 is upregulated in the lung tissue of IPF patients and the liver tissue of PSC patients

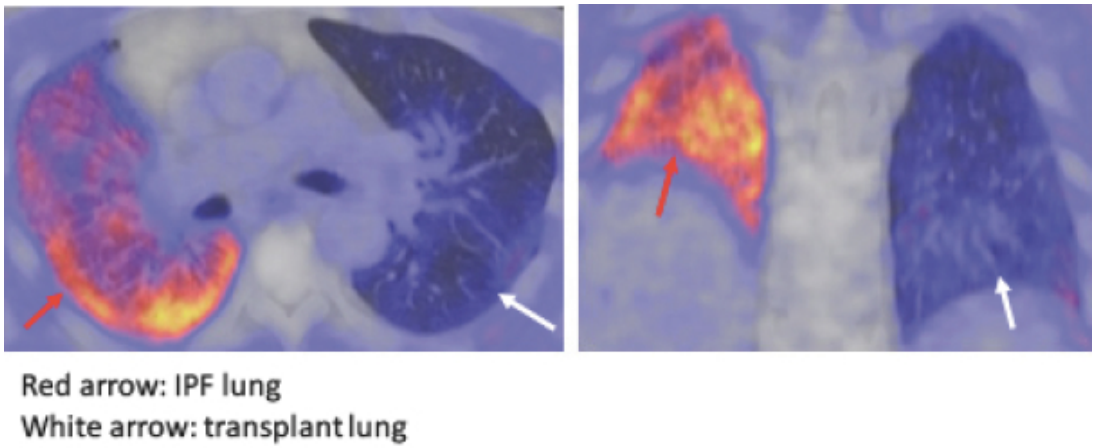


* = $p < 0.05$(1)

(1) A p-value is the probability that the reported result was achieved purely by chance, such that a p-value of less than or equal to 0.05 or 0.01 means that there is a 5.0% or 1.0% or less probability, respectively, that the difference between the control group and the treatment group is purely due to chance. A p-value of 0.05 or less typically represents a statistically significant result.

avß1 expression is upregulated in lung and liver fibrosis

We have conducted a non-interventional clinical trial in IPF patients to assess the expression of integrin avß6 using a PET ligand. This trial confirmed that patients with IPF have high levels of integrin avß6 expression, which tend to be co-localized with fibrotic regions of the lungs. The specificity of this PET ligand can be seen in images from an IPF patient who received a unilateral lung transplant. The PET ligand is only taken up in the diseased lung but not in the transplanted healthy lung.



Pulmonary avß6 PET ligand uptake in an IPF patient with a unilateral lung transplantation is confined to the IPF lung

We have shown that inhibition of both avß6 and avß1 integrins is required to maximally inhibit the expression of *COL1A1*, a key gene that encodes type I collagen, in models of lung and biliary fibrosis as well as in human IPF tissue. *COL1A1* is a TGF-ß regulated gene that is expressed in fibrotic tissue. The expression level of *COL1A1* correlates with the amount of collagen deposited as measured by the standard biochemical method of quantification of hydroxyproline, an amino acid that is a major component of collagen.

Clinical development of PLN-74809

Completed and ongoing trials

We completed a Phase 1a SAD/MAD and food effect clinical trial of PLN-74809 in healthy volunteers. In the SAD portion of the trial, single doses of PLN-74809 were administered orally to 32 volunteers across four cohorts at doses of 15, 30, 50 and 75 mg. Eight additional volunteers in the SAD portion of the trial received placebo. In the MAD portion of the trial, PLN-74809 was administered orally to 27 volunteers, once-daily over 14 days at 10, 20 and 40 mg. Six additional volunteers in the MAD portion of the trial received placebo. In the food effect part of the trial, PLN-74809 was administered orally to 12 volunteers, administered as a single dose of 40 mg with and without food. PLN-74809 was shown to be well tolerated with no dose-related AEs. All but two AEs reported in the entire trial were mild except for a moderate AE of dental abscess (SAD, 30 mg dose cohort) and a moderate AE of viral syndrome (MAD, 40 mg dose cohort). All AEs resolved or recovered and no dose relationship for AEs was observed. No notable findings were observed for laboratory abnormalities, vital signs or ECG/telemetry.

Adverse Events Reported by Participants Receiving PLN-74809

Study Part	PLN-74809 Dose	Adverse Event	Severity
SAD	15 mg	None	-
SAD	30 mg	Constipation [a]	Mild
		Dental abscess [a]	Moderate
		Headache	Mild
SAD	50 mg	None	-
SAD	75 mg	Superficial skin abrasion	Mild
FE-P1	40 mg	None	-
FE-P2	40 mg	Upper respiratory infection	Mild
		Constipation	Mild
MAD	10 mg QD	None	--
MAD	20 mg QD	Back sprain [b]	Mild
		Constipation [b]	Mild
		Constipation	Mild
		Contact dermatitis	Mild
		Nausea [c]	Mild
		Headache [c]	Mild
		Intermittent epigastric discomfort + minty-cool taste [c]	Mild
MAD	40 mg QD	Viral syndrome [d]	Moderate
		Frequent bowel movements [d]	Mild
		Right back muscle spasm [d]	Mild

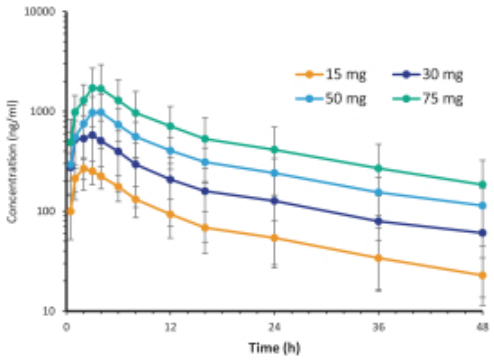
FE = Food effect; MAD = multiple ascending dose; P1 =Period 1; P2 = Period 2; SAD = single ascending dose.
a, b, c, d: Same participant

Additionally, PLN-74809 was well absorbed orally, and displayed a half-life of over 20 hours. PLN-74809 reached steady state plasma concentrations after seven days of dosing. Following 14 days of dosing, PLN-74809 concentrations at the 40 mg dose remained above the predicted protein-adjusted IC_{50} for most of the 24-hour dosing interval. Co-administration of PLN-74809 with food increased drug concentrations relative to the fasted state, with AUC increasing by approximately 60 percent and C_{max} by approximately 100 percent, with patients in the 40 mg dose cohort remaining in the predicted human effective dose range for 24 hours after dosing.

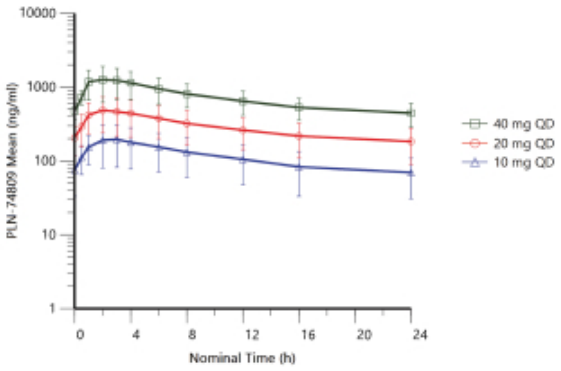
We are currently conducting a Phase 1b proof-of-mechanism trial in healthy volunteers that is similar in design to our previously completed non-human primate mechanistic trial. We will measure PLN-74809's ability to block TGF-ß signaling as measured by pSMAD levels in pulmonary alveolar macrophages collected from broncho-alveolar lavage, or BAL, fluid obtained through bronchoscopy. In this procedure, a bronchoscope is

passed through the mouth or nose and fluid is injected into the lungs then collected along with any displaced cells. These cells can then be assayed for biomarkers such as pSMAD. We are conducting this trial in healthy volunteers due to the safety risk associated with BAL procedure in IPF patients. We believe this trial will allow us to further characterize the PK/PD relationship in humans and will serve to inform our dose selection for Phase 2.

Phase 1a SAD PK

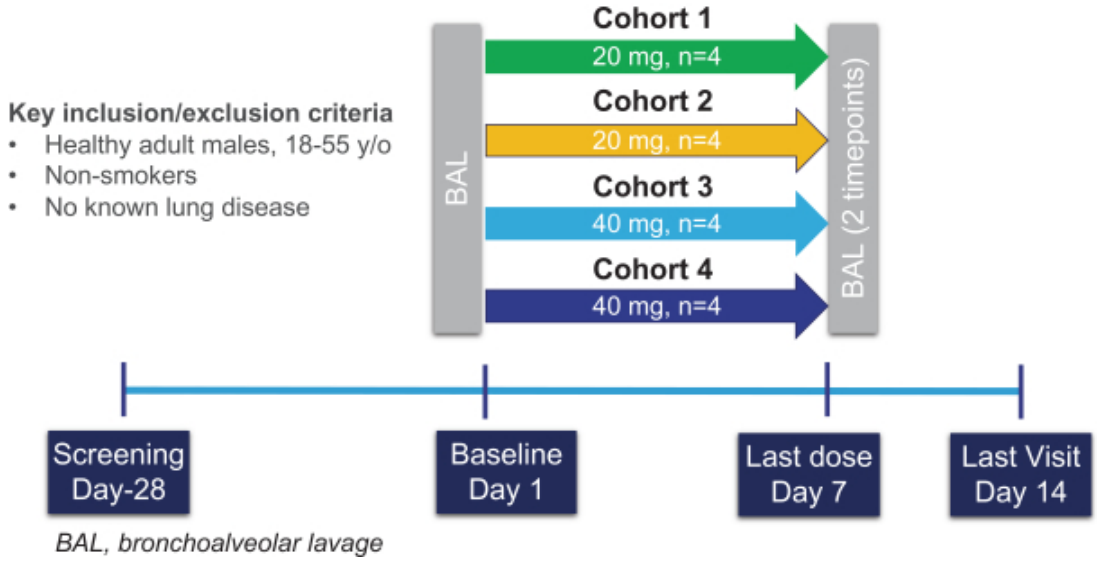


Phase 1a MAD PK at Day 13



In our Phase 1b trial, we expect to enroll 16 volunteers across four equal cohorts (randomized 3:1 active to placebo); two cohorts dosed at 20 mg once daily and two cohorts dosed at 40 mg once daily. We expect that volunteers will undergo an initial BAL procedure prior to treatment to measure baseline pSMAD levels. They will then be treated with PLN-74809 or placebo for seven days, after which they will undergo two additional BAL procedures to measure the amount of pSMAD reduction post-treatment at multiple time points. By utilizing two cohorts each for the 20 mg and 40 mg doses, our objective is to measure pSMAD and drug levels at 4 different time points post treatment for each dose (3, 6, 12 and 24 hours post-dose on day 7), that will allow assessment of PK/PD relationship over a 24-hour period. We expect to receive data from this trial in mid-2019.

Randomization 3:1 (active:placebo)

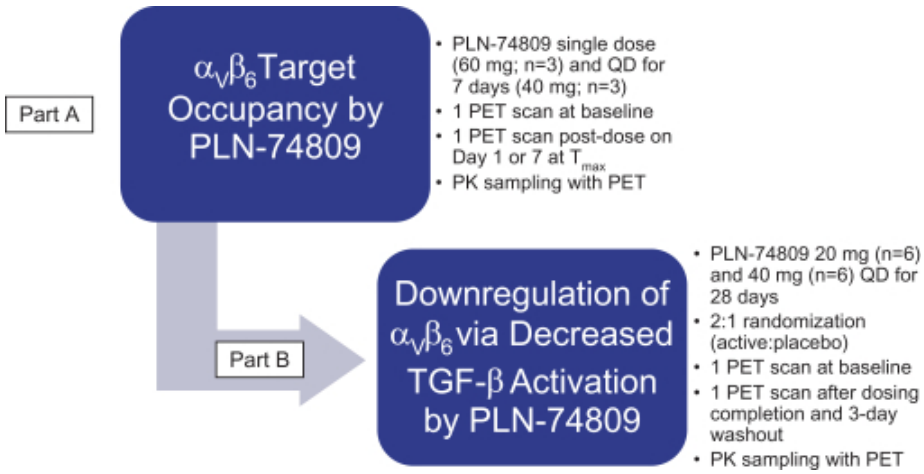


BAL, bronchoalveolar lavage

Planned clinical trials for IPF and PSC

In the second half of 2019, we plan to initiate two Phase 2a trials of PLN-74809 in patients with IPF. In the first of these trials, we plan to utilize a PET ligand to avß6 that allows imaging of target engagement by PLN-74809 in the lungs of IPF patients during treatment. This trial will target enrollment of a total of 18 patients in two parts, A and B. In Part A, we plan to enroll 6 patients in two sequential cohorts: first, a 60 mg single-dose cohort (n=3) followed by a 40 mg multiple-dose cohort (n=3) treated for seven days. We will obtain a PET scan at baseline to evaluate avß6 expression levels in the patients' lungs and then initiate treatment with open-label PLN-74809. In Part A, the post-treatment PET scan will be performed at approximately three hours after administration of the last dose, which will enable us to evaluate PLN-74809's target engagement in patients' lungs at maximum drug concentration. When PLN-74809 binds to the avß6 receptor, we would expect to see decreased PET ligand uptake in the lungs post-treatment when compared to pre-treatment levels. The relationship between dose and target engagement is important to guide dose selection in future studies. We expect data from Part A to be available in the first quarter of 2020.

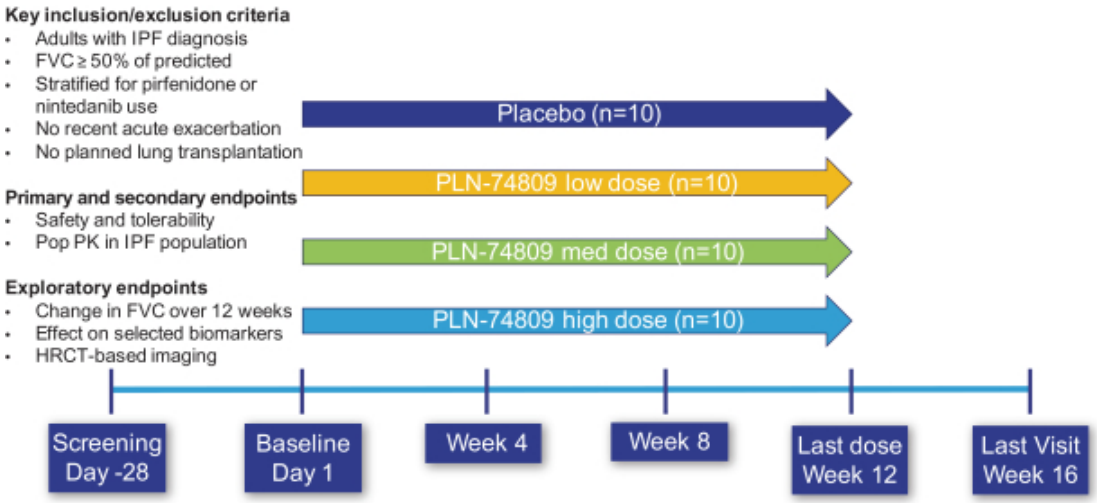
In Part B of our Phase 2a PET imaging trial, we plan to measure whether prolonged treatment with PLN-74809 can break the TGF-ß-driven positive feed-forward loop, as previously described, therefore causing downregulation of avß6 expression in the lungs of IPF patients. We plan to enroll a total of 12 patients randomized across two PLN-74809 dose groups, 20 mg once daily and 40 mg once daily, or placebo (randomized 3:1 active to placebo). After obtaining a pre-treatment baseline PET scan to evaluate avß6 expression levels in the patients' lungs, we will treat patients for 28 days, followed by a 3-day drug washout period. We will obtain a second, post-treatment PET scan following completion of dosing and washout to evaluate post-treatment avß6 expression levels. If prolonged PLN-74809 treatment is successful in causing downregulation of avß6, we would expect to see reduced PET ligand uptake in patient lungs post-treatment vs. baseline. Downregulation of avß6 expression would reflect effective inhibition of the TGF-ß signaling pathway in IPF patients by PLN-74809.



Design of four week Phase 2a IPF PET imaging trial

We plan to initiate our second Phase 2a randomized, double-blind, placebo-controlled IPF trial in the second half of 2019 evaluating up to three doses of PLN-74809 and enrolling approximately 40 IPF patients. This trial is planned to be initiated as a 4-week trial in a limited number of patients and transitioned into a 12-week trial once non-clinical data support longer term dosing. The primary endpoints for this trial will be safety and tolerability, as well as PK in IPF patients. We plan to evaluate exploratory endpoints including pulmonary function tests, biomarkers, and imaging.

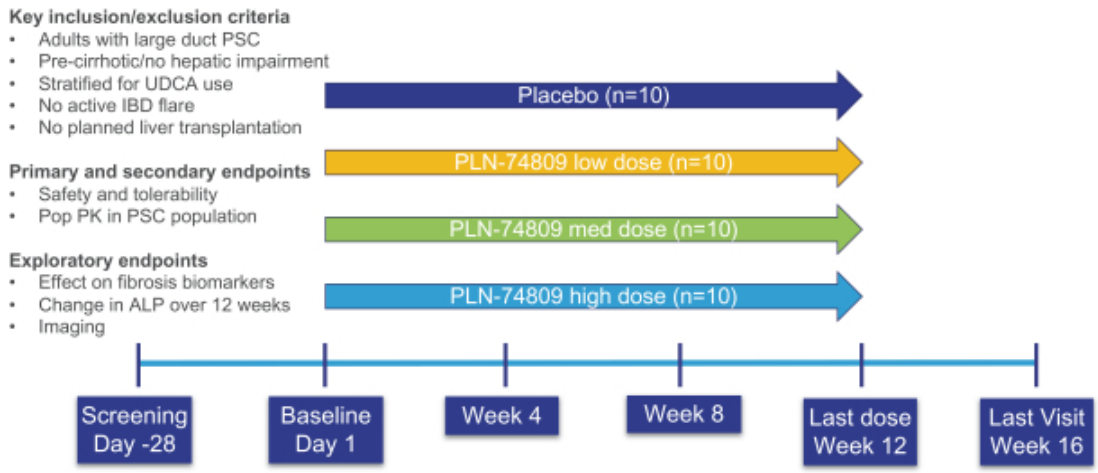
12 Week Safety, PK, Biomarker Trial in IPF Patients



Design of 12 week Phase 2a IPF trial

We plan to file an IND for PLN-74809 in PSC in the second half of 2019 and to initiate our third Phase 2a randomized, double-blind, placebo-controlled trial in PSC patients as soon as possible thereafter. We plan to utilize a similar approach to the previously described IPF study, initiating the trial with a 4-week duration in a limited number of patients and transitioning to a 12-week trial involving approximately 40 PSC patients, evaluating up to three doses of PLN-74809 or placebo. We expect the primary endpoints for this trial will be safety and tolerability, as well as PK. We will also employ exploratory endpoints including fibrosis biomarkers, change in liver function, and imaging.

12 Week Safety, PK, Biomarker Trial in PSC Patients



Design of 12 week Phase 2a PSC trial

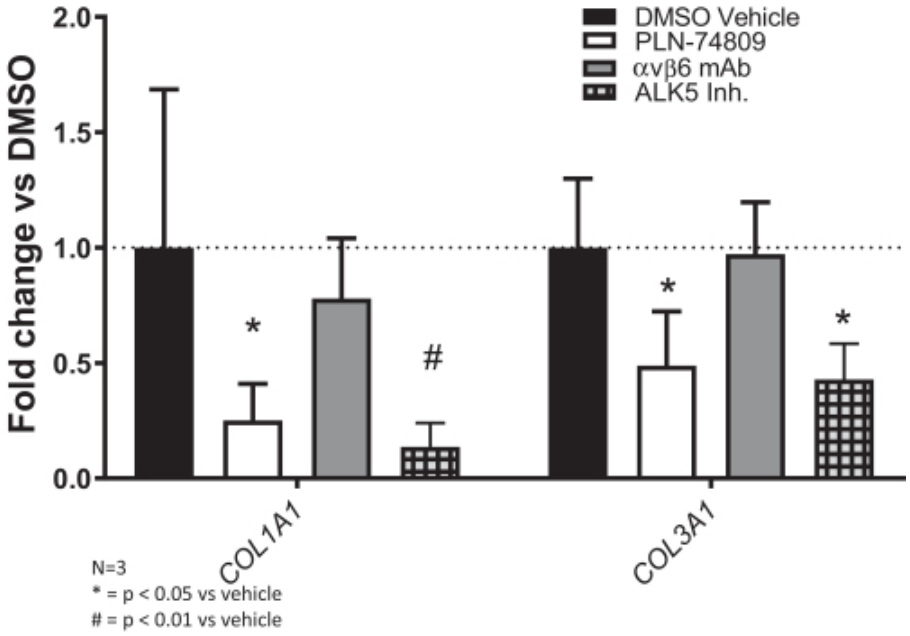
Preclinical data in IPF

Summary Preclinical Data in IPF	
Preclinical Findings	**Observations**
PLN-74809 reduced collagen gene expression in live human IPF lung tissue	• Greater than 50% decrease in expression of *COL1A1* and *COL3A1* relative to DMSO vehicle control • An antibody to avß6 did not significantly decrease expression
pSMAD3 was correlated with extractable collagen levels in patients suspected of having IPF	• pSMAD3 and extractable, or newly formed, collagen 1 were measured in biopsy samples from 18 patients and 5 controls. • pSMAD3 and extractable collagen 1 were correlated with an r value of 0.7807 ($p<0.0001$)
avß6 and avß1 expression is elevated in mouse bleomycin IPF models	• In both acute and chronic bleomycin IPF mouse models, expression of avß6 and avß1 integrins was higher in bleomycin exposed animals compared to healthy controls
Dual avß6 and avß1 inhibition decreased collagen more than avß6 or avß1 single inhibition in mouse chronic bleomycin precision cut lung slices	• Dual inhibition of avß6 and avß1 at 10x IC_{50} significantly decreased *Col1a1* expression relative to DMSO vehicle control • Single inhibition of either avß6 and avß1 at 10x IC_{50} did not show significant decrease in *Col1a1* expression
PLN-74809 showed a dose dependent reduction in collagen fiber density in a mouse bleomycin IPF model	• Three weeks of treatment with PLN-74809 utilizing second-harmonic generation resulted in a dose dependent decrease in collagen fiber density • Fibrous composite score was significantly reduced in a dose dependent manner vs. vehicle control
PLN-74809 decreased TGF-ß activation in chronic bleomycin mouse model	• After two weeks of treatment with PLN-74809 levels of pSMAD3 were significantly reduced compared to PBS vehicle control • Post-treatment pSMAD levels were similar to those of healthy controls
Inhibition of avß6 and avß1 blocked TGF-ß activation in the pulmonary cells of non-human primates	• After seven days of treatment with dual avß6 and avß1 inhibitor pSMAD2 levels were reduced by greater than 75% in pulmonary cells of non-human primates • An anti-avß6 antibody showed approximately 50% decrease • Dual inhibition showed a clear PK/PD relationship with maximal pSMAD suppression was achieved and maintained while drug concentrations were in the effective dose range (i.e., above the plasma protein adjusted IC_{50}, or p.a. IC_{50})
PLN-74809 binds to all conformations of avß6 and avß1 in biochemical assays	• PLN-74809 binds both bent-closed and extended-open conformations of avß6 and avß1 at below 2.0 nM concentrations

PLN-74809 reduced collagen gene expression in live human IPF lung tissue

In an assay using live lung tissue from a patient with IPF, application of PLN-74809 led to significant decrease in expression of *COL1A1* and *COL3A1*, two genes responsible for collagen production. The degree of inhibition observed with PLN-74809 was similar to the degree of inhibition resulting from complete blockade of

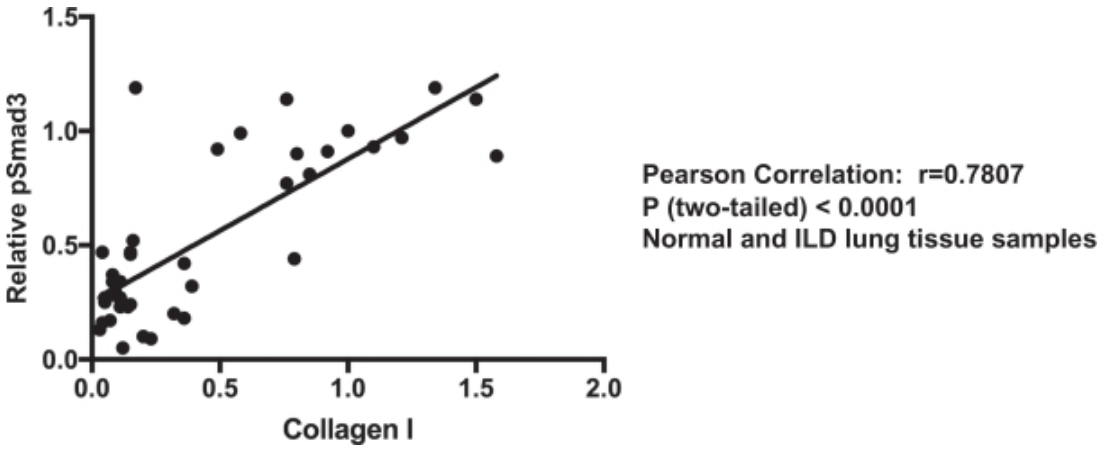
TGF-ß signaling using a direct inhibitor of its TGF-ß type I receptor kinase, also known as ALK5. In contrast, an avß6-specific monoclonal antibody, or mAb, that we synthesized based on publicly available information regarding Biogen's antibody, 3G9, was unable to significantly inhibit *COL1A1* or *COL3A1* expression.



Combined inhibition of avß6 and avß1 provided increased anti-fibrotic activity in live human fibrotic tissue as compared to DMSO vehicle control.

pSMAD3 was correlated with extractable collagen levels in patients suspected of having IPF

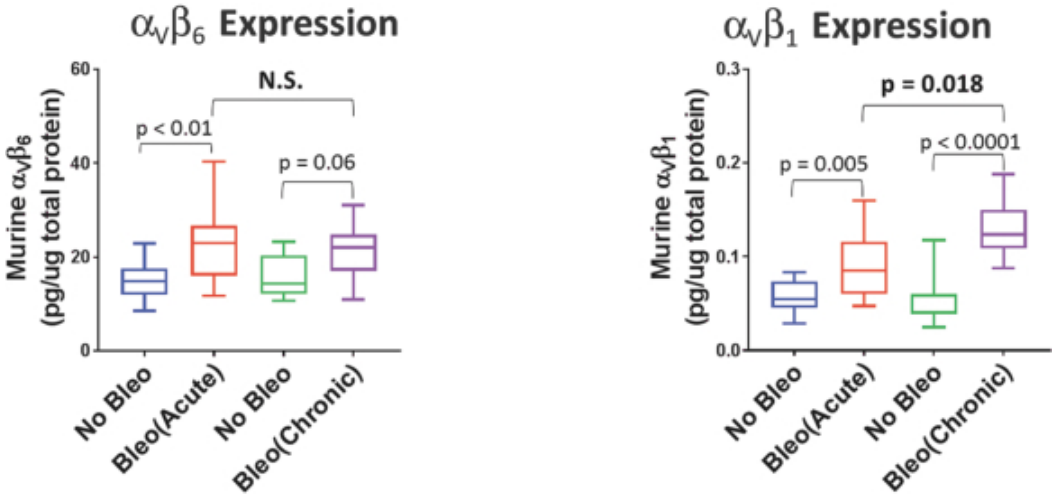
Open lung biopsies for histologic confirmation of IPF diagnosis were performed in 18 patients with interstitial lung disease, or ILD, who were suspected of having IPF. As part of this analysis, five controls (non-transplanted donor lungs) were also included. Multiple biopsies were taken from different lobes of each lung. Total pSMAD3 and extractable collagen 1 were measured by western blot. Extractable collagen 1 is thought to be collagen that has been recently formed and has not been cross-linked to the extracellular matrix. Total pSMAD3 and extractable collagen were significantly correlated. Higher pSMAD3 levels corresponded to higher levels of recently produced collagen.



pSMAD3 levels are correlated with extractable collagen in lung biopsies from patients suspected of having IPF

avß6 and avß1 expression is elevated in mouse bleomycin IPF model

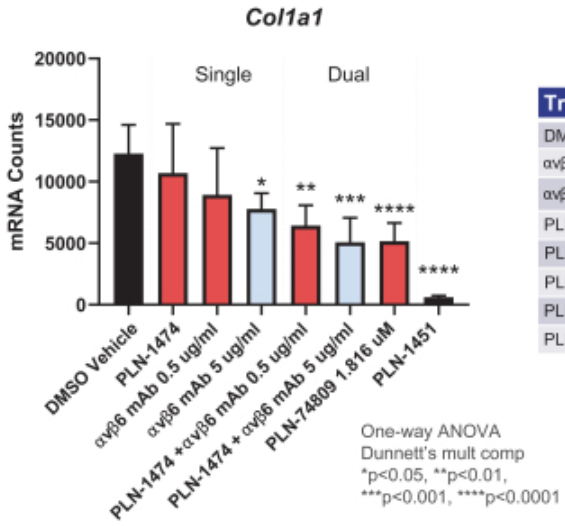
We used the increased expression of both avß6 and avß1 integrins in human disease samples to select animal models with similar characteristics which we then employed for higher-throughput and more extensive testing than would be feasible with primary human tissue. The bleomycin model is the most extensively used model of IPF due to its ability to reproduce many aspects of the disease. The pattern of expression of integrins suggests that the bleomycin model can serve as a valid preclinical surrogate for evaluating the effects of integrin inhibition in IPF. We confirmed that both avß6 and avß1 integrins are upregulated in a mouse model of pulmonary fibrosis induced by exposure to bleomycin. In both acute and chronic versions of this model, expression of avß6 and avß1 integrins were higher in bleomycin-exposed animals compared to healthy controls.



avß6 and avß1 expression in murine bleomycin model

Dual avß6 *and* avß1 *inhibition decreased collagen more than* avß6 *or* avß1 *single inhibition in mouse chronic bleomycin precision cut lung slices*

To further understand the anti-fibrotic effect of single vs. dual integrin inhibition in the murine chronic bleomycin model, we performed assays on precision cut lung slices from chronic bleomycin mouse lungs. We incubated the samples for seven days with either a single selective avß1 inhibitor (PLN-1474), a single selective avß6 inhibitor (avß6 mAb), or a dual selective avß6/avß1 inhibitor. Dual selective inhibition was accomplished with either PLN-74809 or a combination of PLN-1474 and the avß6 mAb. In this assay, we also compared against PLN-1451, an inhibitor of the TGF-ß receptor kinase ALK5, as a positive control. We measured effects on pro-fibrotic gene expression through the mRNA counts for *Col1a1*. PLN-1474, a single selective inhibitor of avß1, and the avß6 mAb, dosed at 10x their IC_{50}, failed to show a significant reduction in *Col1a1* expression. PLN-74809 showed a significant reduction in *Col1a1* expression that was similar to what was seen when PLN-1474 and the avß6 mAb were incubated as a combination therapy. We also evaluated gene expression across a broad panel of 17 additional pro-fibrotic genes. Similar to *Col1a1*, dual inhibition resulted in a greater reduction in gene expression across the panel versus single inhibition.



Treatment	Concentration	Inhibition
DMSO Vehicle		
αvβ6 mAb (10x IC_{50})	0.5 ug/ml	Single (αvβ6)
αvβ6 mAb (100x IC_{50})	5 ug/ml	Single (αvβ6)
PLN-1474	471.4 nM	Single (αvβ1)
PLN-1474 + αvβ6 mAb	471.4 nM + 0.5 ug/ml	Dual
PLN-1474 +αvβ6 mAb	471.4 nM + 5 ug/ml	Dual
PLN-74809	1.816 uM	Dual
PLN-1451	1 uM	ALK5

Dual avß6/avß1 inhibition blocked *Col1a1* expression more than single inhibition (avß6 or avß1) in chronic bleomycin lung slices

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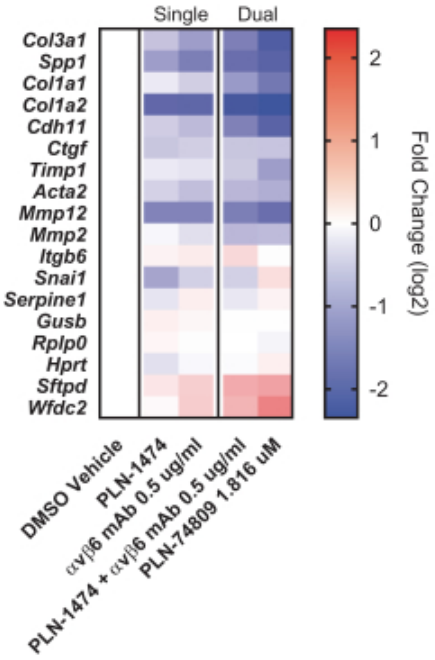
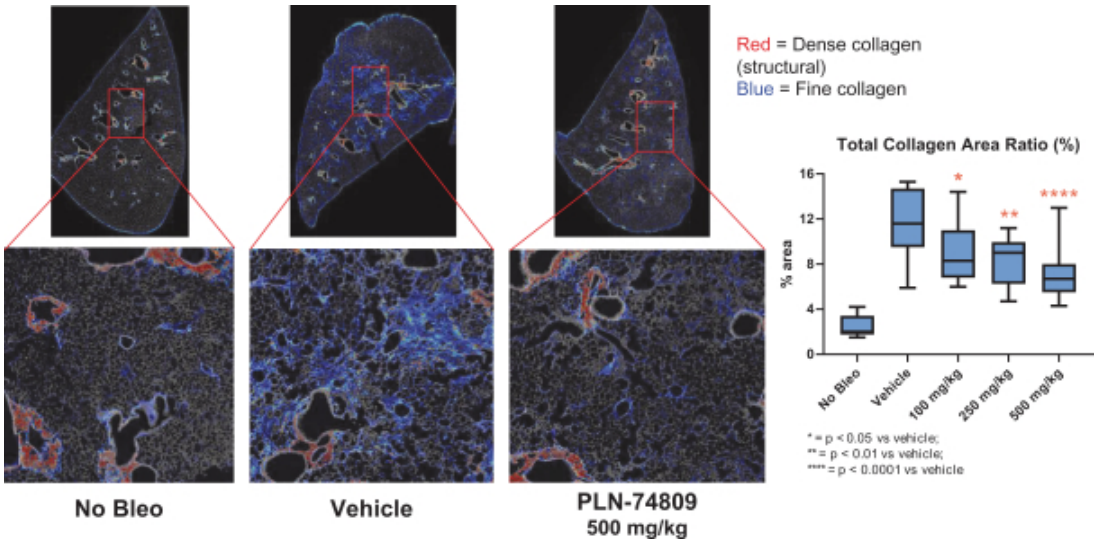


Treatment	Concentration	Inhibition
DMSO		
αvβ6 mAb (10x IC_{50})	0.5 ug/ml	Single (αvβ6)
PLN-1474	471.4 nM	Single (αvβ1)
PLN-1474 + αvβ6 mAb	471.4 nM + 0.5 ug/ml	Dual
PLN-74809	1.816 uM	Dual

Dual avß6/avß1 inhibition blocked profibrotic gene expression more than single inhibition (avß6 or avß1) in chronic bleomycin lung slices

PLN-74809 showed a dose-dependent reduction in collagen fiber density in a mouse bleomycin IPF model

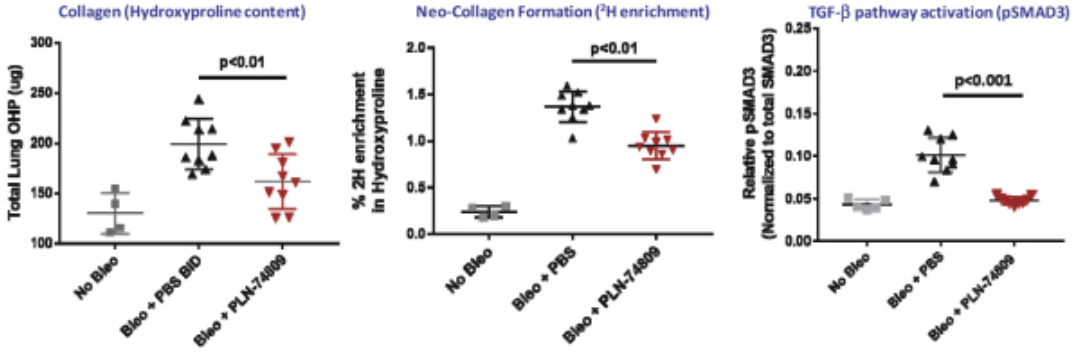
We evaluated three doses of PLN-74809 in a mouse bleomycin IPF model utilizing second-harmonic generation to evaluate the amount of new collagen formation ongoing post-treatment with PLN-74809. We evaluated 100 mg/kg, 250 mg/kg, and 500 mg/kg doses against vehicle control and saw a dose dependent reduction in collagen fiber density and fibrosis composite score.



PLN-74809 resulted in a dose-dependent decrease in collagen fiber density in a mouse bleomycin IPF model as measured through second-harmonic generation

PLN-74809 decreased TGF-ß activation in chronic bleomycin mouse model

We confirmed through biochemical analyses that anti-fibrotic efficacy of PLN-74809 in the bleomycin model was due to blockade of TGF-ß activation. A key biochemical marker of TGF-ß activation is the phosphorylation of SMAD2/3. In the bleomycin model, two weeks of treatment with PLN-74809 reduced pSMAD3 levels to those seen in control mice that had not been exposed to bleomycin in the acute IPF model. In addition, levels of newly formed collagen, or neo-collagen, and total lung hydroxyproline content were significantly reduced in the treatment group.

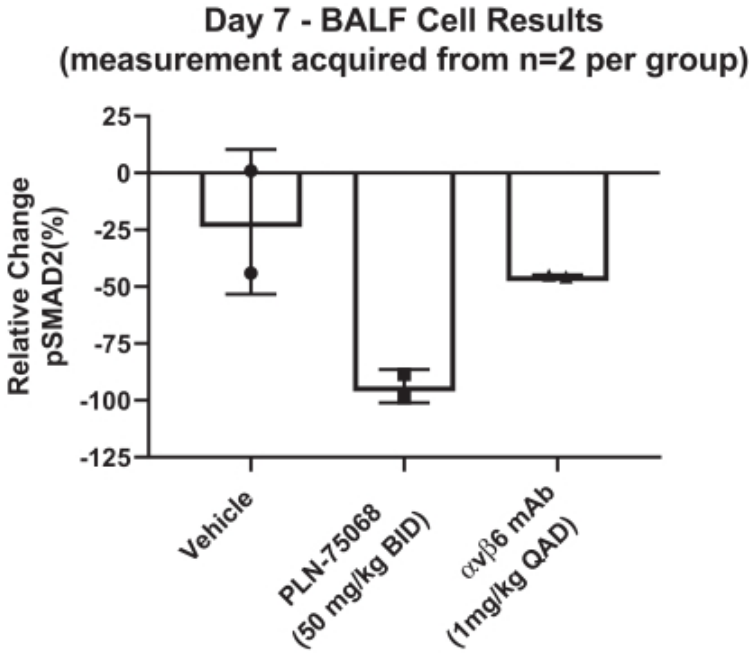


PLN-74809 blocked TGF-ß activation in a chronic bleomycin model

The ability to measure TGF-ß activation through SMAD phosphorylation also provided us with the opportunity to develop SMAD2/3 phosphorylation as a biomarker that correlates with avß6 and avß1 integrin inhibition.

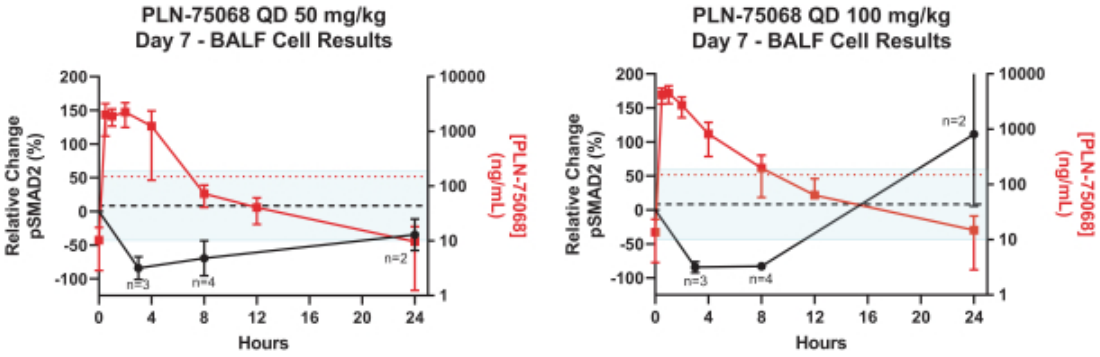
Inhibition of avß6 and avß1 blocked TGF-ß activation in the pulmonary cells of non-human primates

We conducted a non-human primate study to validate pSMAD as a biomarker for TGF-ß activation for future clinical studies. Given that this study will not be part of our regulatory package for our lead compound, PLN-74809, we used PLN-75068, a close analog to PLN-74809, with a similar binding and PK profile for this particular study. In the first stage of this study, we treated non-human primates with PLN-75068 at 50 mg/kg twice daily, or with the avß6 mAb at 1 mg/kg every other day for seven days. We performed BAL procedures on the monkeys pre- and post- treatment and measured pSMAD2 levels in the pulmonary macrophages. BAL fluid collected three hours after dosing showed a significant reduction of pSMAD2 levels when compared to pre-treatment levels. The avß6 mAb showed pSMAD2 level reduction as well, but the effect was less pronounced than for PLN-75068.



BID Dosing of PLN-75068 reduced pSMAD2 levels in non-human primate alveolar fluid

A second stage of this study was designed to evaluate the PK/PD relationship between PLN-75068 and the inhibition of TGF-ß activation. In this stage, we dosed monkeys at either 50 mg/kg or 100 mg/kg once a day for seven days. We designed the study to obtain multiple BAL measurements after the last treatment in order to understand how changes in the pSMAD2 levels relate to serum levels of PLN-75068. Dosing of PLN-75068 in non-human primates showed a decrease in the pSMAD2 levels at both doses. Soon after dosing, when drug concentrations were at their peak, the levels of pSMAD2 levels showed a reduction of more than 75 percent. As the drug concentration decreased, pSMAD2 levels gradually returned to baseline levels. Importantly, the 50 mg/kg and 100 mg/kg dosing groups resulted in similar levels of pSMAD2 level reduction; however, the 100 mg/kg dose stayed in the effective dose range longer, and therefore maintained pSMAD2 level reduction for a longer period.

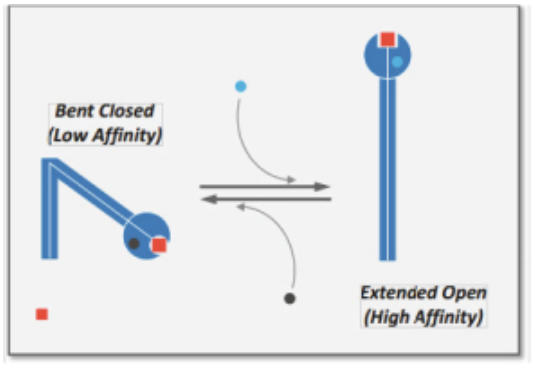


QD dosing of PLN-75068 reduced pSMAD2 levels

PLN-74809 binds to all conformations of avß6 *and* avß1 *in biochemical assays*

Integrins are cellular adhesion proteins having a high degree of structural flexibility with two predominant forms: an extended form with high affinity for binding to ligands, and a bent or closed form in which the ligand binding domain has low affinity for binding to ligands. The conformation of the integrin can also dramatically alter the binding of potential therapeutics such as antibodies.

Biochemical profiling of PLN-74809 confirms that it can inhibit both avß6 and avß1 integrins in both the high-affinity, extended open conformation as well as in the lower-affinity, bent closed conformation and thus has the potential to block integrin interactions regardless of the initial state of the receptor.



	Human Integrin	Conformation	Affinity, K_D (nM)
PLN-74809	$\alpha_v\beta_1$	Bent closed (Mg^{2+})	1.92
		Extended open (Mn^{2+})	0.075
	$\alpha_v\beta_6$	Bent closed (Mg^{2+})	1.32
		Extended open (Mn^{2+})	0.037

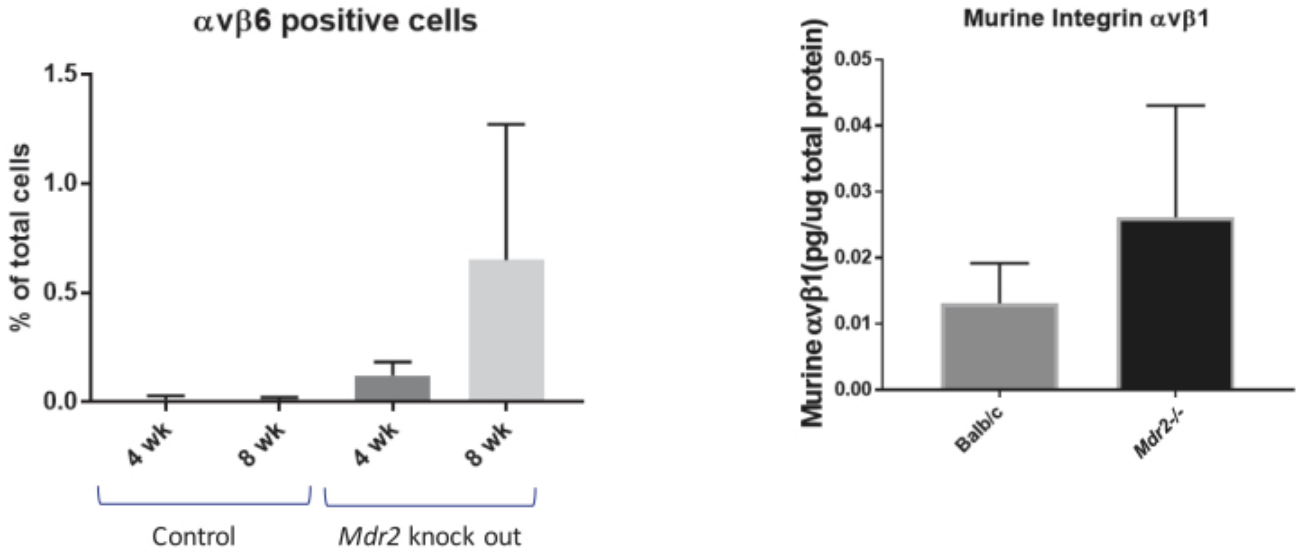
PLN-74809 binds to both high-affinity and low-affinity conformations of avß1 **and** avß6

Preclinical data in PSC

Summary Preclinical Data in PSC	
Preclinical Findings	**Observations**
avß6 and avß1 are overexpressed in human PSC liver tissue as well as a mouse model of PSC	• We confirmed that the widely used *Mdr2* knockout PSC mouse model shows upregulation of both avß6 and avß1, similar to our observations in diseased tissue from PSC patients
PLN-74809 showed a dose dependent reduction in fibrosis in a mouse PSC model	• Six weeks of treatment with PLN-74809 resulted in a significant dose-dependent reduction in fibrosis compared to vehicle treated mice • pSMAD3 levels were also significantly reduced in a dose-dependent manner
PLN-74809 reduced cholestasis markers in PSC model	• After six weeks of treatment with PLN-74809, at the highest dose tested, we observed a significant reduction of alkaline phosphatase and total bilirubin
Dual avß6 and avß1 inhibitor decreased *COL1A1* expression in human PSC liver tissue sample	• After two days incubation with a dual avß6 and avß1 inhibitor we observed a significant reduction in *COL1A1* gene expression in a live liver sample from a PSC patient after transplant

avß6 and avß1 are overexpressed in human PSC liver tissue as well as a mouse model of PSC

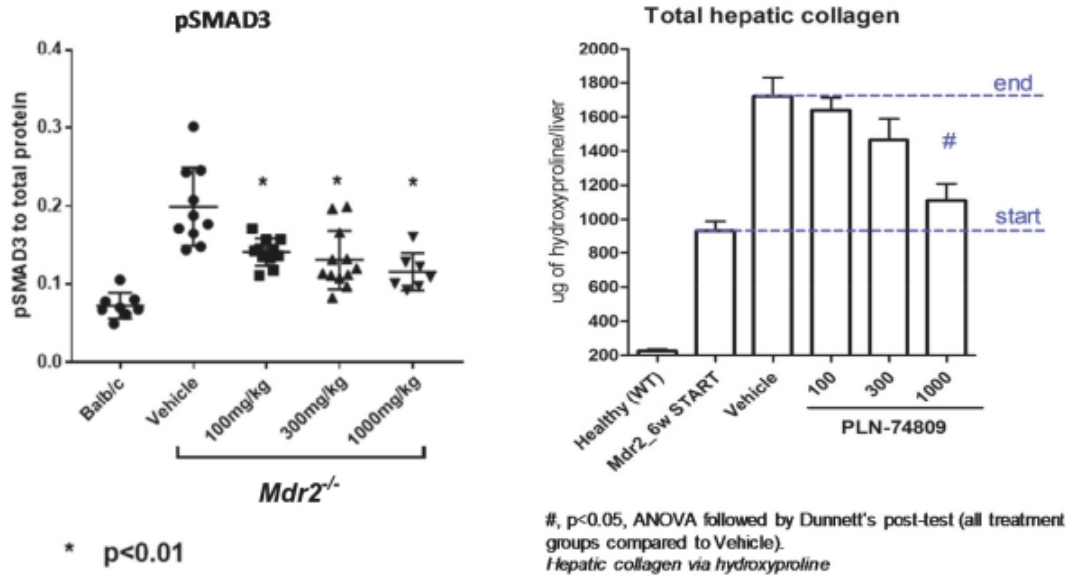
Similar to our approach in diseased tissue from an IPF patient, we examined the expression patterns of integrins in live, diseased tissue obtained from a patient with PSC. We found that both avß6 and avß1 integrins are overexpressed in these tissues. We then went to the standard animal model for PSC based on a deletion of the *Mdr2* gene in mice and confirmed that in this model both avß6 and avß1 are overexpressed compared to normal control mice.



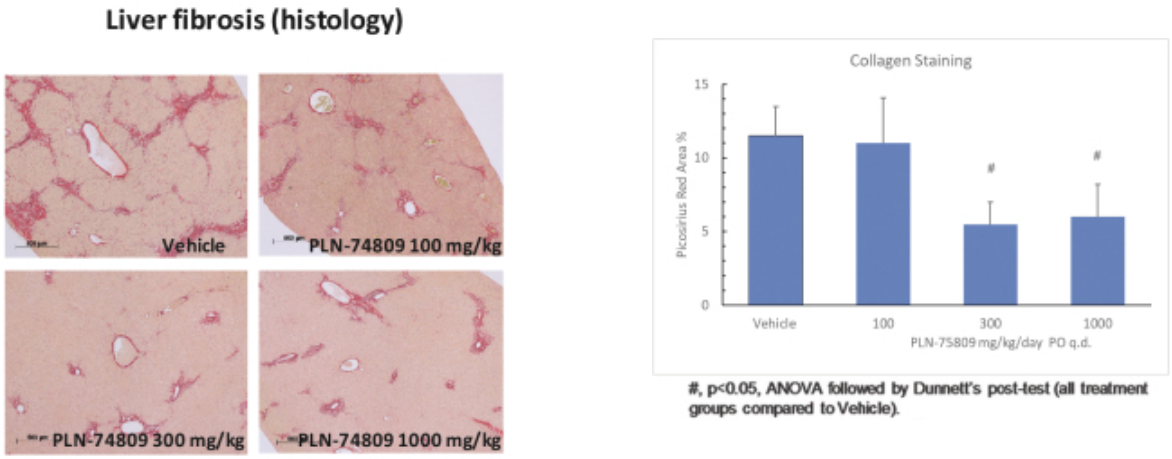
Both avß6 and avß1 are overexpressed in a *Mdr2* knockout model of PSC

PLN-74809 showed a dose dependent reduction in fibrosis in a mouse PSC model

In *Mdr2*-deficient mice that have developed biliary fibrosis resembling PSC, dosing with PLN-74809 for six weeks resulted in a significant, dose-dependent reduction in fibrosis compared to vehicle treated mice. Similar results were observed whether the analyses were based on collagen levels as measured by hydroxyproline, pSMAD3 levels or histological staining.



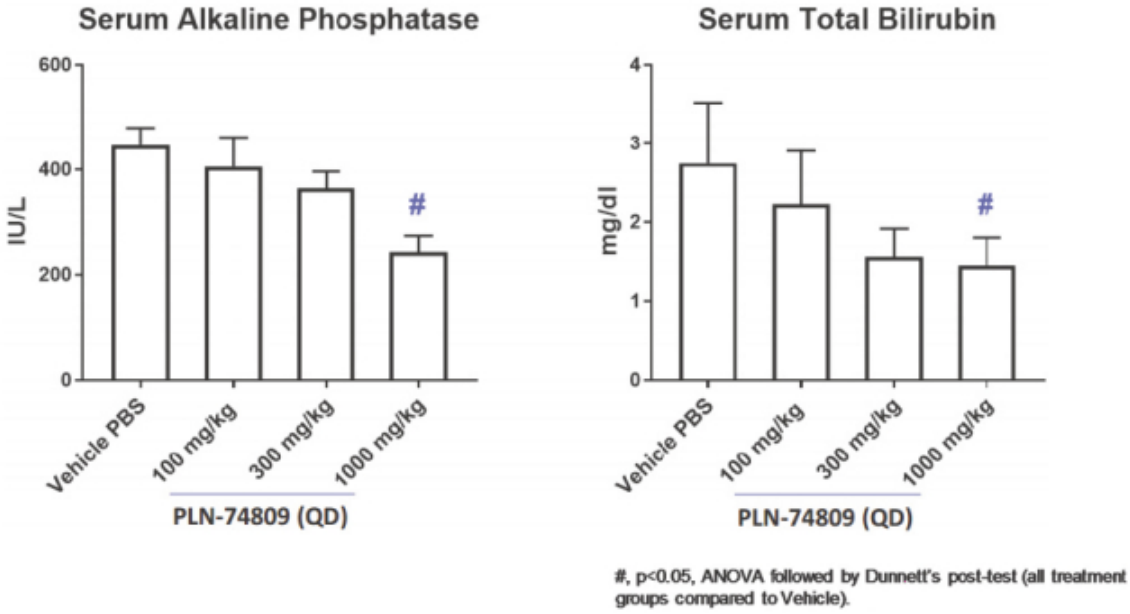
PLN-74809 showed reduction of fibrosis in the *Mdr2* deficient PSC model



PLN-74809 showed improved histology score in the *Mdr2* deficient PSC model

PLN-74809 reduced cholestasis liver biomarkers in PSC model

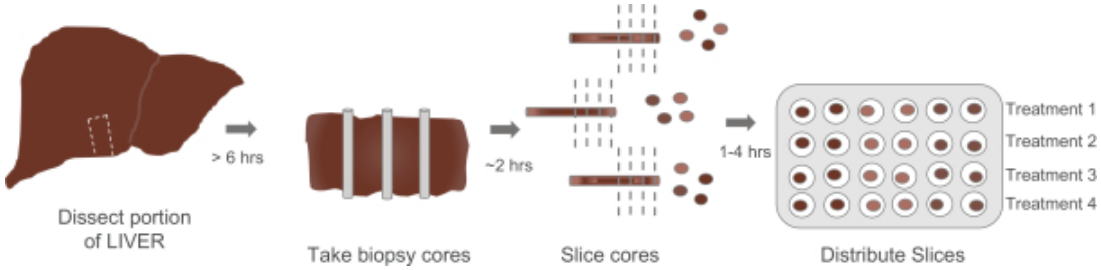
Treatment of *Mdr2*-deficient mice with PLN-74809 also reduced in a dose-dependent manner serum levels of alkaline phosphatase and total bilirubin compared to vehicle controls. Both are markers of cholestasis.



PLN-74809 reduced cholestasis markers in PSC model

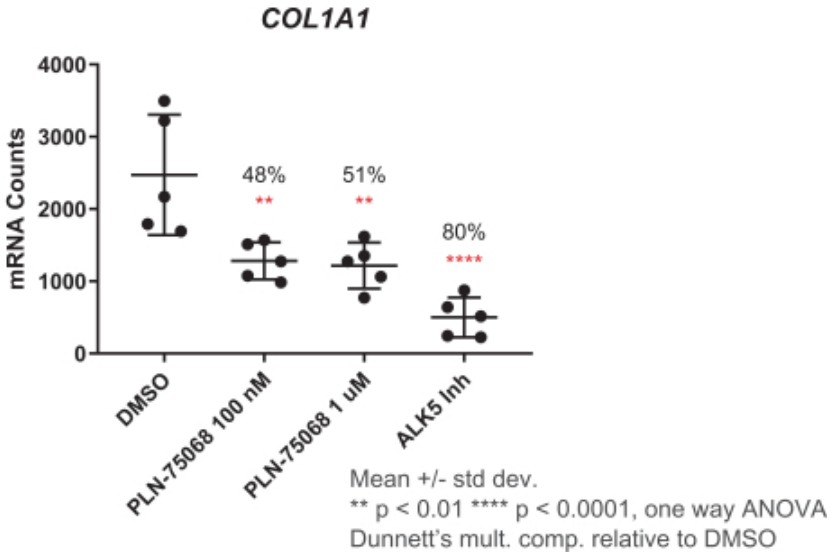
Dual avß6 and avß1 inhibitor decreased COL1A1 expression in human PSC liver tissue sample

We assessed the anti-fibrotic activity of our integrin inhibitors using liver samples obtained from a PSC patient. We used precision-cut tissue slices to establish *ex vivo* tissue culture samples that mimic the multicellular characteristics of organs. The use of these precision-cut tissue culture assays not only provides the opportunity to assess the effects of our compounds directly on diseased human tissue, but also allows this to be done in a three-dimensional, multicellular context that better represents the complexity of the diseased tissue environment.



Assessing anti-fibrotic activity of compounds in live human liver fibrosis tissue

In a tissue sample from a PSC patient, incubation for two days with PLN-75068, a structural analog of PLN-74809, led to a significant decrease of *COL1A1* expression.



PLN-75068 blocked fibrosis in live human PSC liver tissue

PLN-1474 for the treatment of liver fibrosis and NASH

PLN-1474 is a selective inhibitor of avß1 integrin that we are developing for the treatment of stage F3/F4 liver fibrosis in patients with NASH. PLN-1474 is an orally bioavailable inhibitor that has shown anti-fibrotic activity in multiple animal models of liver fibrosis as well as in live human NASH fibrotic liver tissue. We are completing IND enabling studies on PLN-1474 and anticipate filing an IND with the FDA by the end of 2019.

Background on liver fibrosis and NASH

NASH is a severe form of NAFLD that is associated with the development of liver fibrosis and potentially life-threatening liver dysfunction. NAFLD is characterized by increased amounts of fat in the liver, or steatosis. NAFLD is believed to occur due to a combination of factors including high caloric diet, obesity and metabolic syndrome, type 2 diabetes mellitus and genetics. Early stages of the disease often have no symptoms other than slightly elevated or fluctuating levels of liver enzymes in some patients.

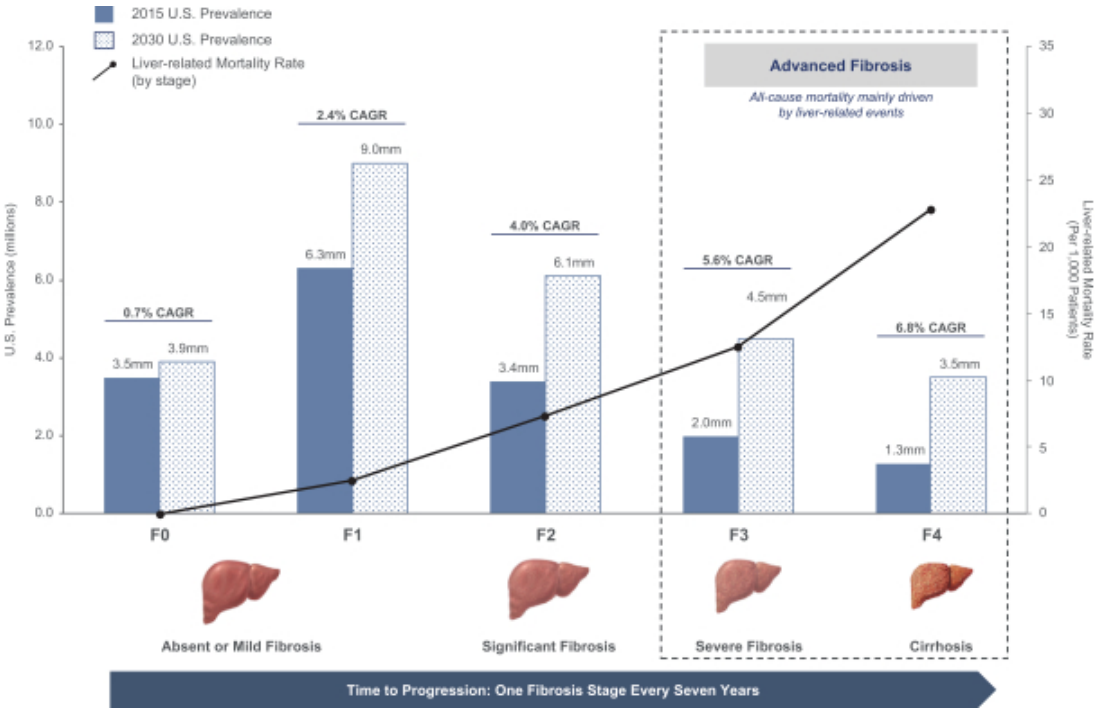
As excess fat builds up in the liver, it can eventually cause lipotoxicity, resulting in inflammation in the liver and leading to injury of hepatocytes, known as ballooning. It is this combination of steatosis, inflammation and hepatocellular ballooning that defines NASH. Over time, NASH can lead to fibrosis of the liver. Fibrosis can progress to cirrhosis, resulting in impaired liver function and increased risk of liver-related complications and mortality. In fact, liver fibrosis is an independent predictor of liver-related morbidity and all-cause mortality in NASH. There are currently no approved therapies for NASH, and to date investigational NASH therapies have only shown modest anti-fibrotic benefits in published clinical trials.

It is estimated that 30 to 40 percent of adults in the United States have NAFLD and approximately 30 percent of these patients, or up to 12 percent of adults, will develop NASH. NASH is already highly prevalent, affecting approximately 16.5 million adults in the United States with approximately 3.3 million at stage F3/F4 liver fibrosis. NASH is a growing problem with U.S. cases expected to top 27 million by 2030, with approximately eight million at stage F3/F4 liver fibrosis.

While NASH is becoming more common in the general population, identifying patients with increased risk of liver-related morbidity and mortality is important for clinical management. While steatosis, inflammation and

hepatocellular ballooning are the measures used to diagnose NASH, to date, the presence and severity of liver fibrosis is the only proven independent predictor of poor clinical outcomes in NASH. Cirrhosis associated with NASH is the fastest growing indication for liver transplantation in the United States.

Approximately 10 to 15 percent of NASH patients will ultimately progress to cirrhosis over time. On average, these patients advance one fibrosis stage every seven years. NASH patients, regardless of stage of fibrosis, have an estimated annual mortality rate of 1.5 to 3.5 percent per year, mostly due to cardiovascular complications. However, when patients progress to stage F2 fibrosis or greater, liver-related complications become the highest risk for mortality. Each progressive stage of fibrosis correlates to a dramatic increase in liver-related mortality risk. Moreover, patients with F3 and F4 fibrosis carry liver-related mortality risk that is 17 times and 42 times greater, respectively, than NASH patients without fibrosis. We believe treatments with a potent anti-fibrotic effect would be more likely to have a meaningful impact on clinical outcomes for NASH patients with F3 to F4 fibrosis.



Stages of liver fibrosis

There are currently no therapies approved for the treatment of NAFLD or NASH. Lifestyle changes and exercise to reduce body weight and treatment of concomitant diabetes and dyslipidemia comprise the cornerstone of treatment but are not sustainable in the majority of patients. For patients with cirrhosis, liver transplantation is the only potential treatment option, but transplant livers are not widely available, and only a minority of these patients will be eligible for a transplant due to the risks, costs and complexities associated with the procedure. NASH is the second leading indication for liver transplantation in the United States, but is also the most rapidly growing indication and is expected to eventually overtake alcoholic liver disease as the largest driver of liver transplant.

There are many candidates in development for the treatment of NASH that target various aspects of the disease. A number of these candidates are directed at reducing the underlying causes of the disease such as

obesity and diabetes or addressing fat accumulation in the liver by altering lipid metabolism. Other candidates are focused on suppressing the inflammatory stage of NASH with the intent of preventing the progression of fibrosis. To date, only modest improvements in liver fibrosis stage or severity have been reported with investigational compounds evaluated in patients with NASH. Our approach is to directly target the fibrosis pathway with the goal of preventing progression or reversing advanced fibrosis (F3/F4). Given TGF- ß's central role to fibrosis pathophysiology, we believe that directly targeting the TGF-ß activation pathway via avß1 integrin inhibition holds the potential to provide a more clinically meaningful anti-fibrotic effect than current investigational therapies, and ultimately prevent disease progression to cirrhosis and liver related complications.

Our solution, PLN-1474

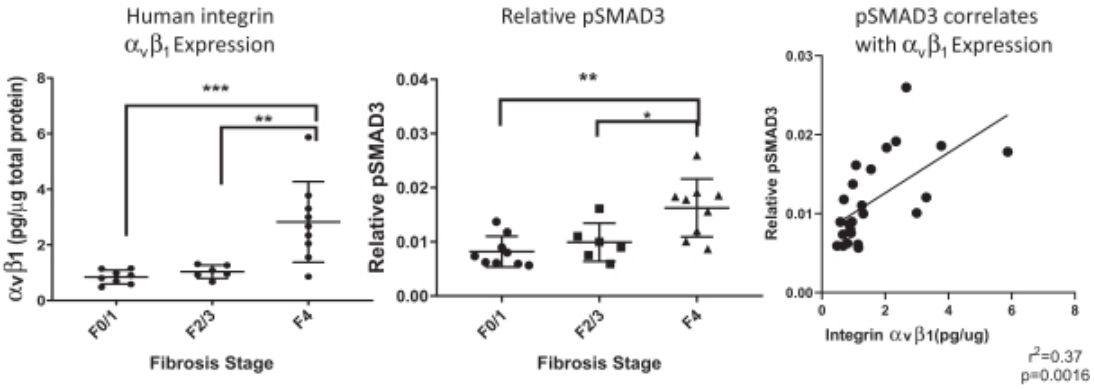
PLN-1474 is an orally bioavailable, small-molecule, selective inhibitor of avß1 mediated TGF-ß activation. We are developing PLN-1474 as an anti-fibrotic therapy for patients with F3/F4 stage liver fibrosis associated with NASH. We have shown that in human fibrotic liver tissue from patients with NASH that the levels of avß1 are significantly elevated in tissue from patients with stage 4 fibrotic disease. Overexpression of avß1 is correlated with TGF-ß activation as measured by pSMAD3 levels. Therefore, we believe a single-selective inhibitor of avß1 is a promising and differentiated approach to treating NASH related liver fibrosis. We are currently conducting IND-enabling studies and plan to submit an IND by the end of 2019.

Preclinical data

Summary of Preclinical Data in NASH	
Preclinical Findings	**Observations**
avß1 and TGF-ß activation are upregulated in human F4 NASH liver biopsies	• Levels of avß1 and pSMAD3 levels are both significantly elevated in tissues from patients with stage F4 liver fibrosis • Levels of avß1 and pSMAD3 levels are highly correlated in NASH liver biopsies
PLN-1474 is associated with anti-fibrotic activity in live human fibrotic NASH liver tissue	• After two days incubation with PLN-1474 we observed a significant reduction in *COL1A1* gene expression in live liver samples from three NASH patients after transplant • Gene expression of *TIMP1*, a strong predictor of mortality in patients with fibrosis, was also reduced after incubation
PLN-1474 resulted in a broad decrease in expression of pro-fibrotic genes in an abbreviated mouse model of NASH liver fibrosis	• In an abbreviated CDA-HFD mouse NASH model, after 3 weeks of treatment, mice treated with PLN-1474 showed decreased expression of a broad set of profibrotic genes relative to vehicle controls
PLN-1474 showed dose-dependent reduction of fibrosis in multiple NASH mouse models	• Six weeks of treatment with PLN-1474, resulted in a significant dose-dependent decrease in expression of *Col1a1* and *Col1a2* as well as hydroxyproline in a CDA-HFD NASH mouse model • After one week of treatment with PLN-1474, we observed significant dose-dependent reductions in *Col1a1*, *Col1a2* and *Col3a1* in a CCL_4 liver fibrosis mouse model
PLN-1474 decreased collagen fiber density and characteristics via 2nd harmonic generation analysis in a NASH fibrosis model	• Six weeks of treatment with PLN-1474 utilizing 2^{nd} harmonic generation, resulted in a dose-dependent decrease in collagen fiber density and fibrosis composite score in a CDA-HFD NASH mouse model
PLN-1474 potently binds to all conformations of avß1	• PLN-1474 binds both bent-closed and extended-open conformations of avß1 at concentrations below 1.1 nM

a*vß1 and TGF-ß activation are upregulated in human F4 NASH liver biopsies*

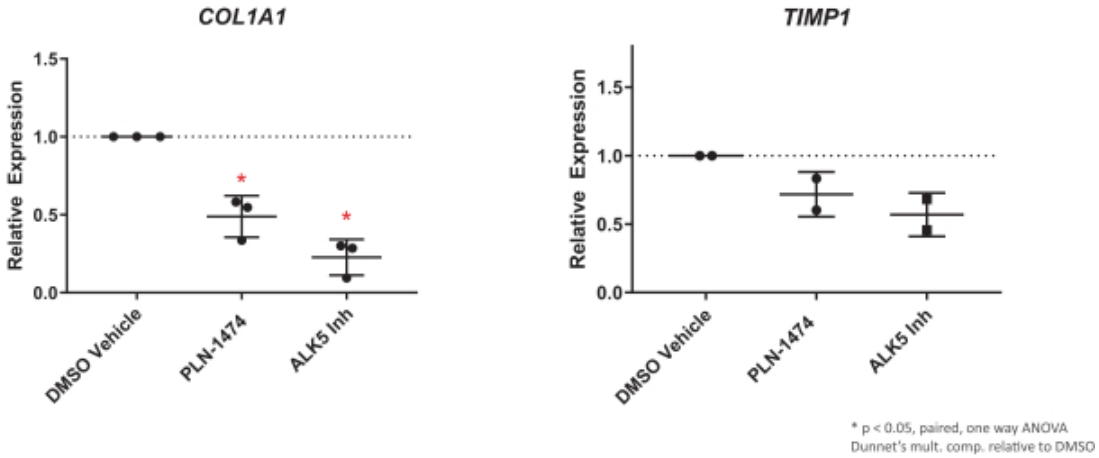
We measured avß1 protein expression and pSMAD3 levels in a group of late-stage liver fibrosis biopsies. In F4 biopsies, avß1 was significantly overexpressed relative to F0/F1 biopsies. Similarly, the pSMAD3 levels were also significantly elevated in F4 biopsies compared to F0/F1.



avß1 and pSMAD3 levels are both upregulated in F4 liver fibrosis

PLN-1474 is associated with anti-fibrotic activity in live human fibrotic NASH liver tissue

We assessed the anti-fibrotic activity of PLN-1474 in live human NASH liver tissue. Precision cut tissue slices from multiple F4 NASH livers treated with PLN-1474 exhibited a mean 50 percent reduction in the levels of *COL1A1* expression compared to vehicle treated controls. In the PLN-1474 treated tissue slices, we also saw a significant reduction in the gene expression of *TIMP1*, which encodes the tissue inhibitor of metallopeptidase, or TIMP-1. In a recent study, TIMP-1 was shown to be a strong predictor of all-cause mortality in patients with fibrosis. TIMP-1 is one of the three components of the Enhanced Liver Fibrosis, or ELF, score, a non-invasive clinical diagnostic test to assess the likelihood of having clinically significant fibrosis. These results suggest that selective inhibition of avß1 could have clinically meaningful anti-fibrotic activity in NASH patients with advanced fibrosis.

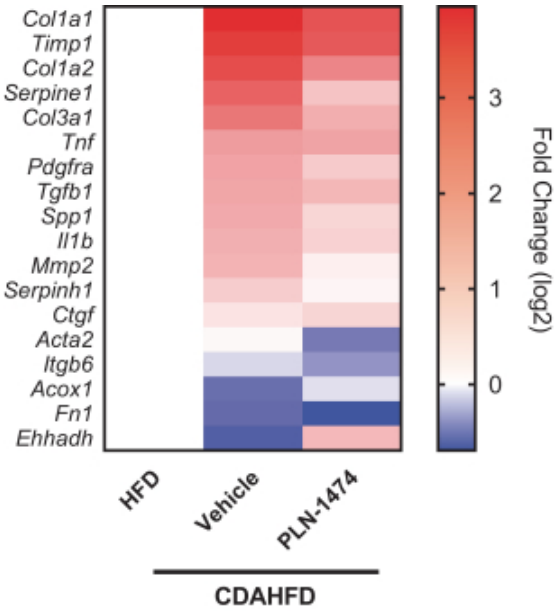


PLN-1474 significantly reduced *COL1A1* and *TIMP1* gene expression in human NASH liver tissue

PLN-1474 resulted in a decrease in expression levels of a broad panel of pro-fibrotic genes in an abbreviated mouse model of NASH liver fibrosis

Mice were treated prophylactically with PLN-1474 for 3 weeks at 30mg/kg BID in an abbreviated CDA-HFD mouse NASH fibrosis model. A broad panel of profibrotic genes showed decreased expression in mice treated with PLN-1474 relative to mice that were treated with a vehicle control.

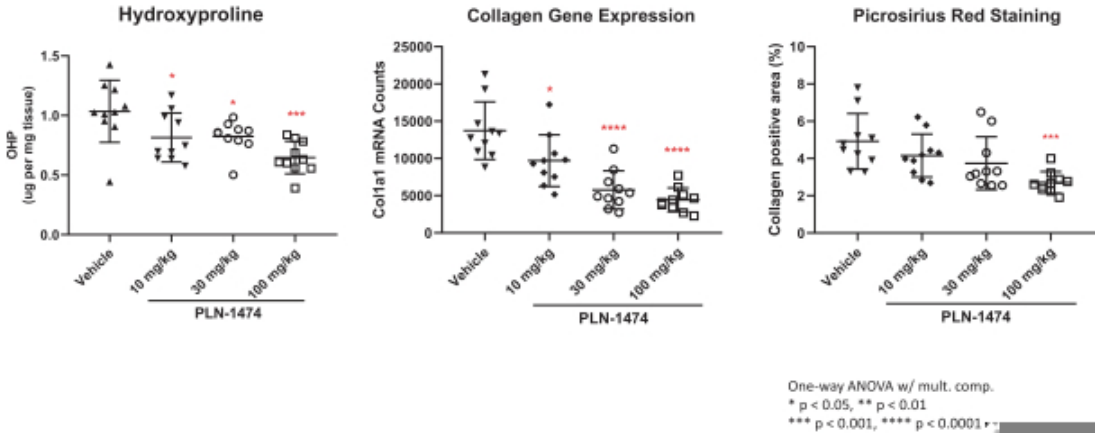
Profibrotic Gene Expression After Treatment with PLN-1474



Treatment with PLN-1474 resulted in decreased expression of a broad set of profibrotic genes in a CDA-HFD mouse NASH liver fibrosis model

PLN-1474 showed dose-dependent reduction of fibrosis in multiple NASH mouse models

We tested the ability of PLN-1474 to inhibit fibrosis in a mouse model of NASH induced by a choline-deficient high fat diet. Treatment of these mice for six weeks, beginning at week five of the high fat diet, resulted in a dose-dependent reduction in collagen production as measured by hydroxyproline levels compared to vehicle-treated controls. Similar dose-dependent decreases in the expression of *Col1a1* genes and picrosirius red staining, a histologic marker for fibrosis, were observed after treatment with PLN-1474. Treatment with PLN-1474 also led to decreases in pSMAD3 levels indicating that PLN-1474 was able to block TGF-ß activation.



PLN-1474 inhibits fibrosis in NASH fibrosis model

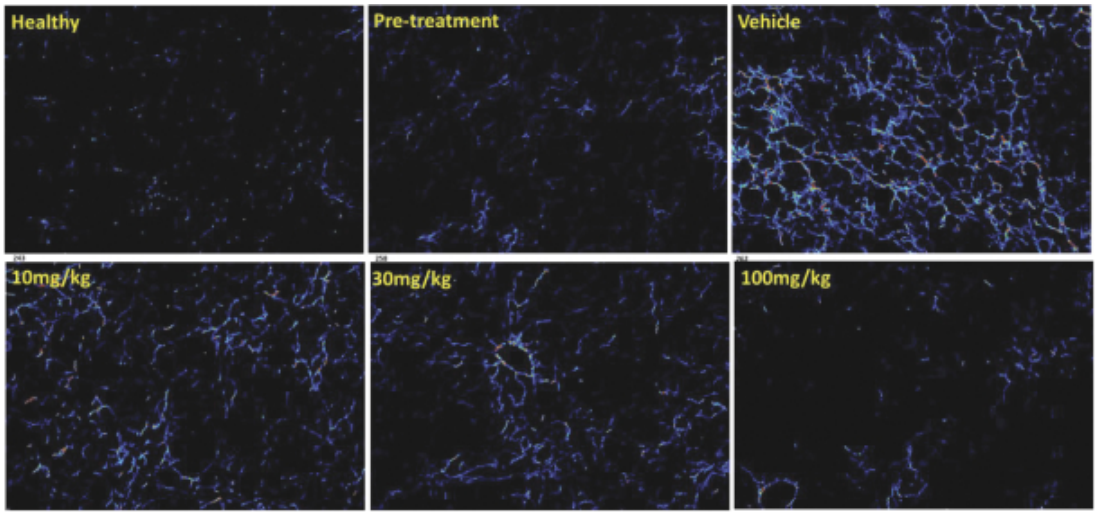
PLN-1474 also inhibited fibrosis in an acute CCl_4 model of liver fibrosis. In this model, liver fibrosis in mice is induced by two weeks of exposure to CCl_4. Treatment with PLN-1474 for one week reduced the expression of *Col1a1*, C*ol1a2* and *Col3a1* compared to vehicle-treated controls. Treatment with PLN-1474 also reduced TGF-ß signaling to baseline levels as measured by pSMAD3 levels.

In the chronic version of the CCL_4 model, fibrosis is induced by 21 days of exposure to CCl_4. Treatment of these mice with PLN-1474 resulted in significant reductions in the expression of collagen genes beginning as soon as two hours after dosing. These results suggest that PLN-1474 has the potential to lead to significant and rapid changes in fibrosis even in livers containing extensive and established fibrotic lesions.

PLN-1474 inhibited collagen expression in a chronic CCl_4 liver fibrosis model

PLN-1474 decreased collagen fiber density and characteristics via second-harmonic generation analysis in a NASH fibrosis model

We evaluated three doses of PLN-1474 in a NASH fibrosis mouse model utilizing second-harmonic generation to evaluate the amount of new collagen formation ongoing post-treatment with PLN-1474. We evaluated 10mg/kg, 30mg/kg and 100mg/kg doses against placebo in a NASH fibrosis model and saw a dose-dependent reduction in collagen fiber density and fibrosis composite score.



PLN-1474 resulted in a dose-dependent decrease in collagen fiber density in a NASH fibrosis model as measured through second-harmonic generation

PLN-1474 potently binds to all conformations of avß1

Similar to our observations with PLN-74809, we have shown that PLN-1474 binds to both the higher-affinity, extended open conformation of integrin avß1 as well as the lower-affinity, bent closed conformation and thus has the potential to block integrin interactions regardless of the state of the receptor.

	Human Integrin	Conformation	Affinity, K_D (nM)
PLN-1474	$\alpha_v\beta_1$	Bent closed (Mg^{2+})	1.10
		Extended open (Mn^{2+})	0.33

PLN-1474 binds to both the extended open and bent closed conformations of avß1 **and** avß6

Planned clinical development of PLN-1474

We are completing IND-enabling studies for PLN-1474 and anticipate filing an IND by the end of 2019. Our initial clinical trials will be conducted in healthy volunteers where we intend to conduct dose-escalation and evaluate safety and tolerability and PK. Initial testing in NASH patients may also include assessment of avß1 expression in the liver using a specific PET ligand and to assess treatment effects via this method.

Applying our fibrosis expertise in developing additional products

We are pursuing potential uses of our existing product candidates, PLN-74809 and PLN-1474, in additional fibrotic indications. We use our precision cut human fibrotic tissue assays in addition to our animal model data to inform our clinical development programs and potentially select additional indications where we think our pipeline candidates could have an effect.

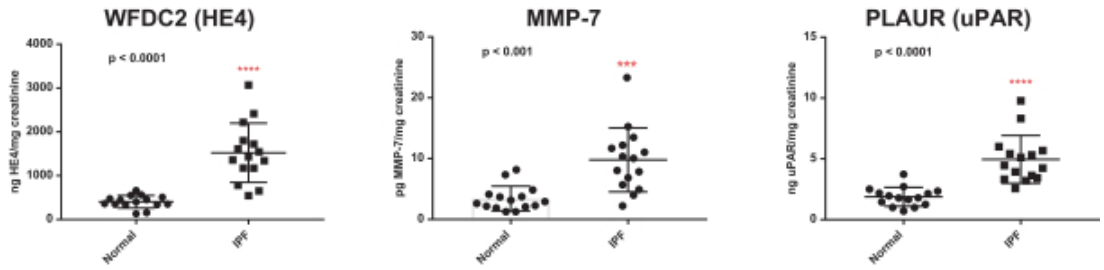
Our mission is to advance the understanding of fibrosis by building a biology-, chemistry- and screening-based engine to drive drug development across the spectrum of fibrotic diseases. While our initial focus is on

small-molecule integrin inhibitors in lung and liver fibrosis, we are actively pursuing additional treatment modalities across fibrosis indications in multiple different organs. We have identified other potential non-integrin targets related to TGF-ß signaling as well as other pathways across multiple fibrosis indications, such as regulators of epithelial-to-mesenchymal transition, a critical process in fibrosis. In addition, while our initial focus is on small-molecule drug candidates, we are agnostic to treatment modalities in the development of our pipeline.

Our biomarker discovery engine

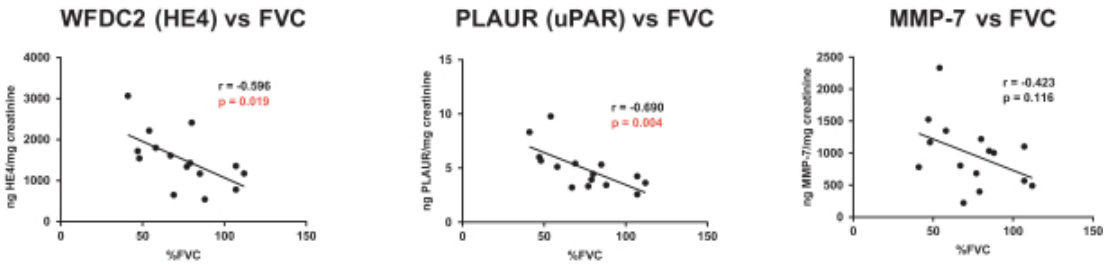
We are developing an extensive biomarker discovery and validation program. We are seeking to develop biomarkers in order to (i) identify patients at high risk of rapid disease progression, (ii) identify those more likely to respond to treatment and (iii) monitor early treatment responses. We are conducting clinical studies and other research with leading academic centers to track disease progression and collect biological samples such as blood, urine, and tissue biopsies which we can use to discover and validate novel biomarkers.

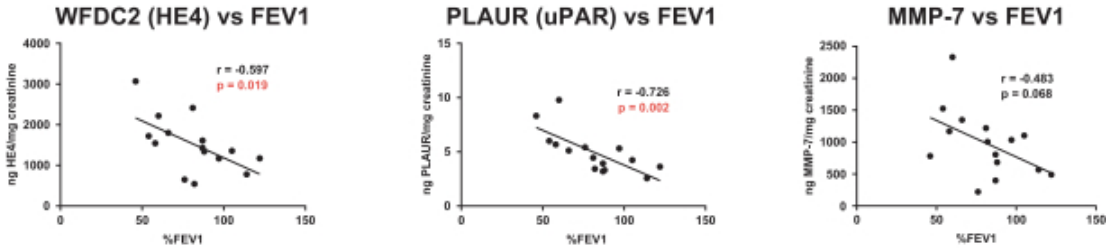
An example of our efforts is the discovery of potential biomarkers for IPF derived from urine and plasma samples. We discovered two novel biomarkers: WFDC2 and PLAUR. We compared these biomarkers to MMP-7, a widely recognized IPF biomarker. All three biomarkers were elevated in a set of urine samples from IPF patients compared to healthy controls.



Potential biomarkers identified in urine samples from IPF patients

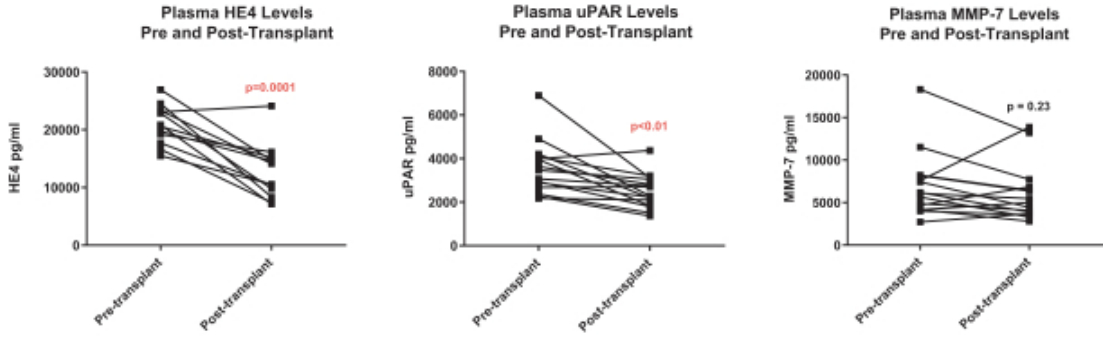
Further support for the potential importance of our novel biomarkers is that their expression levels were highly correlated with reduced lung function in IPF patients while MMP-7 was not. Patients with poor lung function as measured by forced expiratory volume, or FEV_1, or by FVC, have elevated levels of these biomarkers while patients with good lung function do not.





Urine biomarkers of IPF correlate with reduced pulmonary function

We also measured these three biomarkers in urine samples from a cohort of 15 IPF patients who underwent lung transplantation. Levels of our novel biomarkers were significantly reduced following transplant.



Plasma biomarkers of IPF pre- and post-transplant

This data indicates that our biomarkers may be effective in tracking treatment response. We plan to further validate these biomarkers, which will ultimately support our development programs.

Competition

The biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies, strong competition and an emphasis on proprietary products. While we believe that our technology, knowledge, experience and scientific personnel provide us with competitive advantages, we face substantial competition from many different sources, including larger pharmaceutical companies with greater resources. Smaller specialty biotechnology and biopharmaceutical companies, academic research institutions, governmental agencies, as well as public and private institutions are also potential sources of competitive products and technologies, including through collaborative arrangements with large and established biopharmaceutical companies. We also face competition in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and enrolling patients for clinical trials, and acquiring technologies complementary to, or necessary for, our programs. We believe that the key competitive factors affecting the success of any of our product candidates will include efficacy, safety profile, convenience, method of administration, cost, level of promotional activity and intellectual property protection.

There are currently a number of companies targeting the treatment of various fibrosis indications through inhibiting various parts of the TGF-ß pathway, including Biogen Inc., AbbVie Inc., Gilead Sciences, Inc., Indalo Therapeutics, Inc., FibroGen Inc., Galapagos NV, Bristol Myers Squibb Co., or BMS, and Novartis AG. However, we know of no other companies currently in clinical development with an orally bioavailable small-molecule, selective integrin inhibitor.

Although our novel approach is unique from most other existing or investigational therapies across the disease areas where we are focusing our development, we will need to compete with currently approved therapies, and potentially those in currently in development if they are approved. We are aware of several marketed and investigational products in our leading disease areas, including but not limited to:

- *IPF:* There are currently two approved products for the treatment of IPF; Esbriet, marketed by Roche Holding AG, and Ofev, marketed by Boehringer Ingelheim GmbH. Other companies currently developing product candidates in IPF include Biogen, AbbVie, Galapagos, Indalo, Kadmon Holdings, Inc., Prometic Life Sciences, Inc. and Promedior, Inc.
- *PSC*: There are currently no approved therapies for the treatment of PSC. Companies currently developing product candidates in PSC include Gilead, Allergan plc, NGM Biopharmaceuticals, Inc., or NGM, Intercept Pharmaceuticals, Inc. and CymaBay Therapeutics, Inc.
- *NASH:* There are currently no FDA approved therapies for the treatment of NASH. There are a number of companies developing product candidates for the treatment of NASH including Intercept, Pfizer Inc., Gilead, Allergan, Novartis, AstraZeneca plc, Eli Lilly & Company, GlaxoSmithKline plc, Amgen, Inc., BMS, Johnson & Johnson, Merck & Co., Inc., Roche, Sanofi S.A., Takeda Pharmaceuticals, Novo Nordisk, Genfit SA, Madrigal Pharmaceuticals, Inc., Viking Therapeutics, Inc., Cirius Therapeutics, Inc., NGM, Akero Therapeutics, Inc., Conatus Pharmaceuticals Inc., Metacrine, Inc. and CymaBay. Most of the drugs currently in development for NASH are focused on decreasing liver fat or improving liver inflammation as opposed to direct liver anti-fibrotic approaches.

The availability of reimbursement from government and other third-party payors will also significantly affect the pricing and competitiveness of our product candidates, if approved for marketing. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we do, which could result in our competitors establishing a strong market position before we are able to enter the market.

Research and Development Expenses

For the years ended December 31, 2017 and 2018, we had research and development expenses of $14.5 million and $24.4 million, respectively.

Intellectual Property

Overview

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to the development of our business, including seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets relating to our proprietary technology platform and on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen, and maintain our proprietary position in the field of fibrosis that may be important for the development of our business. We additionally may rely on regulatory protection afforded through data exclusivity, market exclusivity, and patent term extensions, where available.

Our commercial success may depend in part on our ability to: obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell, or importing our products may depend on the extent to which we have rights under valid and enforceable licenses, patents, or trade secrets that cover these activities. In some cases, enforcement of these rights may depend on third party licensors. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing

patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same.

As of May 1, 2019, we own or license nineteen pending patent applications, worldwide, including in the United States and corresponding foreign patent applications. At least four pending patent applications have been filed in the United States or corresponding foreign jurisdictions by or on behalf of the Regents of the University of California, which have granted us exclusive license rights to the technology. To date, two patents have issued to us or to our licensors. Our policy is to file patent applications to protect technology, inventions and improvements to inventions that are commercially important to the development of our business. We seek United States and foreign patent protection for a variety of technologies, including: research compounds and methods, candidate compounds and antibodies for modulating the activity of integrins, methods for treating diseases of interest, and methods for manufacturing our products. We also intend to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel products. We seek protection, in part, through confidentiality and proprietary information agreements. We are a party to various other license agreements that give us rights to use specific technologies in our research and development.

Company Owned IP

We own multiple families of patent applications that are directed to small-molecule compositions capable of modulating integrins and methods for treating or preventing diseases associated with integrins. Certain applications in these families relate to our PLN-1474 and PLN-74809 small-molecule product candidates, backup compounds and structural analogs, various unit dosages, dosing regimens, and routes of administration. We are also pursuing innovative ways to modulate integrin function using antibodies, and have one pending patent application to that technology in the United States. Patents that may issue from these company owned applications are generally expected to expire between the years 2037 to 2040, subject to possible patent term adjustment and/or extension.

Licensed IP

We have obtained an exclusive license from the Regents of the University of California to two patent families, which are expected to expire in 2034 and 2036, respectively, subject to possible patent term adjustment and/or extension. Included in these families are two issued U.S. patents with claims directed to small-molecule integrin inhibitors and methods of using such inhibitors for treating fibrotic and other diseases, as well as related patent applications that are pending in Canada, Europe, and Hong Kong.

Trademark Protection

We have registered trademarks for use in connection with our products. We may pursue additional registrations for future products in markets of interest.

Trade Secret Protection

Finally, we may rely, in some circumstances, on trade secrets to protect our technology. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

In addition to the above, we have established expertise and development capabilities focused in the areas of preclinical research and development, manufacturing and manufacturing process development, quality control, quality assurance, regulatory affairs, and clinical trial design and implementation. We believe that our focus and expertise will help us develop products based on our proprietary intellectual property.

License Agreements

Adimab Collaboration Agreement

In October 2018, we entered into a collaboration agreement, or the Adimab Agreement, with Adimab, LLC, or Adimab, for the discovery and optimization of proprietary antibodies as potential therapeutic product candidates. Under the Adimab Agreement, we have initially agreed with Adimab to collaborate on an initial research program. In addition, we may select up to three additional biological targets against which Adimab will use its technology to research and develop antibodies pursuant to a mutually agreed upon research plan.

During the ongoing research period and for a specified evaluation period thereafter, or the Evaluation Term, Adimab will grant us a worldwide, non-exclusive license to Adimab's technology to perform our responsibilities under the specified research plan and to evaluate the program antibodies to determine, at our election, how to proceed with any antibodies discovered as a result of such research program.

On a research program by research program basis, Adimab has granted to us an exclusive option to acquire the rights to up to a certain specified number of discovered antibodies for development and commercialization as biopharmaceutical products. We have also granted Adimab a non-exclusive, non-sublicensable license under our technology during each research program, and during the relevant Evaluation Term solely to perform Adimab's responsibilities under such research plan.

Upon execution of the Adimab Agreement we paid to Adimab a one-time, non-creditable non-refundable technology access fee. For each agreed upon research program that is commenced, we are required to pay Adimab an agreed upon rate for its full-time employees during a given research program, a specified discovery delivery fee, and an optimization completion fee.

If we choose to exercise our option with respect to a specific research program, we are required to pay Adimab a non-creditable, non-refundable high six-figure option exercise fee, payable in installments. If we exercise our option with respect to more than the specified number of antibodies resulting from such research program, we are obligated to make an additional specified payment for each additional optioned antibody. To date, we have not exercised any options under the Adimab Agreement.

We are required to make certain milestone payments to Adimab upon the achievement of certain clinical and regulatory milestone events in the development of therapeutic products and diagnostic products which use the antibodies we have obtained pursuant to our exclusive option. The milestone payments total approximately $12 million for each therapeutic product. For any product that is commercialized pursuant to the Adimab Agreement, we are required to pay Adimab low single digit percentage tiered royalty payments based on annual aggregate worldwide net sales thresholds for such products, subject to reduction as specified in the Adimab Agreement. Royalty terms with respect to each product will expire on a country-by-country basis upon the later of (a) ten years after the first commercial sale of such product in such country and (b) the expiration of the last patent related to any antibody acquired by us pursuant to our option from a specified research program.

Under the Adimab Agreement, we are required to use commercially reasonable efforts to conduct certain research to discover and optimize antibodies directed against the targets that we select. The Adimab Agreement will expire unless earlier terminated (a) in the event that we do not exercise any option pursuant to a research program, upon the conclusion of the last to expire Evaluation Term, or (b) if we do exercise an option, on the expiration of the last royalty term for a product in a particular country. We have the right to terminate the Adimab Agreement at any time upon advance written notice to Adimab. In addition, subject to certain conditions, either we or Adimab may terminate the Adimab Agreement if the other party commits a material breach of the agreement and fails to cure such breach within a specified cure period after written notice is provided. Upon expiration or termination of the Adimab Agreement, all licenses granted to us on a product-by-product and country-by-country basis will continue on a non-exclusive, fully-paid, worldwide, royalty-free, irrevocable basis.

Manufacturing

Our product candidates, PLN-74809 and PLN-1474, are small molecule inhibitors amenable to standard oral formulation technologies. We have validated the synthetic process and manufactured large kilogram quantities similar to the campaigns that will be required to provide drug product for our anticipated Phase 2a clinical trials. The manufacturing process of the drug substance for such product candidates is robust and accessed from readily available starting materials. The synthetic route is amenable to large-scale production and does not require unusual equipment or handling during the manufacturing process. We have obtained an adequate supply chain of the drug substance for PLN-74809 and PLN-1474 from our first North American contract manufacturing organization, or CMO, to satisfy both our clinical and preclinical requirements in 2019. We rely on a sole supplier for the manufacture of PLN-74809. We are engaging secondary raw material suppliers in addition to North American and European CMOs to mitigate global supply chain risk and ensure continuity of supply of drug substance. To maximize flexibility, we have established relationships with non-overlapping vendors for manufacturing of not only raw materials but also drug substance.

We currently rely on third-party manufacturers for the GMP production of larger quantities of our drug product candidates for our clinical trials. Our internal personnel have extensive cGMP manufacturing experience in order to ensure seamless technology transfer and to manage the manufacturing and development processes conducted by third-party manufacturers. Our agreements with third-party manufacturers include confidentiality and intellectual property provisions as well as routine quality audits. In some instances, we have reserved resources from third-party manufacturers for the development and manufacture of our product candidates for near-term clinical programs.

We do not own or operate facilities for clinical drug manufacturing, storage, distribution or quality testing. Currently, all of our clinical manufacturing is outsourced to third-party manufacturers. As our development programs expand and we build new process efficiencies, we expect to continually evaluate this strategy with the objective of satisfying demand for our clinical trials and, if approved, the manufacture, sale and distribution of commercial products.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. government regulation of drug products

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending New Drug Applications, or NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- Completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;

- Submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- Approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug product for each indication;
- Submission to the FDA of an NDA;
- Satisfactory completion of an FDA advisory committee review, if applicable;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- Satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- Payment of user fees and securing FDA approval of the NDA; and
- Compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to initiate.

Clinical trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it initiates at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Marketing approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA, for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. An Agreed Initial Pediatric Study Plan requesting a waiver from the requirement to conduct clinical studies has been submitted to the FDA.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and

provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will be receiving orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan indication or disease as long as the

products contain different active ingredients. Moreover, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

U.S. marketing exclusivity

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an Abbreviated New Drug Application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for a NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for the original non-modified version of the drug. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing regulatory exclusivity periods. This six-month exclusivity may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued “Written Request” for such a trial.

Post-approval requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There are continuing, annual user fee requirements for any marketed products and the establishments where such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product’s safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval of a drug or medical device is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- Restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- Fines, warning letters or holds on post-approval clinical trials;
- Refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- Product seizure or detention, or refusal to permit the import or export of products; and
- Injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs or devices may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Furthermore, on May 10, 2019, the Centers for Medicare and Medicaid Services announced a new pricing transparency rule, which goes into effect on July 9, 2019. This final rule requires direct-to-consumer television advertisements for prescription drugs and biological products for which reimbursement is available, directly or indirectly, through or under Medicare or Medicaid to include the list price of that product, except for a prescription drug or biological product that has a list price of less than $35 per month for a 30-day supply or typical course of treatment. The pricing transparency rule could have a negative effect on our business.

Other healthcare laws

Healthcare providers, physicians, and third party payors play a primary role in the recommendation and prescription of drug products for which we obtain marketing approval. Arrangements with third party payors, healthcare providers and physicians, in connection with the clinical research, sales, marketing and promotion of products, once approved, and related activities, may expose a pharmaceutical manufacturer to broadly applicable fraud and abuse and other healthcare laws and regulations. In the United States, these laws include, without limitation, state and federal anti- kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below:

- the federal Anti-Kickback Statute, or AKS, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer or pay any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, that is intended to induce or reward, referrals including the purchase recommendation, order or prescription of a particular drug for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal civil and criminal false claims laws and civil monetary penalty laws, including the False Claims Act, which impose criminal and civil penalties, including through civil “qui tam” or “whistleblower” actions, against individuals or entities for, among other things, knowingly presenting, or

causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation.

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act, created under Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the Centers for Medicare and Medicaid Services, or CMS, under the Open Payments Program, information related to payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of a pharmaceutical manufacturer's business activities could be subject to challenge under one or more of such laws. Efforts to ensure that business arrangements comply with applicable healthcare laws involve substantial costs. It is possible that governmental and enforcement authorities will conclude that a pharmaceutical manufacturer's business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against a pharmaceutical manufacturer, and it is not successful in defending itself or asserting its rights, those actions could have a significant impact on its 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, integrity and oversight agreements to resolve allegations of non-compliance, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of operations, any of which could adversely affect a pharmaceutical manufacturer's ability to operate its business and the results of operations. In addition, commercialization of any drug product outside the United States will also likely be subject to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Current and future healthcare reform legislation

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system. In particular, in 2010 the ACA was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and provided incentives to programs that increase the federal government's comparative effectiveness research.

There have been a number of significant changes to the ACA and its implementation. The Tax Cuts and Jobs Act of 2017, or Tax Act, includes a provision that repealed effective January 1, 2019 the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. Multiple state Attorneys General filed suit to stop the administration from terminating the subsidies, but their case was dismissed by a federal judge in California on July 18, 2018. Moreover, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-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, also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Similarly, on April 9, 2018, CMS issued a final rule that will give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces by relaxing certain requirements for essential health benefits required under the ACA for plans sold through such marketplaces. Moreover, in July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA 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 ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. 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.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in 2013,

and, due to subsequent legislative amendments, will remain in effect through 2027 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Legislative and regulatory proposals, and enactment of laws, at the foreign, federal and state levels, directed at containing or lowering the cost of healthcare, will continue into the future.

Rest of World Regulation

For other countries outside of the European Union and the United States, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Additionally, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Additionally, to the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

Coverage and reimbursement

Successful commercialization of new drug products depends in part on the extent to which reimbursement for those drug products will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drug products they will pay for and establish reimbursement levels. The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford a drug product. Sales of drug products depend substantially, both domestically and abroad, on the extent to which the costs of drugs products are paid for by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drug products. In many countries, the prices of drug products are subject to varying price control mechanisms as part of national health systems. In general, the prices of drug products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for drug products, but monitor and control company profits. Accordingly, in markets outside the United States, the reimbursement for drug products may be reduced compared with the United States.

In the United States, the principal decisions about reimbursement for new drug products are typically made by CMS, an agency within the HHS. CMS decides whether and to what extent a new drug product will be covered and reimbursed under Medicare, and private payors tend to follow CMS to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists among third-party payors and coverage and reimbursement levels for drug products can differ significantly from payor to payor.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under

Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each Part D prescription drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for drugs for which we obtain marketing approval. Any negotiated prices for any of our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the average manufacturer price, or AMP, and Medicaid rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although under the current state of the law these newly eligible entities (with the exception of children's hospitals) will not be eligible to receive discounted 340B pricing on orphan drugs. As 340B drug pricing is determined based on average manufacturer price, or AMP, and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase. The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures are made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our drug candidates, if any such drug or the condition that they are intended to treat are the subject of a trial. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's drug could adversely affect the sales of our drug candidate. If third-party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our drugs on a profitable basis.

These laws, and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Outside of the United States, the pricing of pharmaceutical products and medical devices is subject to governmental control in many countries. For example, in the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost effectiveness of a particular therapy to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. Other countries may allow companies to fix their own prices for products, but monitor and control product volumes and issue guidance to physicians to limit prescriptions. Efforts to control prices and utilization of pharmaceutical products and medical devices will likely continue as countries attempt to manage healthcare expenditures.

Employees

As of March 31, 2019, we had 48 full-time employees, including 21 with Ph.D. or M.D. degrees and 37 are engaged in research and development activities. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Facilities

We lease a facility containing 32,974 square feet of laboratory and office space, which is located at 260 Littlefield Avenue, South San Francisco, California 94080. The lease expires on February 28, 2025. We believe that our current facilities are sufficient to meet our current and near-term needs and that, should it be needed, suitable additional space will be available.

Legal Proceedings

As of the date of this prospectus, we are not party to any material legal matters or claims. We may become party to legal matters and claims arising in the ordinary course of business. We cannot predict the outcome of any such legal matters or claims, and despite the potential outcomes, the existence thereof may have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

MANAGEMENT

Executive Officers and Directors

The following table sets forth certain information about our executive officers and directors, including their ages as of May 1, 2019.

Name	Age	Position(s)
Executive Officers:		
Bernard Coulie, M.D., Ph.D.	53	President, Chief Executive Officer and Director
Hans Hull	44	Chief Business Officer
Éric Lefebvre, M.D.	55	Chief Medical Officer
Keith Cummings, M.D., MBA	42	Chief Financial Officer
Barbara Howes	54	Chief Human Resource Officer
Non-Employee Directors:		
Hoyoung Huh, M.D., Ph.D.(3)	49	Lead Director
Suzanne Bruhn, Ph.D.(2)	55	Director
John Curnutte, M.D.(2)	67	Director
Neil Exter(2)	60	Director
Charles Homcy, M.D.(3)	70	Director
Kevin Raidy	50	Director
Smital Shah(1)	43	Director

(1) Member of the Audit Committee.
(2) Member of the Compensation Committee.
(3) Member of the Nominating and Corporate Governance Committee.

Executive Officers

Bernard Coulie, M.D., Ph.D., MBA, has served as our Chief Executive Officer and as a Director since February 2016. Prior to joining us, Dr. Coulie cofounded ActoGeniX N.V., a biopharmaceutical company, and held roles of increasing responsibility there, including as Vice President R&D, Chief Medical Officer and Chief Executive Officer, from September 2006 until February 2015, when it was acquired by Intrexon Corporation. Prior to cofounding ActoGeniX, Dr. Coulie held various positions with increasing responsibilities in drug discovery and clinical development at Johnson & Johnson Pharmaceutical Research and Development Europe. Dr. Coulie previously served as a director of ActoGeniX from April 2010 until February 2015, Biogazelle N.V. from July 2015 until November 2018, Myoscience from June 2016 until March 2019. Dr. Coulie is currently serving as a director and Chairman of Calypso BV. Dr. Coulie holds a M.D. and Ph.D. from the University of Leuven, Belgium and a MBA from the Vlerick Management School, Leuven, Belgium. We believe that Dr. Coulie is qualified to serve on our board of directors based on our review of his experience and expertise in operations management and executive leadership at various biopharmaceutical companies.

Hans Hull, J.D., has served as our Chief Business Officer since March 2016. Prior to joining us, Mr. Hull held roles of increasing responsibility at Avalanche Biotechnologies, Inc., a biopharmaceutical company, from March 2011 until December 2015, including as Vice President, Legal and Corporate Development, Senior Vice President, Business Operations and interim President and Chief Executive Officer. Prior to Avalanche, from May 2008 to December 2011, he served as a legal and business development consultant for life sciences companies, including Second Genome, Inc., a biotechnology company, and Aprecia Pharmaceuticals, a pharmaceutical company. Mr. Hull was also the Chief Executive Officer of Orthobond Corporation, a medical device startup from March 2005 to April 2008. Mr. Hull also had an earlier career as an intellectual property attorney at Heller Ehrman LLP and life science consultant at ZS Associates. He holds an A.B. in Chemistry from Princeton University and a J.D. from the University of California, Berkeley.

Éric Lefebvre, M.D., has served as our Chief Medical Officer since May 2018. Prior to joining us, Dr. Lefebvre served as the Vice President of Allergan plc, a global pharmaceutical company, from November 2016 until April 2018. Prior to Allergan, Dr. Lefebvre served as Chief Medical Officer of Tobira Therapeutics, Inc., a clinical-stage biopharmaceutical company, from January 2012 until November 2016. Dr. Lefebvre also led global clinical development and global medical affairs at Janssen Pharmaceuticals for 10 years prior to starting his pharmaceutical career at GlaxoSmithKline Canada. This was preceded by 15 years of providing primary care at Clinique Medicale L'Actuel in Montreal, Canada. He holds a B.S. in Health Sciences from Edouard-Montpetit College and a M.D. from the University of Montreal.

Keith Cummings, M.D., MBA, has served as our Chief Financial Officer since December 2018. Prior to joining us, Dr. Cummings served as Director in the Investment Banking Healthcare Group at Citigroup Global Markets from September 2014 until December 2018. Prior to joining Citigroup, Dr. Cummings worked at Lehman Brothers and subsequently, as the Vice President, Investment Banking Barclays Investment Bank from August 2009 to September 2014. He holds a B.S. in Biochemistry from North Carolina State University, a MBA from Duke University's Fuqua School of Business and a M.D. from Duke University School of Medicine.

Barbara Howes has served as our served as our Chief Human Resource Officer since May 2019. Prior to joining us, Ms. Howes worked full time in consulting full-time in October 2014 where she served as the interim Head of Human Resources for several biotechnology companies, including Pliant prior to joining us full time. Ms. Howes has over 20 years' experience designing and delivering creative and impactful human resources, leadership development and change management solutions with a focus on optimizing organizational performance in the areas of innovation, collaboration, culture and strategy. Prior to founding her consulting practice in October 2014, Ms. Howes led the executive and organization development, career & learning, diversity, and workforce research teams at Genentech from June 2008 through October 2014. Prior to joining Genentech, Ms. Howes spent 12 years at The Walt Disney Company, where she held various development positions at The Disney Stores, Walt Disney Imagineering, and Corporate. She holds a B.A. in Liberal Arts from Mount Saint Mary's College and a MBA with an emphasis in Organizational Behavior from California Lutheran University.

Non-Employee Directors

Hoyoung Huh, M.D., Ph.D., has served as Lead Director of our board of directors since December 2017. He is the founder of pH Pharma and Healthcare & Humanity Foundation. Dr. Huh was a Managing Director of Konus Advisory Group, Inc. from January 2012 to September 2014. Prior to founding Konus Advisory Group, Inc., Dr. Huh was Chief Executive Officer and Chairman of the board of directors of BiPar Sciences, Inc. from February 2008 until December 2010. In addition, Dr. Huh has been involved in the formation, management and board positions of multiple biotechnology and innovation-based companies. He previously served as the Chairman of the board of directors of Geron Corporation from September 2011 to December 2018, and CytomX Therapeutics, Inc. from February 2012 to December 2018, a member of the board of directors of Rezolute, Inc. (f/k/a AntriaBio, Inc.) from 2013 to January 2019, the Chairman of the board of directors of Epizyme, Inc., and as a member of the board of directors of Facet Biotech Corporation, Nektar Therapeutics, Inc., Addex Therapeutics Ltd. and EOS, S.p.A (Milano, Italy). Earlier in his career, Dr. Huh was a partner at McKinsey & Company. He holds A.B. in Biochemistry from Dartmouth College, a M.D. from Cornell University Medical College and a Ph.D. in Cell Biology and Genetics from Cornell University Sloan Kettering Institute. We believe Dr. Huh is qualified to serve on our board of directors based on his significant leadership experience in and familiarity with the biopharmaceutical industry.

Suzanne Bruhn, Ph.D., has served as a member of our board of directors since July 2016. Dr. Bruhn currently serves as President and Chief Executive Officer of Tiaki Therapeutics, a preclinical biotechnology company, since May 2019. Prior to that, Dr. Bruhn served as President and Chief Executive Officer of Proclara Biosciences, Inc, a clinical-stage biotechnology company, from April 2017 until September 2018. Prior to Proclara, Dr. Bruhn served as President and Chief Executive Officer of Promedior, Inc., a private clinical-stage

biotech company developing targeted therapies to treat diseases involving fibrosis, from May 2012 until November 2015. She currently also serves on the board of directors of Aeglea BioTherapeutics, Inc, a publicly traded biotherapeutics company, from February 2017 and Novelion Therapeutics, Inc, a publicly traded pharmaceutical company, from October 2017. She previously served as a member of the board of directors of Raptor Pharmaceuticals Corp., a publicly traded pharmaceutical company, from April 2011 until it was acquired by Horizon Pharma plc in October 2016. She holds a B.S. in Chemistry from Iowa State University and a Ph.D. in Chemistry from Massachusetts Institute of Technology and completed her postdoctoral fellowship in the department of human genetics at Harvard Medical School. We believe Dr. Bruhn is qualified to serve on our board of directors based on her expertise and experience in the biopharmaceutical industry, including her expertise in the development of treatments for rare diseases and diseases involving fibrosis.

John Curnutte, M.D., Ph.D., has served as a member of our board of directors since August 2017. Since February 2011, Dr. Curnutte has served as Executive Vice President of Research and Development at Portola Pharmaceuticals, Inc., a biopharmaceutical company developing product candidates for thrombosis and other hematologic diseases. Prior to that, Dr. Curnutte served as the Chief Executive Officer of 3-V Biosciences, Inc., a biotechnology company. Earlier in his career, he served as a President of Schering-Plough Biopharma and previously held several senior management positions at Genentech, Inc., a biotechnology company. Prior to Genentech, Dr. Curnutte was a tenured faculty member at The Scripps Research Institute, pursuing basic and clinical research in inflammation biochemistry and the molecular genetics of congenital immune deficiencies. He is currently an adjunct clinical professor of pediatrics at Stanford University School of Medicine and a member of the medical staff, where he continues to consult on patients with primary immunodeficiencies. He also currently serves as a member of the board of directors of diaDexus, Inc., a company focused on cardiovascular diagnostics, since February 2015. Dr. Curnutte holds a B.S. in Biochemistry and Molecular Biology from Harvard University and a M.D. and a Ph.D. in Biological Chemistry from Harvard Medical School. We believe Dr. Curnutte is qualified to serve on our board of directors based on his experience in the biopharmaceutical industry, including his operational experience in drug discovery and development.

Neil Exter, MBA, has served as a member of our board of directors since June 2015. He has been a partner at Third Rock Ventures since November 2007. Mr. Exter has more than 30 years of business development, strategy and operating management experience, across the spectrum of emerging and established biotech and technology companies. Mr. Exter is currently the interim chief business officer of Cedilla Therapeutics. Prior to joining Third Rock Ventures, Mr. Exter was CBO of Alantos Pharmaceuticals and led the sale of that company to Amgen. Previously, he served as Vice President of Business Development for Millennium Pharmaceuticals. Mr. Exter presently is a board member of Element Science, Goldfinch Bio, Pliant Therapeutics, Revolution Medicines, Celsius Therapeutics and Decibel Therapeutics. He is a member of the Research Committee of Children's Hospital Boston, the investment committee of the Innovation Research Fund at Partners Healthcare, and the board of directors of the New England Venture Capital Association. He holds an MBA as a Baker Scholar from Harvard Business School, an M.S. from Stanford University, and a B.S. from Cornell University. We believe that Mr. Exter's extensive experience in the life sciences industry as a venture capitalist and senior executive, as well as his service on the boards of directors of numerous biotechnology companies provide him with the qualifications to serve as a director of our company.

Charles Homcy, M.D. has served as a member of our board of directors since July 2015. In 2010, Dr. Homcy joined Third Rock Ventures, a venture capital firm, where he is currently a partner. In 2003, he co-founded Portola Pharmaceuticals, a clinical biotechnology company, and he served as their president and chief executive officer until 2010. Prior to that, Dr. Homcy served as the president of research and development at Millennium Pharmaceuticals, Inc. (currently, Takeda Oncology), a biopharmaceutical company, following its acquisition of COR Therapeutics, Inc. in 2002. He joined COR Therapeutics, Inc., a biopharmaceutical company, in 1995 as executive vice president of research and development, and he served as a director of the company from 1988 to 2002. Dr. Homcy was a clinical professor of medicine at the University of California, San Francisco Medical School, and attending physician at the San Francisco Veterans Affairs Hospital from 1997 to 2011. He was previously president of the medical research division of American Cyanamid-Lederle Laboratories,

a division of Wyeth-Ayest Laboratories. He currently serves on the board of directors of BridgeBio Pharma LLC, a position he has held since November 2018, and of Global Blood Therapeutics, Inc., a position he has held since 2012. Dr. Homcy holds a B.A. and an M.D. from Johns Hopkins University and currently serves on its board of trustees. We believe Dr. Homcy is qualified to serve on our board of directors based on his significant experience building and leading successful biotechnology companies and his scientific expertise.

Kevin Raidy is the Portfolio Manager of Cowen Healthcare Investments. Until October 2017, Mr. Raidy served as Head of Investment Banking at Cowen and Company. He previously served as co-head of Cowen and Company's equity capital markets group, which is responsible for the origination and execution of all equity capital-raising transactions. Before that, he was a managing director at Ramius LLC, where he was portfolio manager for direct investments and convertible bonds, managing a portfolio in excess of $1 billion. Mr. Raidy also was the founder of H4 Capital Management LLC. His sell-side experience includes ten years at Shipley Raidy Capital Partners LP, a boutique investment banking firm that he co-founded, where he was responsible for sourcing, evaluating, and structuring numerous debt and equity financings and also performed M&A advisory services. Prior to founding Shipley Raidy, Mr. Raidy was an associate at Philadelphia First Group. He started his career at Cantor Fitzgerald before moving to Merrill Lynch as an analyst in the municipal finance group. Mr. Raidy holds a BS in economics with a concentration in finance from the Wharton School of the University of Pennsylvania. We believe Mr. Raidy is qualified to serve on our board of directors based on his significant leadership experience in the investment banking industry.

Smital Shah, MBA, has served as a member of our board of directors since March 2019. Since October 2014, Ms. Shah has served in roles of increasing responsibility at ProQR Therapeutics NV, a rare disease company, including as Chief Financial Officer and most recently as Chief Business and Financial Officer. Previously, Ms. Shah managed the multi-billion-dollar debt, cash and investment portfolios of Gilead Sciences, Inc. Prior to Gilead, she was an investment banker at Leerink Partners and JP Morgan focused on capital raising and strategic transactions in the biotechnology space. Previously, Ms. Shah held various research and development roles at Johnson & Johnson Company. She holds a B.S. in Chemical Engineering from the University of Mumbai, a M.S. in Chemical Engineering from Virginia Tech and a MBA from the University of California, Berkeley Haas School of Business. We believe Ms. Shah is qualified to serve on our board of directors due to her extensive experience in the life sciences industry and her leadership experience as a senior financial executive.

Family Relationships

There are no family relationships among any of our executive officers or directors.

Composition of Our Board of Directors

Our board of directors consists of eight members, each of whom are members pursuant to the board composition provisions of our certificate of incorporation and agreements with our stockholders. These board composition provisions will terminate upon the completion of this offering. Upon the termination of these provisions, there will be no further contractual obligations regarding the election of our directors. Our nominating and corporate governance committee and our board of directors may consider a broad range of factors relating to the qualifications and background of nominees. Our nominating and corporate governance committee's and our board of directors' priority in selecting board members is to identify persons who will further the interests of our stockholders through his or her established record of professional accomplishments, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape, and professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal. Our amended and restated certificate of incorporation and amended and restated by-laws that will become effective immediately prior to the closing of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least two-thirds of the votes

that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Director Independence

Upon the completion of this offering, we expect that our common stock will be listed on the Nasdaq Global Market. Applicable Nasdaq rules require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq rules require that (i) on the date of the initial listing, at least one member of each of a listed company's audit, compensation and nominating and corporate governance committees be independent, (ii) within 90 days of the date of the initial listing, a majority of the members of such committees be independent and (iii) within one year of the date of the initial listing, all the members of such committees be independent. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

Our board of directors has determined that all members of the board of directors, except Dr. Coulie, are independent directors, including for purposes of the rules of Nasdaq and the SEC. In making such independence determination, our board of directors considered the relationships that each non-employee director has with us and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each non-employee director. In considering the independence of the directors listed above, our board of directors considered the association of our directors with the holders of more than 5% of our common stock. Upon the completion of this offering, we expect that the composition and functioning of our board of directors and each of our committees will comply with all applicable requirements of Nasdaq and the rules and regulations of the SEC. Dr. Coulie is not an independent director under these rules because he is currently employed as the chief executive officer of our company.

Staggered Board

In accordance with the terms of our amended and restated certificate of incorporation and amended and restated by-laws that will become effective immediately prior to the closing of this offering, our board of directors will be divided into three staggered classes of directors and each will be assigned to one of the three classes. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. The terms of the directors will expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2020 for Class I directors, 2021 for Class II directors and 2022 for Class III directors.

- Our Class I directors will be , , and .
- Our Class II directors will be , , and .
- Our Class III directors will be and .

Our amended and restated certificate of incorporation and amended and restated by-laws that will become effective immediately prior to the closing of this offering will provide that the number of directors shall be fixed from time to time by a resolution of the majority of our board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our board of directors or a change in control.

Board Leadership Structure and Board's Role in Risk Oversight

Hoyoung Huh, M.D., Ph.D. is our current lead director of the board and Bernard Coulie, M.D., Ph.D. is our current chief executive officer, hence the roles of lead director or chairman and the chief executive officer and president are separated. We plan to keep these roles separated following the completion of this offering. We believe that separating these positions allows our chief executive officer to focus on setting the overall strategic direction of the company, expanding the organization to deliver on our strategy and overseeing our day-to-day business, while allowing a lead director of the board to lead the board of directors in its fundamental role of providing strategic advice. Our board of directors recognizes the time, effort and energy that the chief executive officer is required to devote to his position in the current business environment, as well as the commitment required to serve as our lead director, particularly as the board of directors' oversight responsibilities continue to grow. While our amended and restated by-laws and corporate governance guidelines do not require that our lead director and chief executive officer positions be separate, our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

Risk is inherent with every business, and how well a business manages risk can ultimately determine its success. We face a number of risks, including risks relating to our financial condition, development and commercialization activities, operations, strategic direction and intellectual property as more fully discussed in the section entitled "Risk Factors" appearing elsewhere in this prospectus. Management is responsible for the day-to-day management of risks we face, while our board of directors, as a whole and through its committees, has responsibility for the oversight of risk management. In its risk oversight role, our board of directors has the responsibility to satisfy itself that the risk management processes designed and implemented by management are adequate and functioning as designed.

The role of the board of directors in overseeing the management of our risks is conducted primarily through committees of the board of directors, as disclosed in the descriptions of each of the committees below and in the charters of each of the committees. The full board of directors (or the appropriate board committee in the case of risks that are under the purview of a particular committee) discusses with management our major risk exposures, their potential impact on us, and the steps we take to manage them. When a board committee is responsible for evaluating and overseeing the management of a particular risk or risks, the chairperson of the relevant committee reports on the discussion to the full board of directors during the committee reports portion of the next board meeting. This enables the board of directors and its committees to coordinate the risk oversight role, particularly with respect to risk interrelationships.

Committees of Our Board of Directors

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which will operate pursuant to a charter adopted by our board of directors and will be effective upon the effectiveness of the registration statement of which this prospectus is a part. Upon the effectiveness of the registration statement of which this prospectus is a part, the composition and functioning of all of our committees will comply with all applicable requirements of the Sarbanes-Oxley Act of 2002, and with Nasdaq and SEC rules and regulations.

Audit Committee

Effective upon the effectiveness of the registration statement of which this prospectus is a part, Smital Shah, and will serve on the audit committee, which will be chaired by Smital Shah. Our board of directors has determined that each of are "independent" for audit committee purposes as that term is

defined in the rules of the SEC and the applicable Nasdaq rules, and each has sufficient knowledge in financial and auditing matters to serve on the audit committee. Our board of directors has designated as an "audit committee financial expert," as defined under the applicable Nasdaq rules. The audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee's review and discussions with management and our independent registered public accounting firm whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related person transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases.

Compensation Committee

Effective upon the effectiveness of the registration statement of which this prospectus is a part, Suzanne Bruhn, Ph.D., John Curnutte, M.D. and Neil Exter will serve on the compensation committee, which will be chaired by Suzanne Bruhn, Ph.D. Our board of directors has determined that each member of the compensation committee is "independent" as defined in the applicable Nasdaq rules. The compensation committee's responsibilities include:

- annually reviewing and recommending to the board of directors the corporate goals and objectives relevant to the compensation of our principal executive officer;
- evaluating the performance of our principal executive officer in light of such corporate goals and objectives and based on such evaluation: (i) determining cash compensation of our principal executive officer; and (ii) reviewing and approving grants and awards to our principal executive officer under equity-based plans;
- reviewing and approving or recommending to the board of directors the compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;

- evaluating and assessing potential and current compensation advisors in accordance with the independence standards identified in the applicable Nasdaq rules;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and recommending to the board of directors the compensation of our directors;
- preparing the compensation committee report required by SEC rules, if and when required, to be included in our annual proxy statement; and
- reviewing and approving the retention, termination or compensation of any consulting firm or outside advisor to assist in the evaluation of compensation matters.

Nominating and Corporate Governance Committee

Effective upon the effectiveness of the registration statement of which this prospectus is a part, Hoyoung Huh, M.D., Ph.D. and Charles Homcy, M.D., will serve on the nominating and corporate governance committee, which will be chaired by Hoyoung Huh, M.D., Ph.D. Our board of directors has determined that each member of the nominating and corporate governance committee is "independent" as defined in the applicable Nasdaq rules. The nominating and corporate governance committee's responsibilities include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- reviewing the composition of the board of directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;
- developing and recommending to the board of directors a code of business conduct and ethics and a set of corporate governance guidelines; and
- overseeing the evaluation of our board of directors and management.

Our board of directors may from time to time establish other committees.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Corporate Governance

We intend to adopt a written code of business conduct and ethics, effective upon the effectiveness of the registration statement of which this prospectus is a part, that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Following the effectiveness of the registration statement of which this prospectus is a part, a current copy of the code will be posted on the investor relations section of our website, which is located at https://pliantrx.com. The inclusion of our website address in this prospectus does not incorporate by reference the information on or accessible through our website into this prospectus. If we make

any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

Limitation on Liability and Indemnification Matters

Our amended and restated certificate of incorporation, which will become effective immediately prior to the completion of this offering, will contain provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by Delaware law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

Each of our amended and restated certificate of incorporation and amended and restated bylaws, which will become effective immediately prior to the completion of this offering, will provide that we are required to indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. Our amended and restated bylaws will also obligate us to advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under Delaware law. We have entered and expect to continue to enter into agreements to indemnify our directors, executive officers and other employees as determined by our board of directors. With specified exceptions, these agreements provide for indemnification for related expenses including, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these certificate of incorporation and bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and our stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage.

EXECUTIVE COMPENSATION

Overview

The following discussion contains forward-looking statements that are based on our current plans and expectations regarding our future compensation programs. The actual amount and form of compensation that we pay and the compensation policies and practices that we adopt in the future may differ materially from the currently-planned programs that are summarized in this discussion.

The compensation provided to our named executive officers for the fiscal year ended December 31, 2018 is detailed in the 2018 Summary Compensation Table and accompanying footnotes and narrative that follow. Our named executive officers for the fiscal year ended December 31, 2018, which consists of our Chief Executive Officer and our two most highly-compensated individuals (other than our Chief Executive Officer) who were serving as executive officers on December 31, 2018 are:

- Bernard J. Coulie, M.D., Ph.D., our Chief Executive Officer;
- Éric Lefebvre, M.D., our Chief Medical Officer; and
- Hans Hull, J.D., our Chief Business Officer.

2018 Summary Compensation Table

The following table provides information regarding the total compensation awarded to, earned by, and paid to our named executive officers for services rendered to us in all capacities for the fiscal year ended December 31, 2018.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Stock Awards ($)(1)	Option Awards ($)	Non-equity Incentive Plan Compensation ($)(2)	All Other Compensation ($)(3)	Total ($)
Bernard J. Coulie, M.D., Ph.D. *Chief Executive Officer*	2018	413,631		112,682		190,270	44,835	761,418
Éric Lefebvre, M.D. *Chief Medical Officer*(4)	2018	269,167	80,000(5)	342,938		83,067	7,600	782,772
Hans Hull, J.D. *Chief Business Officer*	2018	344,793		18,780		111,712	11,000	486,285

(1) The amounts reported represent the aggregate grant date fair value of the restricted stock awards granted to our named executive officers during the 2018 fiscal year, calculated in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the restricted stock awards reported in this column are set forth in note 11 of our financial statements included elsewhere in this prospectus. The amounts reported in this column reflect the accounting cost for these restricted stock awards and do not correspond to the actual economic value that may be received by our named executive officers upon the vesting of the restricted stock awards or any sale of the underlying shares of common stock. For Dr. Lefebvre, the grant date fair value of his performance-based restricted stock award is reported based on the probable outcome of the applicable performance metrics and the grant date fair value of the such performance-based restricted stock award, based on maximum level of achievement of the applicable performance metrics, is $57,063.

(2) Represents amounts earned by our named executive officers under our short-term incentive program, based on the Company's achievement of certain corporate performance goals and the named executive officers' individual performance during the 2018 fiscal year.

(3) For the 2018 fiscal year, the amounts reported for Dr. Coulie represents—$11,000 for matching contributions made by the Company under its 401(k) plan, $20,000 for a travel allowance, and $13,835 for tax gross-ups paid by the Company for such travel allowance and the amounts reported for Dr. Lefebvre and Mr. Hull represent matching contributions made by the Company under its 401(k) plan.

(4) Dr. Lefebvre commenced employment with us in April 2018 and his annual base salary of $380,000 and annual bonus amounts were pro-rated accordingly.

(5) Represents a one-time lump sum sign-on bonus that Dr. Lefebvre received in connection with his commencement of employment with us.

Narrative to Summary Compensation Table

Base Salaries

From January 1, 2018 through February 15, 2018, the annual base salaries for Dr. Coulie and Mr. Hull were $386,250 and $334,750, respectively. Effective as of February 16, 2018, the annual base salaries for Dr. Coulie and Mr. Hull were increased to $403,631 and $344,793, respectively. Dr. Coulie's annual base salary was further increased to $413,631, effective as of February 20, 2018.

Bonuses

Annual Bonuses

During the fiscal year ended December 31, 2018, our named executive officers were eligible to participate in the Company's short-term incentive program, pursuant to which each was eligible to earn an annual bonus based on the achievement of certain Company performance objectives and individual performance. From January 1, 2018 through February 7, 2018, the target annual bonuses for Drs. Coulie and Lefebvre and Mr. Hull were 35%, 30% and 25%, respectively, of the applicable named executive officer's annual base salary. Effective as of February 8, 2018, the target annual bonuses for Dr. Coulie and Mr. Hull were increased to 40% and 30%, respectively, of the applicable named executive officer's annual base salary.

Sign-on Bonus

In connection with Dr. Lefebvre's commencement of employment with us in April 2018, he received a one-time lump sum bonus equal to $80,000.

Equity Compensation

During the fiscal year ended December 31, 2018, we granted restricted stock awards to each of our named executive officers, as described in more detail in the "Outstanding equity awards at fiscal 2018 year-end" table.

401(k) Plan

We maintain a tax-qualified 401(k) plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax-advantaged basis. Plan participants are able to defer eligible compensation subject to applicable annual Internal Revenue Code limits. We provide a safe harbor matching contribution equal to 100% on the first 3% of participant contributions and an additional 50% on the next 2% of participant contributions, which is 100% vested when contributed. We may also decide to make nonelective contributions, although we are not required to do so pursuant to the terms of the 401(k) plan. The 401(k) plan is intended to be qualified under Section 401(a) of the Internal Revenue Code with the 401(k) plan's related trust intended to be tax exempt under Section 501(a) of the Internal Revenue Code. As a tax-qualified retirement plan, contributions to the 401(k) plan and earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan.

Perquisites

We generally do not provide perquisites to our employees, other than a travel allowance and related tax gross ups to Dr. Coulie.

Executive Employment Arrangements

We initially entered into an offer letter with each of the named executive officers in connection with his employment with us, which set forth the terms and conditions of his employment. Each named executive officer also entered into our standard confidentiality and inventions assignment agreement.

Offer Letters in Place During the Fiscal Year Ended December 31, 2018 for Our Named Executive Officers

Bernard Coulie, M.D., Ph.D.

On October 12, 2015, we entered into an offer letter with Dr. Coulie, who currently serves as our Chief Executive Officer. The offer letter provided for Dr. Coulie's at-will employment and set forth his initial annual base salary, initial target annual bonus opportunity, a $250,000 sign-on bonus, annual travel allowance of up to $20,000, and an initial restricted stock grant for 2,759,780 shares of our common stock, as well as his eligibility to participate in our employee benefit plans generally. Dr. Coulie's initial restricted stock grant vests with respect to 25% of the shares subject thereto on the first anniversary of the vesting commencement date and 1/48th of the shares subject thereto each month thereafter, subject to Dr. Coulie's continued service to the Company through each applicable vesting date. In the event of a termination of his employment by the Company without "cause" (as defined in Dr. Coulie's offer letter) and other than for death or disability, subject to Dr. Coulie's execution of an effective release of claims in favor of the Company and his continued compliance will all legal and contractual obligations to the Company, Dr. Coulie will be entitled to a severance benefit in the form of a lump sum payment equal to six months of his then-base salary.

Éric Lefebvre, M.D.

On February 28, 2018, we entered into an offer letter with Dr. Lefebvre, who currently serves as our Chief Medical Officer. The offer letter provided for Dr. Lefebvre's at-will employment and set forth his initial annual base salary, initial target bonus opportunity, an $80,000 sign-on bonus, an initial restricted stock grant for 1,069,927 shares of our common stock, or the Initial Lefebvre Grant, and an additional restricted stock grant for 178,321 shares of our common stock, or the Additional Lefebvre Grant, as well as his eligibility to participate in our employee benefit plans generally. The Initial Lefebvre Grant vests with respect to 25% of the shares subject thereto on the first anniversary of the vesting commencement date and 1/48th of the shares subject thereto each month thereafter, subject to Dr. Lefebvre's continued service to the Company on each applicable vesting date. The Additional Lefebvre Grant fully vests upon the successful completion of a Phase 1b study with a pharmacodynamic marker in 2019, subject to Dr. Lefebvre's continued service to the Company through such date. In the event of a termination of his employment by the Company without "cause" (as defined in Dr. Lefebvre's offer letter) and other than for death or disability, subject to Dr. Lefebvre's execution of an effective release of claims in favor of the Company and his continued compliance will all legal and contractual obligations to the Company, Dr. Lefebvre will be entitled to a severance benefit in the form of a lump sum payment equal to nine months of his then-base salary. If Dr. Lefebvre becomes re-employed by the Company within nine months of his termination, he must repay his severance amount less the number of months he was unemployed.

Hans Hull, J.D.

On February 10, 2016, we entered into an offer letter with Mr. Hull, who currently serves as our Chief Business Officer. The offer letter provided for Mr. Hull's at-will employment and set forth his initial annual base salary, initial target annual bonus opportunity, and an initial restricted stock grant for 927,000 shares of our common stock, as well as his eligibility to participate in our employee benefit plans generally. Mr. Hull's initial restricted stock grant vests with respect to 25% of the shares subject thereto on the first anniversary of the vesting commencement date and 1/48th of the shares subject thereto each month thereafter, subject to Mr. Hull's continued service to the Company through each applicable vesting date. In the event of a termination of his employment by the Company without "cause" (as defined in Mr. Hull's offer letter) and other than for death or disability, subject to Mr. Hull's execution of an effective release of claims in favor of the Company and his continued compliance will all legal and contractual obligations to the Company, Mr. Hull will be entitled to a severance benefit in the form of a lump sum payment equal to six months of his then-base salary.

Executive Severance Plan

In connection with this offering, our board of directors adopted an Executive Severance Plan, or the Severance Plan, subject to the effectiveness of this offering, in which our named executive officers, and certain other executives, will participate. The benefits provided in the Severance Plan will replace any severance for which our named executive officers may be eligible under their existing offer letters. The severance plan will provide that upon a (i) termination by us for any reason other than for "cause," as defined in the Severance Plan, death or disability, in each case outside of the change in control period (i.e., the period of 12 months after a "change in control," as defined in the Severance plan), an eligible participant will be entitled to receive, subject to the execution and delivery of an effective release of claims in favor of the Company, (i) 12 months of base salary for our Chief Executive Officer and nine months of base salary for the other named executive officers, plus a pro rata target annual bonus for the year of termination, and (ii) health benefits continuation for 12 months for our Chief Executive Officer and nine months for our other named executive officers.

The Severance Plan will also provide that upon a termination by us other than for "cause," as defined in the Severance Plan, death or disability or a resignation for "good reason," as defined in the Severance plan, in each case within the change in control period, an eligible participant will be entitled to receive, in lieu of the payments and benefits above and subject to the execution and delivery of an effective release of claims in favor of the Company, (i) 18 months of base salary plus target annual bonus for our Chief Executive Officer and 12 months of base salary plus target annual bonus for our other named executive officers (ii) health benefits continuation for 18 months for our Chief Executive Officer and 12 months for our other named executive officers, and (iii) full accelerated vesting of all outstanding and unvested equity awards held by such participant.

The payments and benefits provided under the Severance Plan in connection with a change in control may not be eligible for a federal income tax deduction by us pursuant to Section 280G of the Code. These payments and benefits may also subject an eligible participant, including the named executive officers, to an excise tax under Section 4999 of the Code. If the payments or benefits payable in connection with a change in control would be subject to the excise tax imposed under Section 4999 of the Code, then those payments or benefits will be reduced if such reduction would result in a higher net after-tax benefit to the recipient.

Outstanding Equity Awards at Fiscal 2018 Year-End

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2018:

			Stock Awards(1)				
Name	Grant Date	Vesting Commencement Date	Number of Shares or Units of Stock that have Not Vested (#)		Market Value of Shares or Units of Stock that have Not Vested ($)(2)	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights that have Not Vested (#)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights that have Not Vested ($)(2)
Bernard Coulie	2/25/16	9/29/15	517,459	(3)	150,063		
	2/8/18	3/1/18	450,000	(3)	130,500		
Éric Lefebvre	5/17/18	5/1/18	1,069,927	(4)	310,279		
	5/17/18					178,321(5)	51,713
Hans Hull	4/7/16	3/9/16	289,688	(3)	84,010		
	2/8/18	3/1/18	75,000	(3)	21,750		

(1) Each equity award is subject to the terms of our 2015 Equity Incentive Plan, as amended from time to time, or the 2015 Plan.
(2) Based on the fair market value of a share of our common stock on 12/31/18, which was $0.29.
(3) 25% of the shares vest on the first anniversary of the vesting commencement date and the remaining 75% vest in 36 equal monthly installments thereafter, subject to the named executive officer's continuous service relationship with the Company through each applicable vesting date. Notwithstanding the foregoing, the shares are subject to certain acceleration of vesting provisions upon the occurrence of certain events, provided that the named executive officer is in "good standing" (as defined in the applicable restricted stock award agreement) at the time of such event and subject to continued service to the Company through such event: (i) 25% upon the named

executive officer's death; (ii) 12.5% upon a termination of employment by the Company; and (iii) 100% upon a termination in connection with a "sale event" (as defined in the applicable restricted stock award agreement).

(4) 25% of the shares vest on the first anniversary of the vesting commencement date and the remaining 75% vest in 36 equal monthly installments thereafter, subject to the named executive officer's continuous service relationship with the Company through each applicable vesting date.

(5) The restricted stock fully vests upon the successful completion of a Phase Ib study with a pharmacodynamic marker in 2019, subject to Dr. Lefebvre's continued service to the Company through such date. However, during 2019, we decided not to pursue the Phase Ib study and intend to repurchase such shares.

Employee Benefits and Equity Compensation Plans

2019 Stock Option and Incentive Plan

In connection with this offering, our board of directors plans to adopt a 2019 Stock Option and Incentive Plan, or the 2019 Plan. The 2019 Plan will become effective on the date immediately prior to the date on which the registration statement of which this prospectus is part is declared effective by the SEC. The 2019 Plan will replace our 2015 Plan, as our board of directors will not to make additional awards under the 2015 Plan following the closing of this offering. The 2019 Plan will provide flexibility to our compensation committee to use various equity-based incentive awards as compensation tools to motivate our workforce.

We will initially reserve shares of our common stock, or the Initial Limit, for the issuance of awards under the 2019 Plan. The 2019 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2020, by % of the outstanding number of shares of our common stock on the immediately preceding December 31, or such lesser number of shares as determined by our compensation committee. This is referred to herein as the Annual Increase. This number will be subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares we issue under the 2019 Plan will be authorized but unissued shares or shares that we reacquire. The shares of common stock underlying any awards that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without any issuance of stock, expire or are otherwise terminated (other than by exercise) under the 2019 Plan and the 2015 Plan will be added back to the shares of common stock available for issuance under the 2019 Plan.

The maximum aggregate number of shares that may be issued in the form of incentive stock options may not exceed the Initial Limit cumulatively increased on January 1, 2020, and on each January 1 thereafter by the lesser of (i) the Annual Increase for such year or (ii) shares of common stock.

The grant date fair value of all awards made under our 2019 Plan and all other cash compensation paid by us to any non-employee director in any calendar year may not exceed $ for the first year of service and $ for each year of service thereafter.

The 2019 Plan will be administered by our compensation committee. Our compensation committee will have full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of the 2019 Plan. Persons eligible to participate in the 2019 Plan will be those full or part-time employees, non-employee directors and consultants of the Company and its affiliates, as selected from time to time by our compensation committee in its discretion.

The 2019 Plan will permit the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Internal Revenue Code and options that do not so qualify. The option exercise price of each option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant. The term of each option will be fixed by our compensation committee and may not exceed ten years from the date of grant. Our compensation committee will determine at what time or times each option may be exercised.

Our compensation committee will be able to award stock appreciation rights subject to such conditions and restrictions as it may determine. Stock appreciation rights will entitle the recipient to shares of common stock or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right may not be less than 100% of the fair market value of the common stock on the date of grant. The term of each stock appreciation right will be fixed by our compensation committee and may not exceed ten years from the date of grant. Our compensation committee will determine at what time or times each stock appreciation right may be exercised.

Our compensation committee will be able to award restricted shares of common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment or service relationship with us through a specified vesting period. Our compensation committee may also be permitted to grant shares of common stock that are free from any restrictions under the 2019 Stock Plan. Unrestricted stock may be granted to participants in recognition of past services or other valid consideration and may be issued in lieu of cash compensation due to such participant.

Our compensation committee will be able to grant cash bonuses under the 2019 Stock Plan to participants, subject to the achievement of certain performance goals.

The 2019 Stock Plan will provide that upon the effectiveness of a "sale event," as defined in the 2019 Stock Plan, an acquirer or successor entity may assume, continue or substitute outstanding awards under the 2019 Stock Plan. To the extent that awards granted under our 2019 Stock Plan are not assumed or continued or substituted by the successor entity, except as may be otherwise provided in the relevant award certificate, all awards with time-based vesting, conditions or restrictions will become fully vested and nonforfeitable as of the effective time of the sale event, and all awards with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in connection with a sale event in the compensation committee's discretion or to the extent specified in the relevant award certificate. Upon the effective time of the sale event, all outstanding awards granted under the 2019 Stock Plan will terminate to the extent not assumed, continued or substituted for. In the event of such termination, individuals holding options and stock appreciation rights will be permitted to exercise such options and stock appreciation rights (to the extent exercisable) within a specified period of time prior to the sale event. In addition, in connection with the termination of the 2019 Stock Plan upon a sale event, we may make or provide for a payment, in cash or in kind, to participants holding vested and exercisable options and stock appreciation rights equal to the difference between the per share cash consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights and we may make or provide for a payment, in cash or in kind, to participants holding other vested awards.

Our board of directors will be able to amend or discontinue the 2019 Stock Plan and our compensation committee will be permitted, at any time, to amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose but no such action may adversely affect rights under an award without the holder's consent. The compensation committee is specifically authorized to exercise its discretion to reduce the exercise price of outstanding stock options or stock appreciation rights or effect the repricing of such awards through cancellation and re-grants. Certain amendments to the 2019 Stock Plan will require the approval of our stockholders.

No awards will be granted under the 2019 Stock Plan after the date that is 10 years from the date of stockholder approval. No awards under the 2019 Stock Plan will be made prior to the date of this prospectus.

2015 Equity Incentive Plan

Our board of directors adopted, and our stockholders approved, our 2015 Plan, on August 19, 2015. Our 2015 Plan was most recently amended on January 1, 2019. The 2015 Plan allowed for the grant of incentive stock options to employees, including employees of any parent or subsidiary, and for the grant of nonstatutory stock

options, stock appreciation rights, restricted stock awards, restricted stock units and other stock awards to employees, directors, and consultants, including employees and consultants of our affiliates, subject in each case to compliance with applicable tax laws.

Our 2019 Stock Plan will become effective the day before the date that the registration statement of which this prospectus is part is declared effective by the SEC. As a result, we do not expect to grant any additional awards under the 2015 Plan following that date. Any awards granted under the 2015 Plan will remain subject to the terms of our 2015 Plan and applicable award agreements. As of December 31, 2018, options to purchase 809,200 shares of common stock and unexercised rights to purchase 32,600 shares of restricted stock were outstanding under the 2015 Plan.

The maximum number of shares of our common stock that may have been issued under our 2015 Plan was 21,150,000. The maximum number of shares of stock that may have been issued pursuant to the exercise of incentive stock options was three times such maximum number of shares. Shares subject to stock awards granted under our 2015 Plan that expire, are forfeited, are repurchased or otherwise terminate without all the shares covered by such stock awards having been issued, or are settled in cash, do not reduce the number of shares available for issuance under our 2015 Plan. Additionally, shares used to pay the exercise price or purchase price of a stock award or shares reacquired by the Company to satisfy the tax withholding obligations related to a stock award will return to the share reserve under the 2015 Plan. The shares issuable pursuant to stock awards granted under the 2015 Plan are authorized but unissued or reacquired shares, including shares repurchased by the Company on the open market or otherwise.

The Company's board of directors or a duly authorized committee of our board of directors administers our 2015 Plan and the stock awards granted under it, and has the power to interpret and administer our 2015 Plan and any agreement thereunder and to determine the terms of awards, including the recipients, the number of shares subject to each award, the exercise, purchase or strike price, if any, the vesting schedule applicable to the awards together with any vesting acceleration and the terms of the award agreement for use under our 2015 Plan. Under the 2015 Plan, the board of directors also generally has the authority to effect, with the consent of any adversely affected participant, the reduction of the exercise price of any outstanding option or stock appreciation right, the cancellation of any outstanding option or stock appreciation right and the grant in substitution therefore of other awards, cash, or other consideration, or any other action that is treated as a repricing under generally accepted accounting principles.

Pursuant to the 2015 Plan and subject to applicable law, the plan administrator may, in its discretion, delegate to one of more of our officers, the power to designate non-officer employees as recipients of options and/or stock appreciation rights and to determine the number of shares subject to such stock awards to be granted to such employees; provided, however, the plan administrator must specify the total number of shares that may be subject to the stock awards granted by such officer and such officer may not grant options to himself or herself. The board of directors may not delegate the authority to determine the fair market value of our common stock.

Our 2015 Plan provides that in the event of certain specified significant corporate transactions, generally including: (i) a sale of all or substantially all of our assets, (ii) the sale or disposition of at least 90% of our outstanding securities, (iii) the consummation of a merger or consolidation where we do not survive the transaction, and (iv) the consummation of a merger or consolidation where we do survive the transaction but the shares of common stock outstanding before such transaction are converted or exchanged into other property by virtue of the transaction, unless otherwise provided in an award agreement or other written agreement between us and the award holder, the administrator may take one or more of the following actions with respect to such stock awards: (A) arrange for the assumption, continuation or substitution of a stock award by a successor corporation, (B) arrange for the assignment of any reacquisition or repurchase rights held by us to a successor corporation, (C) accelerate the vesting, in whole or in part, of the stock award and provide for its termination before the transaction, (D) arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us,

(E) cancel or arrange for the cancellation of the stock award before the transaction in exchange for a cash payment, if any, determined by the board of directors, or (F) make a payment, in the form determined by the board of directors, equal to the excess, if any, of the value of the property the participant would have received on exercise of the stock award before the transaction over any exercise price payable by the participant in connection with the exercise. The plan administrator is not obligated to treat all stock awards, even those that are of the same type, or all participants, in the same manner. In the event of a change in control, awards granted under the 2015 Plan will not receive automatic acceleration of vesting and exercisability, although the board of directors may provide for this treatment in an award agreement. Under the 2015 Plan, a change in control is defined to include (i) the acquisition by any person of more than 50% of the combined voting power of our then outstanding stock, (ii) a merger, consolidation, or similar transaction in which our stockholders immediately before the transaction do not own, directly or indirectly, more than 50% of the combined voting power of the surviving entity (or the parent of the surviving entity), or (iii) a sale, lease, exclusive license, or other disposition of all or substantially all of the assets to an entity that did not previously hold more than 50% of the voting power of our stock.

Under our 2015 Plan, the board of directors may provide for limitations on the transferability of awards, in its sole discretion. Option awards are generally not transferable other than by will or the laws of descent and distribution, except as otherwise provided under our 2015 Plan.

Our board of directors has the authority to amend, suspend, or terminate our 2015 Plan, although certain material amendments require the approval of our stockholders, and amendments that would impair the rights of any participant require the written consent of that participant.

Our board of directors has determined not to make any further awards under the 2015 Plan following the completion of this offering.

2019 Employee Stock Purchase Plan

In connection with this offering, our board of directors plans to adopt a 2019 Employee Stock Purchase Plan, or an ESPP, which will become effective on the date immediately prior to the date on which the registration statement of which this prospectus is part is declared effective by the SEC. The ESPP will initially reserve and authorize the issuance of up to a total of shares of common stock to participating employees. The ESPP will provide that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2020, by the least of shares of our common stock, % of the outstanding number of shares of our common stock on the immediately preceding December 31, or such lesser number of shares as determined by our compensation committee. This number will be subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

All employees whose customary employment is for more than hours per week and who have completed at least days of employment will be eligible to participate in the ESPP. Any employee who owns 5% or more of the total combined voting power or value of all classes of stock will not be eligible to purchase shares under the ESPP.

We will make one or more offerings, consisting of one or more purchase periods, each year to our employees to purchase shares under the ESPP. Offerings will usually begin every six months and will continue for six-month periods, referred to as offering periods. Each eligible employee may elect to participate in any offering by submitting an enrollment form at least 15 business days before the relevant offering date.

Each employee who is a participant in the ESPP may purchase shares by authorizing contributions of between 1% and % of his or her compensation during an offering period. Unless the participating employee has previously withdrawn from the offering, his or her accumulated contributions will be used to purchase shares on the last business day of the purchase period at a price equal to 85% of the fair market value of the shares on

the first business day of the offering period or the last business day of the purchase period, whichever is lower, provided that no more than shares of common stock (or a lesser number as established by the plan administrator in advance of the purchase period) may be purchased by any one employee during each purchase period. Under applicable tax rules, an employee may purchase no more than $25,000 worth of shares of common stock, valued at the start of the offering period, under the ESPP for each calendar year in which a purchase right is outstanding.

The accumulated contributions of any employee who is not a participant on the last day of a purchase period will be refunded. An employee's rights under the ESPP terminate upon voluntary withdrawal from the plan or when the employee ceases employment with us for any reason.

The ESPP may be terminated or amended by our board of directors at any time, but will automatically terminate on the 10-year anniversary of this offering. An amendment that increases the number of shares of common stock that are authorized under the ESPP and certain other amendments will require the approval of our stockholders. The plan administrator may adopt subplans under the ESPP for employees of our non-U.S. subsidiaries.

Senior Executive Cash Incentive Bonus Plan

In connection with this offering, our board of directors plans to adopt a Senior Executive Cash Incentive Bonus Plan, or the Bonus Plan. The Bonus Plan will provide for cash bonus payments based upon the attainment of performance targets established by our compensation committee. The payment targets will be related to financial and operational measures or objectives with respect to our company, or corporate performance goals, as well as individual performance objectives.

Our compensation committee may select corporate performance goals from among the following: cash flow (including, but not limited to, operating cash flow and free cash flow); sales or revenue; corporate revenue; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of our common stock; economic value-added; development, clinical, regulatory or commercial milestones; acquisitions or strategic transactions, partnerships or joint ventures; operating income (loss); return on capital, assets, equity, or investment; stockholder returns; return on sales; gross or net profit levels; productivity; expense efficiency; margins; operating efficiency; customer satisfaction; working capital; earnings (loss) per share of our common stock; sales or market shares; number of customers; operating income and/or other strategic, financial or operational objectives, any of which may be measured in absolute terms, as compared to any incremental increase, in terms of growth, as compared to results of a peer group, against the market as a whole, compared to applicable market indices and/or measured on a pre-tax or post-tax basis.

Each executive officer who is selected to participate in the Bonus Plan will have a target bonus opportunity set for each performance period. The bonus formulas will be adopted in each performance period by the compensation committee and communicated to each executive. The corporate performance goals will be measured at the end of each performance period after our financial reports have been published or such other appropriate time as the compensation committee determines. If the corporate performance goals and individual performance objectives are met, payments will be made as soon as practicable following the end of each performance period, but not later than 74 days after the end of the fiscal year in which such performance period ends. Subject to the rights contained in any agreement between the executive officer and us, an executive officer must be employed by us on the bonus payment date to be eligible to receive a bonus payment. The Bonus Plan will also permits the compensation committee to approve additional bonuses to executive officers in its sole discretion.

DIRECTOR COMPENSATION

Non-Employee Director Compensation Program

During the fiscal year ended December 31, 2018, we provided compensation to our non-employee directors for their services on our board of directors, other than those associated with Third Rock Ventures or Cowen, pursuant to our non-employee director compensation policies.

The non-employee director compensation policies generally provided for an annual $25,000 cash retainer; however, Dr. Huh's non-employee director compensation policy did not provide for any cash retainers.

In addition, upon initial election to our board of directors, each such non-employee director was granted a certain number of shares of our restricted common stock (approximately 180,000 for Drs. Bruhn and Curnutte and 668,228 for Dr. Huh), or the Initial Pre-IPO Director Grant. The Initial Pre-IPO Director Grant had a per share exercise price equal to the fair market value of a share of our common stock on the date of grant and vests, on the last date of each calendar quarter after the non-employee director's commencement of his or her service to the Company, at a rate of approximately 11,250 shares for Drs. Bruhn and Curnutte and 41,768 for Dr. Huh, subject to continued service to the Company through each applicable vesting date. Upon a "sale event" (as defined in the non-employee director compensation policy), the Initial Pre-IPO Director Grants will vest in full.

On or following the first anniversary of the Initial Pre-IPO Director Grant, and each year thereafter, each continuing non-employee director was granted 29,350 shares of restricted stock, or the Annual Pre-IPO Director Grant. The Annual Pre-IPO Director Grant had a per share exercise price equal to the fair market value of a share of our common stock on the date of grant and vests in equal quarterly installments over one year from the date of grant, subject to continued service to the Company through each applicable vesting date. Upon a sale event, the Annual Pre-IPO Director Grants will vest in full.

Employee directors received no additional compensation for their service as a director.

We reimbursed all reasonable out-of-pocket expenses incurred by directors for their attendance at meetings of our board of directors or any committee thereof.

We plan to adopt a new non-employee director compensation policy which will become effective immediately prior to the completion of this offering, pursuant to which our non-employee directors will be eligible to receive certain cash retainers (which will be prorated for partial years of service) and equity awards.

Non-Employee Director Compensation Table

The following table provides information regarding the total compensation that was earned by or paid to each of our non-employee directors during the fiscal year ended December 31, 2018. Dr. Coulie, who is our Chief Executive Officer, did not receive any additional compensation for his service as a director. The compensation received by Dr. Coulie, as a named executive officer of the Company, is presented in "Executive Compensation —2018 Summary Compensation Table" above.

Name	Fees Earned or Paid in Cash ($)	Stock Awards ($)(1)	All Other Compensation ($)	Total ($)
Suzanne Bruhn, Ph.D.(2)	25,000	8,818		33,818
John Curnutte, M.D.(3)	25,000	8,818		33,818
Neil Exter(4)				
Charles Homcy, M.D.(5)		40,025(6)		40,025
Hoyoung Huh, M.D.(7)			5,000(8)	5,000
Craig Muir(9)				
Kevin Raidy(10)				

(1) The amounts reported represent the aggregate grant date fair value of the restricted stock awards granted to the non-employee directors in the fiscal year ended December 31, 2018, calculated in accordance with FASB ASC Topic 718. Such grant date fair values do not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value of the restricted stock awards reported in this column are set forth in note 11 to our consolidated financial statements included elsewhere in this prospectus. The amounts reported in this column reflect the accounting cost for these restricted stock awards and do not correspond to the actual economic value that may be received by the non-employee directors upon the vesting of the restricted stock awards or any sale of the underlying shares of common stock.
(2) As of December 31, 2018, Dr. Bruhn held 209,350 shares of restricted stock.
(3) As of December 31, 2018, Dr. Curnutte held 209,350 shares of restricted stock.
(4) As of December 31, 2018, Mr. Exter did not hold any outstanding equity awards.
(5) As of December 31, 2018, Dr. Homcy held 500,000 shares of restricted stock.
(6) Dr. Homcy provided us with technical consulting services and received a grant of 125,000 shares of restricted stock for such services.
(7) As of December 31, 2018, Dr. Huh held 713,288 share of restricted stock, which he transferred to pH Pharma Co., Ltd. as of such date. For more information, see Certain Relationships and Related Party Transactions.
(8) Amount represents consulting fees paid to Healthcare & Humanity Foundation on behalf of Dr. Huh for his advisory services to the Company on its strategy and corporate development relating to its business of developing therapeutics for fibrotic disease. Pursuant to a consulting agreement entered into between the Company and Dr. Huh, effective as of February 15, 2017, for his services, Healthcare & Humanity Foundation was paid $5,000 per month on behalf of Dr. Huh and Dr. Huh was granted 45,000 shares of restricted stock that vests 25% for each quarter of continuous service. Dr. Huh's consulting relationship with the Company terminated in January 2018. For more information, see "Certain Relationships and Related Party Transactions."
(9) Mr. Muir's service as a member of our board of directors ended in July 2018. As of December 31, 2018, Mr. Muir did not hold any outstanding equity awards.
(10) Mr. Raidy was appointed a member of our board of directors in July 2018. As of December 31, 2018, Mr. Raidy did not hold any outstanding equity awards.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

In addition to the compensation arrangements, including employment, termination of employment and change in control arrangements, with our directors and executive officers, including those discussed in the sections entitled "Management" and "Executive and Director Compensation," and the registration rights described in the section entitled "Description of Capital Stock—Registration Rights," the following is a description of each transaction since January 1, 2016 and each currently proposed transaction in which:

- we have been or are to be a participant;
- the amounts involved exceeded or will exceed $120,000; and
- any of our directors, executive officers or holders of more than 5% of our capital stock, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

Private Placements of Securities

Series A redeemable convertible preferred stock financing

From August 2015 through March 2018, we sold an aggregate of 56,000,000 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share, for an aggregate purchase price of $56.0 million.

All purchasers of our Series A redeemable convertible preferred stock are entitled to specified registration rights. See the section entitled "Description of Capital Stock—Registration Rights" for more information regarding these registration rights.

The following table summarizes the Series A redeemable convertible preferred stock purchased by members of our board of directors or their affiliates and holders of more than 5% of our outstanding capital stock.

Name of stockholder	Shares of Series A redeemable convertible preferred stock		Total purchase price
Entities affiliated with Third Rock Ventures(1)	55,000,000	$	55,000,000
pH Pharma Co., Ltd.(2)	1,000,000	$	1,000,000

(1) Consists of 39,750,000 shares held by Third Rock Ventures III, L.P., or TRV III, and 15,250,000 shares held by Third Rock Ventures IV, L.P., or TRV IV.
(2) Hoyoung Huh, M.D., Ph.D., our lead director, has a majority ownership in pH Pharma Co. Ltd., or pH Pharma, and has voting power over the shares.

Series B redeemable convertible preferred stock financing

From July 2018 through November 2018, we sold an aggregate of 49,501,221 shares of our Series B redeemable convertible preferred stock at a purchase price of $1.3767 per share, for an aggregate purchase price of approximately $68.1 million.

All purchasers of our Series B redeemable convertible preferred stock are entitled to specified registration rights. See the section entitled "Description of Capital Stock—Registration Rights" for more information regarding these registration rights.

The following table summarizes the Series B redeemable convertible preferred stock purchased by members of our board of directors or their affiliates and holders of more than 5% of our outstanding capital stock.

Name of stockholder	Shares of Series B redeemable convertible preferred stock	Total purchase price
Entities affiliated with Cowen Healthcare Investments(1)	10,895,619	$ 14,999,999
Entities affiliated with Eventide Asset Management LLC(2)	10,895,619	$ 14,999,999
Bernard Coulie and Barbara Leyman, as Trustees of The Coulie/Leyman Family Trust(3)	181,594	$ 250,000
Hans Hull	36,319	$ 50,000

(1) Consists of (a) 10,154,302 shares of Series B convertible preferred stock held by Cowen Healthcare Investments II LP, or Cowen II and (b) 741,317 shares of Series B convertible preferred stock held by CHI EF II LP, or CHI EF II. Cowen Healthcare Investments II GP LLC is the sole general partner of Cowen II and CHI EF II.

(2) Consists of (a) 7,263,746 shares of Series B convertible preferred stock and (b) 3,631,873 shares of Series B convertible preferred stock held by Eventide Healthcare & Life Science Fund. Eventide Gilead Fund and Eventide Healthcare & Life Sciences Fund are registered investment companies for which Eventide Asset Management, LLC acts as investment advisor. Eventide Asset Management, LLC has voting and investment power with respect to the shares.

(3) Consists of 181,594 shares of Series B convertible preferred stock held by Bernard Coulie and Barbara Leyman, as Trustees of The Coulie/Leyman Family Trust, or Coulie/Leyman Family Trust, of which Dr. Coulie and his spouse are the sole trustees.

Agreements with Stockholders

Investors' rights agreement

On July 10, 2018, we entered into an Amended and Restated Investors' Rights Agreement, as amended to date, which we refer to as our investors' rights agreement, with certain holders of our outstanding redeemable convertible preferred stock, including entities with which certain of our directors are affiliated. After the completion of this offering, the holders of shares of our common stock issuable in connection with the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into common stock, are entitled to rights with respect to the registration of their shares following this offering under the Securities Act. See the section entitled "Description of Capital Stock—Registration Rights" for more information regarding these registration rights.

Right of first refusal and co-sale agreement

On July 10, 2018, we entered into an Amended and Restated Right of First Refusal and Co-Sale Agreement, as amended to date, which we refer to as our right of first refusal and co-sale agreement, which imposes restrictions on the transfer of our capital stock. Upon the completion of this offering, the right of first refusal and co-sale agreement will terminate and the restrictions on the transfer of our capital stock set forth in this agreement will no longer apply.

Voting agreement

On July 10, 2018, we entered into an Amended and Restated Voting Agreement, as amended to date, which we refer to as our voting agreement, under which certain holders of our capital stock, including persons who hold more than 5% of our outstanding capital stock and entities with which certain of our directors are affiliated, have agreed to vote their shares on certain matters, including with respect to the election of directors. Upon the completion of this offering, the voting agreement will terminate and none of our stockholders will have any special rights regarding the election or designation of members of our board of directors or the voting of our capital stock of the company.

Consulting or research agreements with related parties

Certain employees of Third Rock Ventures, one of our stockholders, provide consulting services to us. Consulting service expenses of $132,000 and $54,000 were recorded for the years ended December 31, 2017 and 2018, respectively.

Charitable contributions

In 2018, we made charitable contributions to the University of California, San Francisco Foundation ("UCSF Foundation"), which were directed to support research performed in the laboratories of two of our scientific founders. Charitable contributions made to the UCSF Foundation during the year ended December 31, 2018 were $0.5 million.

Executive Officer and Director Compensation

See the sections entitled "Executive Compensation" and "Director Compensation" for information regarding compensation of our executive officers and directors.

Other Relationships

Other than as described above, since January 1, 2016, we have not entered into any transactions, nor are there any currently proposed transactions, between us and a related party where the amount involved exceeds, or would exceed, $120,000, and in which any related person had or will have a direct or indirect material interest.

Indemnification Agreements

In connection with this offering, we intend to enter into new agreements to indemnify our directors and executive officers. These agreements and our amended and restated certificate of incorporation and amended and restated bylaws will, among other things, require us to indemnify these individuals for certain expenses (including attorneys' fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on behalf of our company or that person's status as a member of our board of directors to the maximum extent allowed under Delaware law.

Policies for Approval of Related Party Transactions

Prior to this offering, we have not had a formal policy regarding approval of transactions with related parties. Prior to the completion of this offering, we expect to adopt a written related person transaction policy that sets forth our procedures for the identification, review, consideration and approval or ratification of related person transactions. The policy will become effective immediately upon the execution of the underwriting agreement for this offering. For purposes of our policy only, a related person transaction is a transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we and any related person are, were, or will be participants and in which the amount involved exceeds $120,000. Transactions involving compensation for services provided to us as an employee or director are not covered by this policy. A related person is any executive officer, director, or beneficial owner of more than 5% of any class of our voting securities, including any of their immediate family members and any entity owned or controlled by such persons.

Under the policy, if a transaction has been identified as a related person transaction, including any transaction that was not a related person transaction when originally consummated or any transaction that was not initially identified as a related person transaction prior to consummation, our management must present information regarding the related person transaction to our audit committee, or, if audit committee approval would be inappropriate, to another independent body of our board of directors, for review, consideration, and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related persons, the benefits to us of the transaction, and whether the transaction is on terms that are comparable to the terms available to or from, as the case may be, an unrelated third party or to or from employees generally. Under the policy, we will collect information that we deem reasonably necessary from each director, executive officer, and, to the extent feasible, significant stockholder to enable us to identify any existing or potential related person transactions and to effectuate the terms of the policy.

In addition, under our Code of Conduct, which we intend to adopt in connection with this offering, our employees and directors have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest.

In considering related person transactions, our audit committee, or other independent body of our board of directors, will take into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs, and benefits to us;
- the impact on a director's independence in the event that the related person is a director, immediate family member of a director, or an entity with which a director is affiliated;
- the availability of other sources for comparable services or products; and
- the terms available to or from, as the case may be, unrelated third parties or to or from employees generally.

The policy requires that, in determining whether to approve, ratify, or reject a related person transaction, our audit committee, or other independent body of our board of directors, must consider, in light of known circumstances, whether the transaction is in, or is not inconsistent with, our best interests and those of our stockholders, as our audit committee, or other independent body of our board of directors, determines in the good faith exercise of its discretion. All of the transactions described above were entered into prior to the adoption of the written policy, but all were approved by our board of directors considering similar factors to those described above.

PRINCIPAL STOCKHOLDERS

The following table presents information concerning the beneficial ownership of the shares of our common stock as of May 1, 2019 by:

- each person we know to be the beneficial owner of 5% or more of our outstanding shares of our capital stock;
- each of our directors;
- each of our named executive officers; and
- all of our current executive officers and directors as a group.

We have determined beneficial ownership in accordance with SEC rules. The information does not necessarily indicate beneficial ownership for any other purpose. Under these rules, a person is deemed to be a beneficial owner of our common stock if that person has a right to acquire ownership within 60 days by the exercise of options or the conversion of our redeemable convertible preferred stock. A person is also deemed to be a beneficial owner of our common stock if that person has or shares voting power, which includes the power to vote or direct the voting of our common stock, or investment power, which includes the power to dispose of or to direct the disposition of such capital stock. Except in cases where community property laws apply or as indicated in the footnotes to this table, we believe that each stockholder identified in the table possesses sole voting and investment power over all shares of common stock shown as beneficially owned by the stockholder.

Percentage of beneficial ownership in the table below is based on 120,415,178 shares of common stock deemed to be outstanding as of May 1, 2019, assuming the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into common stock, immediately prior to the completion of this offering. The table below assumes that the underwriters do not exercise their option to purchase additional shares. Shares of common stock subject to options that are currently exercisable or exercisable within 60 days of May 1, 2019 are considered outstanding and beneficially owned by the person holding the options for the purpose of computing the percentage ownership of that person but are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated below, the address of each individual listed below is c/o Pliant Therapeutics, Inc., 260 Littlefield Avenue, South San Francisco, California 94080.

Name and address of beneficial owner	Number of shares beneficially owned	Percentage of shares beneficially owned before offering	Percentage of shares beneficially owned after offering
5% or Greater Stockholders:			
Entities affiliated with Third Rock Ventures(1)	57,000,000	47.3%	%
Entities affiliated with Cowen Healthcare Investments(2)	10,895,619	9.0%	%
Entities affiliated with Eventide Asset Management LLC(3)	10,895,619	9.0%	%
Named Executive Officers and Directors:			
Bernard Coulie, M.D., Ph.D.(4)	3,683,040	3.1%	%
Hans Hull(5)	1,053,944	*	%
Éric Lefebvre, M.D.(6)	1,295,123	1.1%	%
Hoyoung Huh, M.D., Ph.D.(7)	1,713,288	1.4%	%
Suzanne Bruhn, Ph.D.(8)	238,350	*	%
John Curnutte, M.D.(9)	209,350	*	%
Neil Exter(10)	—	—	%
Charles Homcy, M.D.(11)	500,000	*	%
Kevin Raidy(2)	10,895,619	9.0	%
Smital Shah(12)	22,500	*	%
All executive officers and directors as a group (12 persons)(13)	19,611,214	16.2%	%

* Represents beneficial ownership of less than one percent.

(1) Consists of (a) 2,000,000 shares of common stock held by TRV III, (b) 39,750,000 shares of common stock issuable upon conversion of Series A redeemable convertible preferred stock held by TRV III, (c) 15,250,000 shares of common stock issuable upon conversion of Series A redeemable convertible preferred stock held by TRV IV. The general partner of TRV III is Third Rock Ventures GP III, L.P., or TRV GP III LP. The general partner of TRV GP III LP is TRV GP III, LLC, or TRV GP III LLC. Mark Levin, Kevin Starr and Robert Tepper, M.D. are the managing members of TRV GP III LLC who collectively make voting and investment decisions with respect to shares held by TRV III. Each of TRV GP III, TRV GP III LLC, Mr. Levin, Mr. Starr and Dr. Tepper disclaims beneficial ownership of the shares held by TRV III, except to the extent of its or his proportionate pecuniary interest therein, if any. The general partner of TRV IV is Third Rock Ventures GP IV, L.P., or TRV GP IV LP. The general partner of TRV GP IV LP is TRV GP IV, LLC, or TRV GP IV LLC. Abbie Celniker, Ph.D., Dr. Tepper, Alexis Borisy, Craig Muir and Cary Pfeffer, M.D. are the managing members of TRV GP IV LLC who collectively make voting and investment decisions with respect to shares held by TRV IV. Each of TRV GP IV, TRV GP IV LLC, Dr. Celniker, Dr. Tepper, Mr. Borisy, Mr. Muir and Dr. Pfeffer disclaims beneficial ownership of the shares held by TRV III, except to the extent of its, his or her proportionate pecuniary interest therein, if any. The address for TRV III and TRV IV is 29 Newbury Street, Suite 401, Boston, Massachusetts 02116.

(2) Consists of (a) 10,154,302 shares of common stock issuable upon conversion of Series B redeemable convertible preferred stock held by Cowen II and (b) 741,317 shares of common stock issuable upon conversion of Series B redeemable convertible preferred stock held by CHI EF II. Cowen Healthcare Investments II GP LLC is the sole general partner of Cowen II and CHI EF II. As managing partner of Cowen II and CHI EF II, Kevin J. Raidy exercises sole voting and investment power of the securities held by Cowen II and CHI EF II. Mr. Raidy disclaims beneficial ownership of the shares held by Cowen II and CHI EF II, except to the extent of any actual pecuniary interest. The address for Cowen II and CHI EF II is 599 Lexington Avenue, New York, New York 10022.

(3) Consists of (a) 7,263,746 shares of common stock issuable upon conversion of Series B redeemable convertible preferred stock and (b) 3,631,873 shares of common stock issuable upon conversion of Series B redeemable convertible preferred stock held by Eventide Healthcare & Life Science Fund. Eventide Gilead Fund and Eventide Healthcare & Life Sciences Fund are registered investment companies for which Eventide Asset Management, LLC acts as investment advisor. Eventide Asset Management, LLC has voting and investment power with respect to the shares. The principal business address of each of Eventide Gilead Fund and Eventide Healthcare & Life Science Fund is One International Place, Suite #3510, Boston, MA 02110.

(4) Consists of (a) 181,594 shares of common stock issuable upon conversion of Series B redeemable convertible preferred stock held by Bernard Coulie and Barbara Leyman, as Trustees of The Coulie/Leyman Family Trust, or Coulie/Leyman Family Trust, of which Dr. Coulie and his spouse are the trustees; (b) 3,209,780 shares of common stock held by Coulie/Leyman Family Trust, of which 606,228 shares are subject to repurchase by us at the original purchase price as of May 1, 2019; and (c) 291,666 shares of common stock underlying options held by Dr. Coulie exercisable within 60 days of May 1, 2019.

(5) Consists of (a) 36,319 shares of common stock issuable upon conversion of Series B redeemable convertible preferred stock held by Mr. Hull; (b) 1,002,000 shares of common stock held by Mr. Hull, of which 265,563 shares are subject to repurchase by us at the original purchase price as of May 1, 2019 and (c) 15,625 shares of common stock underlying options held by Mr. Hull exercisable within 60 days of May 1, 2019.

(6) Consists of (a) 1,248,248 shares of common stock held by Dr. Lefebvre, of which 980,767 shares are subject to repurchase by us at the original purchase price as of May 1, 2019; and (b) 46,875 shares of common stock underlying options held by Dr. Lefebvre exercisable within 60 days of May 1, 2019.

(7) Consists of (a) 1,000,000 shares of common stock issuable upon conversion of Series A redeemable convertible preferred stock held by pH Pharma Co., Ltd., or pH Pharma and (b) 713,288 shares of common stock held by pH Pharma, of which 417,680 shares are subject to repurchase by us at the original purchase price as of May 1, 2019. Dr. Huh has a majority ownership in pH Pharma and also has voting power over the shares. Dr. Huh disclaims beneficial ownership of the shares held by pH Pharma, except to the extent of his proportionate pecuniary interest therein. The address for pH Pharma is 9th Fl., The-K Twin Towers, Tower A 50 Jongro 1-gil, Jongno-gu, Seoul 03142, Korea.

(8) Consists of (a) 209,350 shares of common stock held by Dr. Bruhn, of which 56,250 shares are subject to repurchase by us at the original purchase price as of May 1, 2019; and (c) 29,000 shares of common stock underlying options held by Dr. Bruhn exercisable within 60 days of May 1, 2019.

(9) Consists of 209,350 shares of common stock held by Dr. Curnutte, of which 101,250 shares are subject to repurchase by us at the original purchase price as of May 1, 2019.

(10) Mr. Exter is a partner of Third Rock Ventures. Mr. Exter does not have voting or investment power over any of the shares directly held by TRV III and TRV IV referenced in footnote (1) above.

(11) Consists of 500,000 shares of common stock held by Dr. Homcy, of which 85,938 shares are subject to repurchase by us at the original purchase price as of May 1, 2019. Dr. Homcy is a partner of Third Rock Ventures. Dr. Homcy does not have voting or investment power over any of the shares directly held by TRV III and TRV IV referenced in footnote (1) above.

(12) Consists of 22,500 shares of common stock underlying options held by Ms. Shah exercisable within 60 days of May 1, 2019.

(13) See notes 4 through 12 above.

DESCRIPTION OF CAPITAL STOCK

Upon the completion of this offering, our authorized capital stock will consist of shares of common stock, par value $0.0001 per share, and shares of preferred stock, par value $0.0001 per share, all of which will be undesignated, and there will be shares of common stock outstanding and no shares of preferred stock outstanding. As of May 1, 2019, we had approximately 77 record holders of our capital stock. All of our outstanding shares of redeemable convertible preferred stock will convert into shares of our common stock immediately prior to the completion of this offering. In addition, upon the completion of this offering, options to purchase shares of our common stock will be outstanding and shares of our common stock will be reserved for future grants under our equity incentive plans.

The following description of our capital stock and provisions of our amended and restated certificate of incorporation and bylaws are summaries of material terms and provisions and are qualified by reference to our amended and restated certificate of incorporation and bylaws, copies of which have been filed with the SEC as exhibits to the registration statement of which this prospectus is a part. The descriptions of our common stock and preferred stock reflect amendments to our amended and restated certificate of incorporation and bylaws that will become effective immediately prior to the completion of this offering.

Common Stock

Upon the completion of this offering, we will be authorized to issue one class of common stock. Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Except as described under “Anti-takeover Effects of Delaware Law and Provisions of our Amended and Restated Certificate of Incorporation and Bylaws” below, a majority vote of the holders of common stock is generally required to take action under our amended and restated certificate of incorporation and bylaws. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights and no sinking fund provisions are applicable to our common stock. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred stock

Immediately prior to completion of this offering, all outstanding shares of our redeemable convertible preferred stock will be converted into shares of our common stock. Upon the completion of this offering, our board of directors will be authorized, without action by the stockholders, to designate and issue up to an aggregate of shares of preferred stock in one or more series. Our board of directors can designate the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes could, under certain circumstances, have the effect of restricting dividends on our common stock, diluting the voting power of our common stock, impairing the liquidation rights of our common stock, or delaying, deferring or preventing a change in control of our company, which might harm the market price of our common stock. See also “—Anti-takeover effects of Delaware Law and provisions of our amended and restated certificate of incorporation and bylaws—Provisions of our amended and restated certificate of incorporation and bylaws—Undesignated preferred stock” below.

Our board of directors will make any determination to issue such shares based on its judgment as to our company's best interests and the best interests of our stockholders. Upon the completion of this offering, we will have no shares of preferred stock outstanding and we have no current plans to issue any shares of preferred stock following completion of this offering.

Options

As of December 31, 2018, we had outstanding options to purchase 809,200 shares of our common stock, with a per share weighted-average exercise price of $0.29 under our 2015 Plan.

Registration Rights

Upon the completion of this offering, the holders of shares of our common stock, including shares issuable upon the automatic conversion of our redeemable convertible preferred stock, or their permitted transferees, which we refer to as our registrable securities, are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of the investor rights agreement. The investor rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses incurred in connection with registrations under the investor rights agreement will be borne by us, and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand registration rights

Beginning 180 days after the effective date of this registration statement, the holders of our registrable securities are entitled to demand registration rights. Under the terms of our investor rights agreement, we will be required, upon the request of holders of at least a majority of our outstanding registrable securities, to file a registration statement and use commercially reasonable efforts to effect the registration of these shares for public resale. We are required to effect up to two registrations pursuant to this provision of the investor rights agreement.

Short form registration rights

Upon the completion of this offering, the holders of our registrable securities are also entitled to short form registration rights. Pursuant to our investor rights agreement, if we are eligible to file a registration statement on Form S-3, upon the request of holders of at least 20% of our outstanding registrable securities to sell registrable securities with an anticipated aggregate offering amount of at least $5.0 million net of certain expenses related to the offering, we will be required to use our commercially reasonable efforts to effect a registration of such shares. We are required to effect up to two registrations in any twelve month period pursuant to this provision of the investor rights agreement.

Piggyback registration rights

The holders of our registrable securities are entitled to piggyback registration rights. If we register any of our securities either for our own account or for the account of other security holders, the holders of our outstanding registrable securities are entitled to include their shares in the registration. Subject to certain exceptions contained in the investor rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering if the underwriters determine that marketing factors require a limitation of the number of shares to be underwritten.

Indemnification

Our investor rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the

registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expenses of registration

We will pay the registration expenses, subject to certain limited exceptions contained in the investor rights agreement, of the holders of the shares registered pursuant to the demand, short form and piggyback registration rights described above, including the expenses of one counsel for the selling holders.

Expiration of registration rights

The registration rights granted under the investor rights agreement will terminate upon the earlier of (i) a deemed liquidation event, as defined in our amended and restated certificate of incorporation (as in effect prior to the completion of this offering) or certain other events constituting a sale of the company, (ii) at such time after our initial public offering when all registrable securities could be sold under Rule 144 of the Securities Act or a similar exemption without limitation during a three-month period without registration or (iii) the fifth anniversary of our initial public offering.

Anti-Takeover Effects of Delaware Law and Provisions of Our Amended and Restated Certificate of Incorporation and Bylaws

Certain provisions of the Delaware General Corporation Law and of our amended and restated certificate of incorporation and bylaws that will become effective immediately prior to the completion of this offering could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our board of directors. These provisions might also have the effect of preventing changes in our board of directors or management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Delaware takeover statute

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or

- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Provisions of our amended and restated certificate of incorporation and bylaws

Our amended and restated certificate of incorporation and bylaws to be in effect immediately prior to completion of this offering will include a number of provisions that may have the effect of delaying, deferring or discouraging another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board composition and filling vacancies. In accordance with our amended and restated certificate of incorporation, our board is divided into three classes serving staggered three-year terms, with one class being elected each year. Our amended and restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum.

No written consent of stockholders. Our amended and restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholder without holding a meeting of stockholders.

Meetings of stockholders. Our bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements. Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in our bylaws.

Amendment to certificate of incorporation and bylaws. As required by the Delaware General Corporation Law, any amendment of our amended and restated certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our amended and restated certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability and the amendment of our amended and restated certificate of incorporation must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority vote of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated preferred stock. Our amended and restated certificate of incorporation provides for authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our amended and restated certificate of incorporation grants our board of directors' broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Exclusive forum. Our certificate of incorporation provides that the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on behalf of our company, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors or officers to the company or our stockholders, (iii) any action asserting a claim against our company arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or bylaws, (iv) any action to interpret, apply, enforce, or determine the validity of our certificate of incorporation or bylaws, or (v) any action asserting a claim against our company governed by the internal affairs doctrine. This exclusive forum provision will not apply to any causes of action arising under the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Although our certificate of incorporation contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Transfer agent and registrar

The transfer agent and registrar for our common stock is . The transfer agent and registrar's address is .

Listing

We intend to apply to list our common stock on The Nasdaq Global Market under the symbol "PLRX."

Limitations of liability and indemnification matters

For a discussion of liability and indemnification, see the section entitled "Management — Limitation on liability and indemnification matters."

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Sale of Restricted Shares

Based on the number of shares of common stock outstanding as of May 1, 2019, upon completion of this offering, shares of common stock will be outstanding, assuming no exercise by the underwriters of their option to purchase additional shares and no exercise of options. All of the shares sold in this offering will be freely tradable. The remaining shares of common stock outstanding after this offering will be restricted as a result of securities laws or lock-up agreements as described below. Following the expiration of the lock-up period, all shares will be eligible for resale in compliance with Rule 144 or Rule 701 under the Securities Act. “Restricted securities” as defined under Rule 144 of the Securities Act were issued and sold by us in reliance on exemptions from the registration requirements of the Securities Act. These shares may be sold in the public market only if registered or qualified for an exemption from registration, such as under Rule 144 or Rule 701 under the Securities Act.

Rule 144

In general, a person who has beneficially owned restricted stock for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Persons who have beneficially owned restricted shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares then outstanding, which will equal approximately shares immediately after this offering assuming no exercise of the underwriters’ option to purchase additional shares, based on the number of shares outstanding as of May 1, 2019; or
- the average weekly trading volume of our common stock on The Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

Rule 701

Rule 701 under the Securities Act, or Rule 701, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and under “Underwriting” included elsewhere in this prospectus and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

Lock-up Agreements

In connection with this offering, we, each of our directors and executive officers, and holders of substantially all of our securities have agreed with the underwriters that for a period of 180 days following the date of this prospectus, subject to certain exceptions, we and they will not offer, sell, assign, transfer, pledge, contract to sell or otherwise dispose of or hedge any shares of our common stock or any securities convertible into or exchangeable for shares of our common stock. The representatives of the underwriters may, in their sole discretion, at any time, release all or any portion of the shares from the restrictions in this agreement.

Rule 10b5-1 Trading Plans

Following the completion of this offering, certain of our officers, directors and significant stockholders may adopt written plans, known as Rule 10b5-1 trading plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis to diversify their assets and investments. Under these 10b5-1 trading plans, a broker may execute trades pursuant to parameters established by the officer, director or stockholder when entering into the plan, without further direction from such officer, director or stockholder. Such sales would not commence until the expiration of the applicable lock-up agreements entered into by such officer, director or stockholder in connection with this offering.

Registration Rights

We are party to an investor rights agreement which provides that holders holding shares of our common stock, including shares issuable upon the automatic conversion of our redeemable convertible preferred stock, have the right to demand that we file a registration statement or request that their shares of our common stock be covered by a registration statement that we are otherwise filing. See the section entitled “Description of Capital Stock — Registration Rights” in this prospectus. Except for shares purchased by affiliates, registration of their shares under the Securities Act would result in these shares becoming freely tradable without restriction under the Securities Act immediately upon effectiveness of the registration, subject to the expiration of the lock-up period described above and in the section entitled “Underwriting” in this prospectus, and to the extent such shares have been released from any repurchase option that we may hold.

Equity Incentive Plans

As soon as practicable after the completion of this offering, we intend to file a Form S-8 registration statement under the Securities Act to register shares of our common stock subject to options and other equity awards outstanding or reserved for issuance under our equity incentive plans. This registration statement will become effective immediately upon filing, and shares covered by this registration statement will thereupon be eligible for sale in the public markets, subject to Rule 144 limitations applicable to affiliates and any lock-up agreements. For a more complete discussion of our equity incentive plans, see “Executive and Compensation — Employee Benefits and Equity Compensation Plans.”

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

- a non-resident alien individual;
- a foreign corporation or any other foreign organization taxable as a corporation for U.S. federal income tax purposes; or
- a foreign estate or trust, the income of which is not subject to U.S. federal income tax on a net income basis.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code, generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances including the alternative minimum tax, or the Medicare tax on net investment income, the rules regarding qualified small business stock within the meaning of Section 1202 of the Code and any election to apply Section 1400Z-2 of the Code to gains recognized with respect to shares of our common stock. This discussion also does not address any U.S. state, local or non-U.S. taxes or any other aspect of any U.S. federal tax other than the income tax. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt or governmental organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- "qualified foreign pension funds," or entities wholly owned by a "qualified foreign pension fund";
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and partners and investors therein);

- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- persons who have elected to mark securities to market;
- persons who have a functional currency other than the U.S. dollar;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- certain U.S. expatriates; and
- persons subject to special tax accounting rules as a result of any item of gross income with respect to the common stock being taken into account in an applicable financial statement under Section 451(b) of the Code.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on our common stock

Distributions, if any, on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on sale or other taxable disposition of our common stock." Any such distributions will also be subject to the discussions below under the sections titled "Backup withholding and information reporting" and "Withholding and information reporting requirements—FATCA."

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence. If we or another withholding agent apply over-withholding or if a non-U.S. holder does not timely provide us with the required certification, the non-U.S. holder may be entitled to a refund or credit of any excess tax withheld by timely filing an appropriate claim with the IRS.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) to the applicable withholding agent and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing a U.S. tax return with the IRS.

Gain on sale or other taxable disposition of our common stock

Subject to the discussions below under "Backup withholding and information reporting" and "Withholding and information reporting requirements—FATCA," a non-U.S. holder generally will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale or other taxable disposition of shares of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on Our Common Stock" also may apply;
- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or
- we are, or have been, at any time during the five-year period preceding such sale of other taxable disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation," unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup withholding and information reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in "Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of

information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and information reporting requirements — FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, generally imposes a U.S. federal withholding tax at a rate of 30% on payments of dividends on our common stock paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Under applicable U.S. Treasury regulations, withholding under FATCA currently applies to payments of dividends on our common stock. Currently proposed U.S. Treasury Regulations provide that FATCA withholding does not apply to gross proceeds from the disposition of property of a type that can produce U.S. source dividends or interest; however, prior versions of the rules would have made such gross proceeds subject to FATCA withholding. Taxpayers (including withholding agents) can currently rely on the proposed Treasury Regulations. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

UNDERWRITING

Citigroup Global Markets Inc., Cowen and Company, LLC and Piper Jaffray & Co. are acting as joint book-running managers of this offering and as representatives of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus, each underwriter named below has severally agreed to purchase, and we have agreed to sell to that underwriter, the number of shares of common stock set forth opposite the underwriter's name in the following table.

Underwriters	Number of Shares
Citigroup Global Markets Inc.	
Cowen and Company, LLC	
Piper Jaffray & Co.	
Needham & Company, LLC	
Total	

The underwriting agreement provides that the obligations of the underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the shares (other than those covered by the underwriters' option to purchase additional shares described below) if they purchase any of the shares.

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus. Any shares sold by the underwriters to securities dealers may be sold at a discount from the initial public offering price not to exceed $ per share. If all the shares are not sold at the initial offering price, the underwriters may change the offering price and the other selling terms. The representatives have advised us that the underwriters do not intend to make sales to discretionary accounts.

If the underwriters sell more shares than the total number set forth in the table above, we have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to additional shares at the public offering price less the underwriting discount. The underwriters may exercise the option solely for the purpose of covering over-allotments, if any, in connection with this offering. To the extent the option is exercised, each underwriter must purchase a number of additional shares approximately proportionate to that underwriter's initial purchase commitment. Any shares issued or sold under the option will be issued and sold on the same terms and conditions as the other shares that are the subject of this offering.

We, our officers, directors and holders of substantially all of our securities have agreed that, subject to specified limited exceptions, for a period of 180 days from the date of this prospectus, we and they will not, without the prior written consent of the representatives, dispose of or hedge any shares or any securities convertible into or exchangeable for shares of our common stock. The representatives, in their sole discretion, may release any of the securities subject to these lock-up agreements at any time, which, in the case of officers and directors, shall be with notice.

Prior to this offering, there has been no public market for our shares. Consequently, the initial public offering price for the shares will be determined by negotiations between us and the representatives. Among the factors considered in determining the initial public offering price will be our results of operations, our current financial condition, our future prospects, our markets, the economic conditions in and future prospects for the industry in which we compete, our management and currently prevailing general conditions in the equity securities markets, including current market valuations of publicly traded companies considered comparable to our company. We cannot ensure however, that the price at which the shares will sell in the public market after this offering will not be lower than the initial public offering price or that an active trading market in our shares will develop and continue after this offering.

We intend to apply to have our shares listed on the Nasdaq Global Market under the symbol “PLRX”.

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters’ option to purchase additional shares.

	Paid by Pliant Therapeutics, Inc.	
	No Exercise	Full Exercise
Per share	$	$
Total	$	$

We estimate that our portion of the total expenses of this offering will be $. We have also agreed to reimburse the underwriters for certain FINRA-related and other expenses incurred by them in connection with this offering in an amount up to $.

In connection with the offering, the underwriters may purchase and sell shares in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the option to purchase additional shares, and stabilizing purchases.

- Short sales involve secondary market sales by the underwriters of a greater number of shares than they are required to purchase in the offering.
  - “Covered” short sales are sales of shares in an amount up to the number of shares represented by the underwriters’ option to purchase additional shares.
  - “Naked” short sales are sales of shares in an amount in excess of the number of shares represented by the underwriters’ option to purchase additional shares.
- Covering transactions involve purchases of shares either pursuant to the underwriters’ option to purchase additional shares or in the open market in order to cover short positions.
  - To close a naked short position, the underwriters must purchase shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.
  - To close a covered short position, the underwriters must purchase shares in the open market or must exercise the option to purchase additional shares. In determining the source of shares to close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.
- Stabilizing transactions involve bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the shares to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

Relationships

The underwriters are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal

investment, hedging, financing and brokerage activities. The underwriters and their respective affiliates may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans and credit default swaps) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and short positions in such securities and instruments.

Affiliates of Cowen and Company, LLC purchased 10,895,619 shares of our Series B redeemable convertible preferred stock in our July 2018 Series B redeemable convertible preferred stock financing. Those shares of Series B redeemable convertible preferred stock will automatically convert into shares of common stock immediately prior to and in connection with the completion of this offering.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area, no offer of shares which are the subject of the offering has been, or will be made to the public in that Member State, other than under the following exemptions under the Prospectus Directive:

i) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

ii) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the representatives for any such offer; or

iii) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares referred to in (i) to (iii) above shall result in a requirement for the company or any representative to publish a prospectus pursuant to Article 3 of the Prospectus Directive, or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person located in a Member State to whom any offer of shares is made or who receives any communication in respect of an offer of shares, or who initially acquires any shares will be deemed to have represented, warranted, acknowledged and agreed to and with each representative and the company that (i) it is a “qualified investor” within the meaning of the law in that Member State implementing Article 2(1)(e) of the Prospectus Directive; and (ii) in the case of any shares acquired by it as a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, the shares acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the representatives has been given to the offer or resale; or where shares have been acquired by it on behalf of persons in any Member State other than qualified investors, the offer of those shares to it is not treated under the Prospectus Directive as having been made to such persons.

The company, the representatives and their respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgments and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers

of shares. Accordingly any person making or intending to make an offer in that Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the company or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the company nor the representatives have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the company or the representatives to publish a prospectus for such offer. For the purposes of this provision, the expression an "offer of shares to the public" in relation to any shares in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (as amended) and includes any relevant implementing measure in each Member State.

The above selling restriction is in addition to any other selling restrictions set out below.

Notice to Prospective Investors in the United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated (each such person being referred to as a "relevant person").

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Notice to Prospective Investors in France

Neither this prospectus nor any other offering material relating to the shares described in this prospectus has been submitted to the clearance procedures of the *Autorité des Marchés Financiers* or of the competent authority of another member state of the European Economic Area and notified to the *Autorité des Marchés Financiers*. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus nor any other offering material relating to the shares has been or will be:

- released, issued, distributed or caused to be released, issued or distributed to the public in France; or
- used in connection with any offer for subscription or sale of the shares to the public in France.

Such offers, sales and distributions will be made in France only:

- to qualified investors (*investisseurs qualifiés*) or to a restricted circle of investors (*cercle restreint d'investisseurs*), in each case investing for their own account, all as defined in, and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French *Code monétaire et financier*;
- to investment services providers authorized to engage in portfolio management on behalf of third parties; or
- in a transaction that, in accordance with article L.411-2-II-1° -or-2° -or 3° of the French *Code monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l'épargne*).

The shares may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French *Code monétaire et financier*.

Notice to Prospective Investors in Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to professional investors, as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong ("SFO") and any rules made under that Ordinance; or in other circumstances which do not result in the document being a prospectus, as defined in the Companies Ordinance (Cap. 32) of Hong Kong ("CO") or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors, as defined in the SFO and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Notice to Prospective Investors in Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the initial purchaser will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Notice to Prospective Investors in Singapore

This prospectus has not been and will not be lodged or registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever

described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- where no consideration is or will be given for the transfer;
- where the transfer is by operation of law;
- as specified in Section 276(7) of the SFA; or
- as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Solely for the purposes of its obligations pursuant to Section 309B of the SFA, we have determined, and hereby notify all relevant persons (as defined in the CMP Regulations 2018), that the shares are "prescribed capital markets products" (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Notice to Prospective Investors in Australia

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

You confirm and warrant that you are either:

- a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the Company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
- a person associated with the Company under Section 708(12) of the Corporations Act; or
- a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the securities issued to you pursuant to this prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for us by Goodwin Procter LLP, Redwood City, California. Certain legal matters in connection with our patents and intellectual property interests will be passed upon for us by Morrison Foerster LLP, San Francisco, California. Legal matters in connection with the offering will be passed upon for the underwriters by Cooley LLP, San Francisco, California.

EXPERTS

The financial statements included in this prospectus have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report appearing herein (which report expresses an unqualified opinion on the financial statements and includes an explanatory paragraph referring to the Company's ability to continue as a going concern as described in Note 2). Such financial statements have been so included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock being offered by this prospectus, which constitutes a part of the registration statement. This prospectus does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the common stock offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at www.sec.gov. Upon completion of this offering, we will be subject to the information reporting requirements of the Exchange Act, and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available via the SEC's website at www.sec.gov. We also maintain a website at www.plianttrx.com, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. However, the information contained in or accessible through our website is not part of this prospectus or the registration statement of which this prospectus forms a part, and investors should not rely on such information in making a decision to purchase our common stock in this offering.

Pliant Therapeutics, Inc.
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Pliant Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Pliant Therapeutics, Inc. (the "Company") as of December 31, 2017 and 2018, the related statements of operations, redeemable convertible preferred stock and stockholders' deficit, and cash flows, for each of the two years in the period ended December 31, 2018, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2018, in conformity with accounting principles generally accepted in the United States of America.

Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 2 to the financial statements, the Company has suffered recurring losses from operations and has forecasted cash needs in excess of current liquidity that raises substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 2. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

San Jose, CA
May 10, 2019

We have served as the Company's auditor since 2018.

Pliant Therapeutics, Inc.
Balance Sheets

(In thousands, except share and per share amounts)	As of December 31, 2017	As of December 31, 2018	Pro Forma as of December 31, 2018 (unaudited)
Assets			
Current assets			
Cash and cash equivalents	$ 4,251	$ 60,949	$
Tax credit receivable	250	500	
Prepaid expenses and other current assets	206	284	
Total current assets	4,707	61,733	
Property and equipment, net	1,846	4,260	
Other non-current assets	—	536	
Total assets	$ 6,553	$ 66,529	
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Deficit			
Current liabilities			
Accounts payable	$ 1,594	$ 2,576	
Accrued liabilities	1,594	2,508	
Total current liabilities	3,188	5,084	
Other long term liabilities	20	811	
Total liabilities	3,208	5,895	
Commitments and Contingencies (Note 13)			
Series A redeemable convertible preferred stock, $0.0001 par value; 62,500,000 and 56,000,000 shares authorized at December 31, 2017 and 2018, respectively; 36,500,000 and 56,000,000 shares issued and outstanding, at December 31, 2017 and 2018, respectively; aggregate liquidation preference of $39,910 and $61,516 at December 31, 2017 and 2018, respectively; shares issued and outstanding pro forma (unaudited)	39,910	61,516	$
Series B redeemable convertible preferred stock, $0.0001 par value; no shares and 58,109,973 shares authorized at December 31, 2017 and 2018, respectively; no shares and 49,501,221 shares issued and outstanding at December 31, 2017 and 2018, respectively; aggregate liquidation preference of $0 and $70,587 at December 31, 2017 and December 31, 2018, respectively; shares issued and outstanding pro forma (unaudited)	—	70,587	$
Stockholders' deficit:			
Common stock, $0.0001 par value; 80,500,000 and 147,682,655 shares authorized at December 31, 2017 and 2018; and 7,171,605 and 9,745,453 shares issued and outstanding at December 31, 2017 and 2018, respectively; shares issued and outstanding, pro forma (unaudited)	1	1	
Additional paid-in capital	—	—	
Accumulated deficit	(36,566)	(71,470)	
Total stockholders' deficit	(36,565)	(71,469)	$
Total liabilities, redeemable convertible preferred stock and stockholders' deficit	$ 6,553	$ 66,529	

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

Pliant Therapeutics, Inc.
Statements of Operations

(In thousands, except share and per share amounts)	Years Ended December 31, 2017	2018
Operating expenses:		
Research and development	$ 14,526	$ 24,415
General and administrative	3,823	6,500
Total operating expenses	18,349	30,915
Loss from operations	(18,349)	(30,915)
Interest income	16	688
Other expense, net	—	(49)
Net loss	$ (18,333)	$ (30,276)
Accretion to redemption value and cumulative dividends on redeemable convertible preferred stock	$ (2,289)	$ (4,876)
Net loss attributable to common stockholders	$ (20,622)	$ (35,152)
Net loss per share, attributable to common stockholders, basic and diluted	$ (3.59)	$ (4.22)
Shares used in computing net loss per share attributable to common stockholders, basic and diluted	5,745,000	8,333,000
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		$
Shares used in computing pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		

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

Pliant Therapeutics, Inc.
Statements of Redeemable Convertible Preferred Stock and Stockholders' Deficit

(In thousands, except share amounts)	Redeemable Convertible Preferred Stock				Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Deficit
	Series A		Series B						
	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at December 31, 2016	16,500,000	$17,621	—	$ —	4,512,336	$ —	$ —	$ (15,998)	$ (15,998)
Issuance of Series A redeemable preferred stock	20,000,000	20,000							
Vesting of founders' common stock and restricted stock awards	—	—	—	—	2,659,269	1	21	—	22
Accretion to redemption value and cumulative dividends on redeemable convertible preferred stock		2,289					(54)	(2,235)	(2,289)
Stock-based compensation expense							33		33
Net loss	—	—	—	—	—	—	—	(18,333)	(18,333)
Balance at December 31, 2017	36,500,000	39,910	—	—	7,171,605	1	—	(36,566)	(36,565)
Issuance of Series A redeemable preferred stock, net of issuance costs of $16	19,500,000	19,484						—	—
Issuance of Series B redeemable preferred stock, net of issuance costs of $315	—	—	49,501,221	67,833	—	—	—		—
Vesting of founders' common stock and restricted stock awards	—	—	—	—	2,573,848	—	20	—	20
Accretion to redemption value and cumulative dividends on redeemable convertible preferred stock		2,122	—	2,754			(248)	(4,628)	(4,876)
Stock-based compensation expense							228		228
Net loss	—	—	—	—	—	—	—	(30,276)	(30,276)
Balance at December 31, 2018	56,000,000	$61,516	49,501,221	$70,587	9,745,453	$ 1	$ —	$ (71,470)	$ (71,469)

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

Pliant Therapeutics, Inc.
Statements of Cash Flows

(In thousands)	Years Ended December 31, 2017	2018
Cash flows from operating activities		
Net loss	$ (18,333)	$ (30,276)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	292	666
Stock-based compensation expense	33	228
Changes in operating assets and liabilities:		
Tax credit receivable	(250)	(250)
Prepaid expenses and other current assets	(131)	(78)
Other non-current assets	142	(505)
Accounts payable	441	760
Accrued liabilities	882	776
Deferred rent	—	351
Net cash used in operating activities	(16,924)	(28,328)
Cash flows from investing activities		
Purchase of property and equipment	(1,405)	(2,323)
Net cash used in investing activities	(1,405)	(2,323)
Cash flows from financing activities		
Proceeds from issuance of Series A preferred stock, net of issuance costs	20,000	19,484
Proceeds from issuance of Series B preferred stock, net of issuance costs	—	67,833
Proceeds from the issuance of restricted common stock	18	32
Repurchase of unvested common stock	(12)	—
Net cash provided by financing activities	20,006	87,349
Net increase in cash and cash equivalents	1,677	56,698
Cash and cash equivalents at beginning of period	2,574	4,251
Cash and cash equivalents at end of period	$ 4,251	$ 60,949
Supplemental disclosures of noncash investing and financing activities:		
Purchase of property and equipment in accounts payable and accrued liabilities	107	191
Reclassification of restricted stock awards from liabilities to common stock upon vesting	22	20
Accretion to redemption value and cumulative dividends on redeemable convertible preferred stock	2,289	4,876
Tenant improvement paid for by the landlord	—	566
Deferred offering costs in accounts payable and accrued liabilities	—	31

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

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1. Description of Business

Pliant Therapeutics, Inc. (the "Company") is a clinical stage biopharmaceutical company focused on discovering and developing novel therapies for the treatment of fibrosis with an initial focus on treating fibrosis by inhibiting integrin-mediated activation of TGF-ß. Fibrosis refers to the abnormal thickening and scarring of connective tissue due to the production and deposition of excess collagen in the extra-cellular matrix. Fibrosis can occur in many different tissues including lung, liver, kidney, muscle, skin and the GI tract, and often causes severe and debilitating disease leading to organ failure. The Company is located in South San Francisco, California, and was incorporated in the state of Delaware in June 2015.

2. Going Concern

The Company has devoted substantially all its efforts to organizing and staffing, business planning, raising capital and developing its technology and preclinical assets since its inception. The Company has funded its operations primarily with the net proceeds from the issuance of redeemable convertible preferred stock. The Company expects to continue to incur significant losses and require significant additional capital to advance its clinical and preclinical development programs, support its operations and business development efforts.

The Company has incurred net losses and negative cash flows from operations since inception and had an accumulated deficit of $71.5 million as of December 31, 2018 and cash used in operations of $28.3 million during the year ended December 31, 2018. As of December 31, 2018, the Company had cash and cash equivalents of $60.9 million. Based on its current forecast the Company does not have sufficient cash and cash equivalents for at least the next year following the date that the financial statements are issued. These conditions raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued.

Management plans to raise additional capital through a combination of preferred stock equity financing, public equity offerings and strategic transactions, however, there can be no assurance that the Company will be able to complete financing or equity offerings on acceptable terms, or in amounts required to support its operations, if at all, or identify and enter into any strategic transactions that will bring the capital that it will require.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business, and do not include any adjustments relating to recoverability and classification of recorded assets amounts or the amounts and classification of liabilities that might be necessary should we be unable to continue as a going concern.

3. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP").

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, and expenses as well as the disclosure of contingent assets and liabilities as of and during the reporting period. The Company bases its

Pliant Therapeutics, Inc.
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estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. Significant estimates and assumptions reflected in these financial statements include, but are not limited to, useful lives assigned to property and equipment, the fair values of common and redeemable convertible preferred stock, stock-based compensation expense, accruals for research and development costs, income taxes and uncertain tax positions. The Company assesses estimates on an ongoing basis; however, actual results could materially differ from those estimates.

Fair Value Measurements

Fair value accounting is applied for all financial assets and liabilities and non-financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually). The carrying amount of the Company's financial instruments, including cash equivalents, prepaid expenses and other current assets, accounts payable and accrued liabilities approximate fair value due to their short-term maturities.

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash and cash equivalents and short-term investments. The Company invests in money market funds, treasury bill and notes and government notes. The Company limits its credit risk associated with its cash and cash equivalents by placing them with banks and institutions it believes are highly credit worthy and in highly rated investments.

The Company's future results of operations involve several other risks and uncertainties. Factors that could affect the Company's future operating results and cause actual results to vary materially from expectations include, but are not limited to, uncertainty of results of clinical trials and reaching milestones, uncertainty of regulatory approval of the Company's product candidates, uncertainty of market acceptance of the Company's product candidates, competition from substitute products, including those that may be developed or marketed by larger companies, securing and protecting intellectual property, strategic relationships and dependence on key individuals and sole source suppliers.

The Company's product candidates require approvals from the U.S Food and Drug Administration ("FDA") and comparable foreign regulatory agencies prior to commercial sales in their respective jurisdictions. There can be no assurance that any product candidates will receive the necessary approvals. If the Company was denied approval, approval was delayed or the Company was unable to maintain approval for any product candidate, it could have a materially adverse impact on the Company.

Segments

The Company operates and manages its business as one reportable and operating segment, which is the business of developing and commercializing novel therapies for fibrotic diseases. The Company's chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for allocating and evaluating financial performance. All long-lived assets are maintained in the United States of America.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with original maturities of three months or less from the purchase date to be cash equivalents. Cash equivalents consist primarily of amounts invested in treasury and government securities (collectively "money market funds") and are stated at fair value.

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Property and Equipment, Net

Property and equipment are recorded at cost net of accumulated depreciation and amortization. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the assets. The useful lives of property and equipment are as follows:

Laboratory equipment	5 years
Computer equipment and software	3 years
Leasehold improvements	Shorter of remaining lease term or estimated useful life

Upon retirement or sale of the assets, the cost and related accumulated depreciation and amortization are removed from the balance sheets and the resulting gain or loss is recorded to the statements of operations. Repairs and maintenance are expensed as incurred.

Impairment of Long-Lived Assets

Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to future net cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, an impairment charge is recognized by the amount by which the carrying amount of the asset exceeds the fair value of the asset. There was no impairment of long-lived assets during the years ended December 31, 2017 and 2018.

Redeemable Convertible Preferred Stock

The Company classifies redeemable convertible preferred stock outside of stockholders' deficit because, upon the occurrence of certain change in control events that are outside the Company's control, including liquidation, sale or transfer of the Company's assets, holders of the redeemable convertible preferred stock can cause redemption for cash. At any time on or after July 10, 2023, the holders of a majority of the outstanding redeemable convertible preferred stock can also require the Company to redeem the redeemable convertible preferred stock by providing the Company a written notice requesting such redemption. The Company recognizes changes in the redemption value immediately as they occur, for example changes in fair value of preferred stock, and adjusts the carrying amount of the redeemable convertible preferred stock to equal the redemption value at the end of each reporting period. In the absence of retained earnings these accretion charges are recorded against additional paid in capital, if any, and then to accumulated deficit. The Company analyzed all embedded derivatives and beneficial conversion features in issued redeemable convertible preferred stock and concluded that none requires bifurcation and recording under relevant accounting standards.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses consist primarily of personnel costs for the Company's research and product development employees. Also included are non-personnel costs such as fees paid to consultants and third parties for preclinical and clinical studies, research and development services, laboratory supplies and equipment maintenance costs, license costs, contract manufacturing costs and allocations of facilities related costs.

The Company estimates preclinical and clinical studies and research expenses based on the services performed, pursuant to contracts with research institutions that conduct and manage preclinical and clinical

studies and research services on its behalf. The Company estimates these expenses based on discussions with internal management personnel and external service providers as to the progress or stage of completion of services and the contracted fees to be paid for such services. If the actual timing of the performance of services or the level of effort varies from the original estimates, the Company will adjust the accrual accordingly. Payments made to third parties under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and are expensed over the time when services are rendered.

Payments associated with licensing agreements to acquire exclusive licenses to develop, use, manufacture and commercialize products that have not reached technological feasibility and do not have alternate commercial use are expensed as incurred.

Tax Credit Receivable

The Company is eligible for federal and California research and development credits for its research and development activities performed within the United States and California, respectively. The credits are generally available to offset federal and California income tax liabilities. The Company has applied $250,000 of federal research and development credits to offset its federal payroll tax expenses for the years ended December 31, 2017 and 2018 due to its small business status.

Stock-Based Compensation

The Company's stock-based equity awards include restricted stock awards and stock options that are granted to employees and consultants and accounted at fair value on the award grant date. Stock-based compensation expense is recognized over the awards' vesting period on a straight-line basis and recorded as either research and development or general and administrative expenses in the statements of operations based on the function to which the related services are provided. Forfeitures are accounted for as they occur.

The Company adopted the Accounting Standards Update ("ASU") No. 2018-07, "*Compensation—Stock Compensation ("Topic 718"): Improvements to Nonemployee Share-Based Payment Accounting*, as discussed below under "Recently Adopted Accounting Pronouncements," as of January 1, 2017. The measurement date for non-employee awards was generally the date when the services were completed, resulting in financial reporting period adjustments to stock-based compensation expense during the vesting term for changes in the fair value of the awards. After the adoption of ASU No. 2018-07, the measurement date for non-employee awards is the later of the adoption date of ASU No. 2018-07 or the grant date, without changes in the fair value of the award.

The Black-Scholes option-pricing model requires the use of the following assumptions:

- *Expected term*—The expected term represents the period that the stock-based awards are expected to be outstanding. The expected term for the Company's stock options was calculated based on the weighted-average vesting term of the awards and the contract period, or simplified method.
- *Expected volatility*—Since the Company is not yet a public company and does not have any trading history for its common stock, the expected volatility was estimated based on the average historical volatilities of common stock of comparable publicly traded entities over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their size, stage in the life cycle or area of specialty. The Company will continue to apply this process until enough historical information regarding the volatility of its stock price becomes available.
- *Risk-free interest rate*—The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the expected term of the awards.

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- *Expected dividend*—The Company has never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

The fair value of the common stock has been determined using independent third-party valuations based on relevant valuation methodologies as outlined in the American Institute of Certified Public Accountants (AICPA) Practice Aid, "*Valuation of Privately-Held-Company Equity Securities Issued as Compensation*". The Company also considered the amount of time between the independent third-party valuation dates and the grant dates and used interpolation of the fair value between the two valuation dates to estimate common stock fair value at each grant date. This determination included an evaluation of whether the subsequent valuation indicated that any significant change in valuation had occurred between the previous valuation and the grant date.

Deferred Offering Costs

Deferred offering costs, consisting of direct legal, accounting, filing and other fees directly related to the Company's proposed initial public offering ("IPO") are capitalized. The deferred offering costs will be reclassified to additional paid in capital upon completion of the IPO. No amounts were deferred as of December 31, 2017. The Company deferred $0.2 million as of December 31, 2018, which is recorded as other non-concurrent assets in the balance sheets. In the event the IPO is aborted, including postponement of 90 days or greater, all capitalized deferred offering costs will be expensed.

Leases and Rent Expense

The Company records rent expense on a straight-line basis over the life of the lease. In cases where there is a free rent period or future fixed rent escalations, the Company records a deferred rent liability. Additionally, the receipt of any lease incentives is recorded as a deferred rent liability which is amortized over the lease term as a reduction of rent expense. Building improvements made with the lease incentives or tenant allowances are capitalized as leasehold improvements and included in property and equipment in the balance sheets.

Income Taxes

The Company provides for income taxes under the asset and liability method. Current income tax expense or benefit represents the amount of income taxes expected to be payable or refundable for the current year. Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax basis of assets and liabilities and net operating loss and credit carryforwards and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all the tax benefits will not be realized.

The Company accounts for uncertain tax positions in accordance with ASC No. 740-10, *Accounting for Uncertainty in Income Taxes*. The Company assesses all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and the Company will determine whether (i) the factors underlying the sustainability assertion have changed and (ii) the amount of the recognized tax benefit is still appropriate. The recognition and measurement of tax benefits requires significant judgment. Judgments concerning the recognition and measurement of a tax benefit might change as new information becomes available.

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The Company includes any penalties and interest expense related to income taxes as a component of income tax expense, as necessary.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' deficit that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2017 and 2018 there was no difference between net loss and comprehensive loss in the accompanying financial statements.

Net Loss Per Share

Basic net loss per share is computed by dividing net loss attributed to common stockholders by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is computed using the weighted-average number of shares of common stock outstanding during the period and, if dilutive, the weighted-average number of potential shares of common stock. Net loss per share attributable to common stockholders is calculated using the two-class method, which is based on an earnings allocation formula that determines net loss per share for the Company's common stockholders and holders of participating securities. The Company's redeemable convertible preferred stock contains participation rights in any dividend paid by the Company and is deemed to be a participating security. Net loss attributable to common stockholders and participating preferred shares are allocated to each share on an as-converted basis as if all the earnings for the period had been distributed. The participating securities do not include a contractual obligation to share in losses of the Company and are not included in the calculation of net loss per share in the periods in which a net loss is recorded.

Diluted net loss per share is computed using the more dilutive of (a) the two-class method or (b) the as-converted method. The Company allocates earnings first to redeemable convertible preferred shares stockholders based on dividend rights and then to common and preferred stockholders based on ownership interests. The weighted-average number of shares of common stock included in the computation of diluted net loss gives effect to all potentially dilutive common equivalent shares, including outstanding stock options and preferred stock.

Common stock equivalent shares are excluded from the computation of diluted net loss per share if their effect is antidilutive. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is generally the same as basic net loss per share attributable to common stockholders since dilutive common shares are not assumed to have been issued if their effect is antidilutive. The Company reported a net loss attributable to common stockholders for the years ended December 31, 2017 and 2018.

Unaudited Pro Forma Information

Immediately prior to the completion of the Company's IPO resulting in net proceeds of at least $45.0 million to the Company all outstanding shares of redeemable convertible preferred stock will automatically convert into common stock. Unaudited pro forma balance sheet information as of December 31, 2018, assumes the conversion of all outstanding redeemable convertible preferred stock into shares of common stock. The shares of common stock issuable and the proceeds expected to be received in the IPO are excluded from such pro forma financial information.

The unaudited pro forma net loss per share for the year ended December 31, 2018 was computed using the weighted-average number of shares of common stock outstanding, including the pro forma effect of the

conversion of all outstanding shares of redeemable convertible preferred stock, as if such conversion had occurred at the beginning of the period, or their issuance dates, if later. The unaudited pro forma net loss per share does not include the shares expected to be sold and related proceeds to be received from the IPO. Net loss attributable to common stockholders used in the unaudited pro forma net loss per share calculation was adjusted for the accretion of redeemable convertible preferred stock, as preferred stock is not considered outstanding prior to the closing of the IPO.

Recently Adopted Accounting Pronouncements

The Company is an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 ("JOBS Act"), and may take advantage of reduced reporting requirements that are otherwise applicable to public companies. Section 107 of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies are required to comply with those standards. The Company has elected to use the extended transition period for complying with new or revised accounting standards with certain exceptions that follow; and as a result of this election, its financial statements may not be comparable to companies that comply with public company effective dates.

In May 2014, the Financial Accounting Standards Board ("FASB"), issued ASU No. 2014-09, *Revenue from Contracts with Customers*. In August 2015, the FASB issued ASU No. 2015-14, *Revenue from Contracts with Customers: Deferral of the Effective date*, which delayed the effective date of ASU No. 2014-09 by one year. The objective of this update is to provide a single, comprehensive revenue recognition model for all contracts with customers to improve comparability within industries, across industries, and across capital markets. This standard update contains principles that the Company will apply to determine the measurement of revenue and timing of when it is recognized. ASU No. 2014-09, as amended, is effective for annual periods beginning after December 15, 2018 for public entities. Early adoption was permitted based on ASU No. 2014-09 original adoption date. The Company adopted ASU No. 2014-09 as amended on of January 1, 2017. As the Company does not generate any revenues and does not have other agreements with customers, the new standard adoption did not have any impact on the Company's financial statements.

In March 2016, the FASB issued ASU No. 2016-09, *Improvements to Employee Share-Based Payment Accounting*, which simplifies share-based payment accounting through a variety of amendments. The Company elected to record forfeitures as they occur for all periods presented. Adoption of ASU No. 2016-09 did not have a material impact on the Company's financial statements.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations ("Topic 805"): Clarifying the Definition of a Business*, which changes the definition of a business to assist entities with evaluating when a set of transferred assets and activities is deemed to be a business. Determining whether a transferred set of assets and activities constitutes a business is important because the accounting for a business combination differs from that of an asset acquisition. The definition of a business also affects the accounting for dispositions. Under the new standard, when substantially all the fair value of assets acquired is concentrated in a single asset, or a group of similar assets, the assets acquired would not represent a business and business combination accounting would not be required. The new standard may result in more transactions being accounted for as asset acquisitions rather than business combinations. The standard is effective for public entities for interim and annual periods beginning after December 15, 2017 and shall be applied prospectively. Early adoption is permitted. The Company elected to early adopt ASU No. 2017-01 on January 1, 2017 and will apply the new guidance to applicable future transactions.

In June 2018, the FASB issued ASU No. 2018-07, which amends and expands the scope of ASC 718, *Compensation—Stock Compensation*, (which currently only includes accounting guidance for share-based

awards granted to employees) to include share-based awards issued to nonemployees for goods or services. Consequently, the accounting for share-based awards to nonemployees and employees will be substantially aligned. The ASU supersedes Subtopic 505-50, *Equity—Equity-Based Payments to Non-Employees*. This standard is effective for public companies for annual periods beginning after December 15, 2018, including interim periods within those fiscal years, with early adoption permitted if ASU No. 2014-09 has been adopted by an entity. The Company early adopted ASU No. 2018-07 as of January 1, 2017, which did not have a material impact on the Company's financial statements.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases ("Topic 842")*, which requires an entity to recognize assets and liabilities arising from a lease for both financing and operating leases. For public entities, ASU No. 2016-02 is effective for fiscal years beginning after December 15, 2018. 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. As a result of the Company having elected the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the JOBS Act, ASU No. 2016-02 is effective for the Company in the fiscal years beginning after December 15, 2019, with early adoption permitted. The Company is currently in the process of evaluating the impact of the adoption of ASU No. 2016-02 on the Company's financial statements.

4. Fair Value Measurements

Assets and liabilities recorded at fair value on a recurring basis in the balance sheets, as well as assets and liabilities measured at fair value on a non-recurring basis or disclosed at fair value, are categorized based upon the level of judgment associated with inputs used to measure their fair values. The accounting guidance for fair value provides a framework for measuring fair value and requires certain disclosures about how fair value is determined. Fair value is defined as the price that would be received upon the sale of an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the measurement date. The accounting guidance also establishes a three-level valuation hierarchy that prioritizes the inputs to valuation techniques used to measure fair value based upon whether such inputs are observable or unobservable. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect market assumptions made by the reporting entity. The three-level hierarchy for the inputs to valuation techniques is briefly summarized as follows:

- *Level 1*—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;
- *Level 2*—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and
- *Level 3*—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

The Company's cash equivalent money market funds are classified as Level 1 because they are valued using quoted market prices.

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The following table presents information about the Company's financial assets that are measured at fair value and indicates the fair value hierarchy of the valuation (in thousands):

	As of December 31, 2017			
	Level 1	Level 2	Level 3	Total
Financial assets:				
Money market funds	$ 3,263	$ —	$ —	$ 3,263
Total financial assets	$ 3,263	$ —	$ —	$ 3,263

	As of December 31, 2018			
	Level 1	Level 2	Level 3	Total
Financial assets:				
Money market funds	$ 59,911	$ —	$ —	$ 59,911
Total financial assets	$ 59,911	$ —	$ —	$ 59,911

There were no liabilities measured at fair value on a recurring basis as of December 31, 2017 and 2018. There have been no transfers between fair value measurement levels during the years ended December 31, 2017 and 2018.

The Company records interest income and accretion income earned on money market funds to interest income in its statement of operations.

5. Property and Equipment, net

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

	As of December 31,	
	2017	2018
Computer equipment and software	$ —	$ 6
Laboratory equipment	2,235	4,708
Leasehold improvements	20	621
Total property and equipment, gross	2,255	5,335
Less: Accumulated depreciation	(409)	(1,075)
Total property and equipment, net	$ 1,846	$ 4,260

Depreciation expense for the years ended December 31, 2017 and 2018 was $0.3 million and $0.7 million, respectively.

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6. Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	As of December 31,	
	2017	2018
Accrued compensation and benefits	$ 896	$ 1,470
Accrued research and development expenses	538	633
Other	160	405
Total accrued liabilities	$ 1,594	$ 2,508

Accrued compensation and benefits consist primarily of accrued bonuses and accrued vacation.

7. License Agreement

In August 2015, the Company entered into an exclusive, worldwide license agreement (the "UC Agreement") with the Regents of the University of California (the "UC Regents") relating to the use of certain patents and technology relating to avb1 compounds in fibrosis indications. Pursuant to the UC Agreement, the Company is obligated to (i) make a non-refundable upfront license fee payment of $0.4 million and annual license maintenance fee payments of $10,000 per year beginning on the first anniversary of the UC Agreement escalating to $25,000 per year thereafter (ii) make royalty payments to the UC Regents of 3% of net sales of a therapeutic licensed product or 1% of net sales of a method of use licensed product, subject to an annual minimum of $1.0 million, (iii) make milestone payments up to an aggregate of $18.2 million to the UC Regents upon the occurrence of certain events, (iv) make a milestone payment based on the number of outstanding shares and a price per share as defined in the UC Agreement within 30 days of the closing of an IPO or change of control, and (v) reimburse the UC Regents for prosecution and maintenance expenses of the licensed patents without limitation. The Company will expense any payments for milestones to research and development expenses prior to receiving Federal Drug and Administration ("FDA") approval for any of its product candidates. These costs will be capitalized when FDA approval is obtained for any products being selected for commercialization and amortized over the remaining life of the patent. If the Company sublicenses its rights under the UC Agreement, it is obligated to pay the UC Regents a percentage of the total gross proceeds received in consideration of the grant of the sublicense, which total amount would be first reduced by the aggregate amount of certain research and development related expense incurred by the Company. The UC Regents have the right to purchase an amount equal to a low single-digit percent of any securities offered by the Company to investors other than to Third Rock Ventures III, L.P. ("TRV") or an affiliate of TRV. This participation right expires immediately before the completion of the IPO.

The UC Agreement can be terminated at any time upon the material breach of contract terms by either party to the agreement. The Company has the right to terminate the agreement at any time upon providing written notice to the UC Regents. Unless terminated early, the UC Agreement will remain in effect from the effective date until the later of (i) the expiration or abandonment of the patent rights licensed under the UC Agreement, or (ii) ten years from the date of the first commercial sale of the first licensed product under the agreement.

The Company recorded $10,000 as research and development expenses related to the annual license maintenance fee for each of the years ended December 31, 2017 and 2018, respectively.

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8. Research Agreement

Adimab Development and Option Agreement

In October 2018, the Company and Adimab LLC ("Adimab") entered into a development and option agreement (the "Adimab Agreement") for the discovery and optimization of proprietary antibodies as potential therapeutic product candidates. Under the Adimab Agreement, the Company will select biological targets against which Adimab will use its proprietary platform technology to research and develop antibody proteins using a mutually agreed upon research plan.

Upon the Company's selection of a target, the Company and Adimab will initiate a research plan and the discovery term begins. During the discovery term, Adimab will grant the Company a non-exclusive, non-sublicensable license under its technology with respect to the target, to research, design and preclinically develop and use antibodies that were modified or derived using Adimab technology, solely to evaluate such antibodies, perform the Company's responsibilities under the research plan and use such antibodies for certain diagnostic purposes. The Company will also grant to Adimab a non-exclusive, non-sublicensable and non-transferable license with respect to the target under the Company's technology that covers or relates to such target, solely to perform its responsibilities under the research plan during the discovery period. The Company is required to pay Adimab at an agreed upon rate for its full-time employees during the discovery period while Adimab performs research on each target under the applicable research plan.

Adimab granted the Company an exclusive option to obtain a worldwide, royalty-bearing, sublicensable license under Adimab platform patents and other Adimab technology to research, develop and commercialize up to twenty four antibodies selected by the Company (the "Program Antibodies") against specific biological targets (the "Commercialization Option"). Upon the exercise of a Commercialization Option, and payment of the applicable option fee to Adimab, Adimab will assign the patents that cover the Program Antibodies to Company. The Company will be required to use commercially reasonable efforts to develop, seek market approval of, and commercialize at least one antibody against the target covered by the Commercialization Option in specified markets upon the exercise of a Commercialization Option.

Pursuant to the Adimab Agreement, the Company is obligated to (i) make a nonrefundable upfront license fee payment for access to Adimab's technology; (ii) pay Adimab at an agreed upon rate for each full-time employee ("FTE") during the research period; (iii) make additional payments upon the Company making other research related elections; (iv) pay up to a dollar amount in the low double digit millions for the achievement of certain research and development milestones for each research target program which can vary by target type; (v) make royalty payments to Adimab on Company net sales of its products covered under the Adimab Agreement, subject to varying royalty payments on certain product types. Currently, no product types have been selected by the Company.

During the year ended December 31, 2018, the Company recognized research and development expense under the Adimab Agreement of $0.1 million related to the upfront license fee and FTE costs.

9. Redeemable Convertible Preferred Stock

Under the Company's Amended and Restated Certificate of Incorporation ("Certificate of Incorporation"), the Company is authorized to issue two classes of shares: preferred and common stock. The preferred stock may be issued in series, and the Company's board of directors is authorized to determine the rights, preferences, and

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terms of each series. The following is a summary of the Company's redeemable convertible preferred stock (in thousands except share amounts):

Preferred stock consisted of the following as of December 31, 2017:

	Preferred Shares Authorized	Shares Issued and Outstanding	Redemption Value/ Liquidation Preference	Carrying Value
Series A	62,500,000	36,500,000	$ 39,910	$39,910
	62,500,000	36,500,000	$ 39,910	$39,910

Preferred stock consisted of the following as of December 31, 2018:

	Preferred Shares Authorized	Shares Issued and Outstanding	Redemption Value/ Liquidation Preference	Carrying Value
Series A	56,000,000	56,000,000	$ 61,516	$ 61,516
Series B	58,109,973	49,501,221	70,587	70,587
	114,109,973	105,501,221	$ 132,103	$ 132,103

Series A Preferred

In August 2015, the Company entered into a Series A Preferred Stock Purchase Agreement (the "Series A Purchase Agreement") pursuant to which it agreed to sell, and the purchasers agreed to purchase up to $45.0 million of Series A Redeemable Convertible Preferred Stock ("Series A Preferred") in three anticipated tranches based on the achievement of defined performance milestones. The Series A Preferred stockholders may not assign the rights to purchase shares of Series A Preferred at any future milestone closing tranches separately without a transfer of already purchased shares. The Company determined that these future tranche obligations did not meet the definition of a freestanding financial instrument because, while separately exercisable, they were not legally detachable. Further, the Company determined that the embedded future tranche obligation did not require bifurcation for accounting purposes as it was clearly and closely related to the economic characteristics and risks of the Series A Preferred and would not meet the definition of a derivative on a standalone basis.

Under the Series A Purchase Agreement, as part of the initial closing, the Company issued 6.5 million shares of Series A Preferred at $1.00 per share in exchange for cash proceeds of $6.4 million and the conversion of convertible promissory notes in the amount of $0.1 million representing outstanding principal and accrued interest.

In April 2016, the Company issued 5.0 million shares of Series A Preferred at $1.00 per share in exchange for cash proceeds of $5.0 million in an additional closing of the first tranche. The final closing of the first tranche occurred in September of 2016, when the Company issued 5.0 million additional shares of Series A Preferred at $1.00 per share in exchange for cash proceeds of $5.0 million.

In February 2017, the Company issued 8.0 million shares of Series A Preferred at $1.00 per share in exchange for cash proceeds of $8.0 million in a closing of the second tranche.

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In July 2017, the Company issued 12.0 million shares of Series A Preferred at $1.00 per share in exchange for cash proceeds of $12.0 million in an initial closing of the third tranche.

In January 2018, the Company issued 8.5 million shares of Series A Preferred at $1.00 per share in exchange for cash proceeds of $8.5 million in an additional closing of the third tranche.

In March 2018, based on the amendment to the Series A Purchase Agreement, the Company issued 11.0 million additional shares of Series A Preferred at $1.00 per share in exchange for cash proceeds of $11.0 million in the final closing of the third tranche.

Series B Preferred

In July 2018, the Company entered into a Series B Preferred Stock Purchase Agreement (the "Series B Purchase Agreement") in which it agreed to sell, and the purchasers agreed to purchase, up to $70.0 million of Series B Redeemable Convertible Preferred Stock ("Series B Preferred"). Under the Series B Purchase Agreement, the Company initially issued 45.1 million shares of Series B Preferred at $1.3767 per share in exchange for cash proceeds of approximately $62.1 million.

In November 2018, the Company issued 4.4 million additional shares of Series B Preferred at $1.3767 per share in exchange for cash proceeds of approximately $6.0 million.

The Series A Preferred and Series B Preferred (collectively, the "Preferred Stock") have the following rights and privileges:

Voting

Each holder of shares of Series A Preferred and Series B Preferred is entitled to the number of votes equal to the number of shares of common stock into which such shares could be converted and has voting rights and powers equal to the voting rights and powers of the common stock, and except as provided by law or by other provisions of the Company's Certificate of Incorporation, as amended, shall vote together with the common stock as a single class on an as-converted basis on all matters as to which holders of common stock have the right to vote.

The holders of Series A Preferred, voting separately as a single class, are entitled to elect two members of the Company's board of directors. At any time when at least 12.5 million shares of Series B Preferred are outstanding, the holders of Series B Preferred are entitled to elect one member of the Company's board of directors. The holders of shares of common stock, voting separately as a single class, are entitled to elect one member of the Company's board of directors. All remaining members of the Company's board of directors are elected by the holders of the common stock and Preferred Stock voting together as a single class.

Conversion

Shares of the Preferred Stock are convertible at any time at the option of the holder into such number of shares as is determined by dividing the original issuance price by the conversion price in effect at the time. The original conversion price is the original issuance price for each series of Preferred Stock, or $1.00 for Series A Preferred and $1.3767 for Series B Preferred, subject to certain adjustments. As of December 31, 2018, the Preferred Stock was convertible into shares of the Company's common stock on a one-for-one basis.

All outstanding shares of Preferred Stock will automatically convert upon the completion of an IPO resulting in net proceeds to the Company of at least $45.0 million or the vote or written consent of a requisite majority of holders of the then outstanding shares of Preferred Stock on an as-converted to common stock basis.

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Dividends

The holders of Series A Preferred were originally entitled to receive cumulative dividends from their respective dates of issuance at the rate of 8.0% on their original issue price. In July 2018, in conjunction with the execution of the Series B Purchase Agreement, the Series A Preferred accreted dividends were cancelled.

Under the Series B Purchase Agreement, the holders of both shares of Series A and Series B Preferred are entitled to receive cumulative dividends commencing on July 10, 2018, the issuance date of Series B Preferred, at an annual rate of 8.0% on their original issuance price. The Series A Preferred and Series B Preferred dividends accrue from day-to-day, whether declared or not, and are payable only when and if declared by the Company's board of directors. Since inception, the Company has never declared or paid any dividends.

Liquidation Preferences

Upon liquidation, dissolution, or winding up of the Company or a deemed liquidation event as defined in the Company's Certificate of Incorporation, the holders of shares of Preferred Stock will receive, in preference to any distribution to the holders of common stock, an amount per share equal to the greater of (i) the original issue price per share of the respective series of Preferred Stock, plus all dividends declared but unpaid on such shares, or (ii) the amount the holders would receive on an as-converted into common stock basis. Series B Preferred holders are entitled to receive their liquidation preference before any distributions are made to Series A Preferred holders and common stock holders. Series A Preferred holders are entitled to receive their liquidation preference before any distributions are made to common stock holders. After payments of the full liquidation preferences of the Series A and B Preferred described above, any remaining assets of the Company shall be distributed to the holders of the common stock in proportion to the number of shares of common stock that they hold.

Redemption

The Series A Preferred were redeemable at any time on or after five years from August 19, 2015, the original issuance date of the 6.5 million shares of Series A Preferred, upon receipt of a written notice from the holders of a majority of the shares of Series A Preferred. The initial redemption price was the greater of (i) the Series A Preferred original issuance price per share, plus any accrued and unpaid dividends, whether or not declared by the board of directors, and (ii) the fair market value of Series A Preferred as mutually agreed upon by the Company and the holders of a majority of the shares of Series A Preferred then outstanding.

In July 2018, in conjunction with the execution of the Series B Preferred Purchase Agreement, the Series A Preferred redemption provision was amended as follows:

All outstanding shares of Preferred Stock shall be redeemed by the Company at a price equal to the original issuance price per share, plus any accrued and unpaid dividends, whether or not declared, together with any other dividends declared but unpaid in three annual installments commencing not more than sixty (60) days after receipt by the Company at any time on or after five years from the Series B Preferred original issuance date, July 10, 2018, a written notice from the holders of a majority of the shares of Preferred Stock.

The Company accounted for the changes in Series A Preferred redemption provision as a modification as there was no significant difference in Series A Preferred fair value before and after the modification.

10. Common Stock

The voting, dividend, and liquidation rights of the holders of the common stock are subject to and qualified by the rights, powers, and preferences of the holders of the Preferred Stock. As of December 31, 2018, the

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Company had 147,682,655 authorized shares of common stock at a par value of $0.001 per share. The common stock has the following rights and privileges:

Voting

The holders of shares of common stock are entitled to one vote for each share of common stock held at any meeting of stockholders and at the time of any written action in lieu of a meeting.

Dividends

The holders of shares of common stock are entitled to receive dividends, when declared by the Company's board of directors. Cash dividends may not be declared or paid to holders of shares of common stock until all unpaid dividends on the Preferred Stock have been paid in accordance with their terms. No dividends have been declared or paid by the Company since its inception.

Liquidation

After payment of the respective liquidation preferences to the holders of shares of Preferred Stock, the holders of shares of common stock are entitled to share ratably in the Company's remaining assets available for distribution to its stockholders in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or upon occurrence of a deemed liquidation event.

Shares reserved for future issuance

	As of December 31,	
	2017	2018
Conversion of redeemable convertible preferred stock	36,500,000	105,501,221
Exercises of outstanding stock option awards	—	809,200
Shares of common stock available for future grants under the 2015 Equity Incentive Plan, as amended	3,119,766	7,029,718
Total shares reserved for future issuance	39,619,766	113,340,139

Founders' Common Stock Awards

During 2015, the Company's board of directors granted common stock awards to the Company's founders in exchange for services provided to the Company. The purchase price of the common stock awards was the estimated fair value at the issuance date. The shares vest from one to four years and vesting could be accelerated upon a change in control. The vesting of certain performance-based grants of restricted stock awards were contingent upon the filing of an Investigational New Drug Application by the Company with the FDA.

If the holder of founders' common stock award terminates their relationship with the Company during the vesting period, the Company may repurchase any unvested restricted common stock held by these individuals at their original purchase price. During the vesting term, holders of founders' common stock awards are deemed to be common stockholders and have dividend and voting rights. The Company issued 5,328,500 shares of founders' common stock during 2015. No founders' common stock awards were granted in subsequent years. Total compensation expense was $25,000 for these founders' common stock awards, which are recorded to operating expenses in the statements of operations over their respective vesting period. As of December 31, 2018, 333,729 shares of founders' common stock awards were not vested and are expected to vest in 2019.

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11. 2015 Equity Incentive Plan and Stock-Based Compensation

In August 2015, the board of directors adopted the 2015 Equity Incentive Plan, as amended (the "Plan"), which provides for the grant of incentive stock options, nonqualified stock options or other awards including stock appreciation rights and restricted stock awards to the Company's employees, officers, directors, advisors, and consultants for the purchase of up to 11.0 million shares of the Company's common stock. In July 2018, the Plan was amended to increase the number of shares reserved thereunder by 7.2 million shares. As of December 31, 2018, 7.0 million shares remained available for issuance under the Plan.

Options under the Plan may be granted for periods of up to 10 years and at prices no less than 100.0% of the estimated fair value of the shares on the date of grant as determined by the board of directors, provided, however, that the exercise price of an incentive stock option granted to a 10.0% shareholder shall not be less than 110.0% of the estimated fair value of the shares on the date of grant and the option is not exercisable after the expiration of five years from the date of grant.

Restricted Common Stock Awards

The Company granted restricted stock awards under the Plan. The purchase price of the restricted common stock awards was the estimated fair value as determined by the board of directors at the issuance date. The shares vest from one to four years and vesting could be accelerated upon a change in control. A holder of an award may pay a total purchase price or a part of the purchase price for granted shares at any time during the vesting periods. Upon termination of employment, the Company has the right to repurchase any unvested restricted shares. The repurchase price for unvested shares of common stock will be the lower of (i) the fair market value on the date of repurchase or (ii) their original purchase price. During the vesting term, holders of restricted stock awards are deemed to be a common stock shareholders and have dividends and voting rights.

The Company accounted for restricted stock awards as early exercised options and recognized a liability in other liabilities when cash was received for the purchase of shares of restricted stock. As shares of restricted stock vested, the Company reclassified the liability to common stock and additional paid in capital. As of December 31, 2017, and 2018, the Company recorded a liability included in accrued expenses and other liabilities of $42,000 and $52,000, respectively.

The Company used Black-Scholes option pricing model to estimate stock-based compensation expense related to restricted stock awards with the following assumptions for the years ended December 31, 2017 and 2018:

	2017	2018
Expected volatility	75.15% - 80.90%	69.60% - 76.20%
Risk-free interest rate	1.05% - 1.79%	1.80% - 2.48%
Expected dividend	— %	— %
Expected term (in years)	0.55 - 2.15	0.92 - 2.16
Underlying common stock fair value	$0.04 - $0.22	$0.26 - $0.33

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The following table summarizes restricted stock activity during the years ended December 31, 2017 and 2018:

	Number of Shares	Weighted-Average Grant Date fair value
Outstanding and unvested, as of December 31, 2016	6,285,967	$ 0.01
Issued	1,624,288	$ 0.16
Vested	(2,089,144)	$ 0.01
Repurchased	(1,217,834)	$ 0.01
Outstanding and unvested, as of December 31, 2017	4,603,277	$ 0.06
Issued	2,428,248	$ 0.29
Vested	(2,003,725)	$ 0.05
Outstanding and unvested, as of December 31, 2018	5,027,800	$ 0.17

Restricted stock awards of 32,600 shares with a weighted-average grant date fair value of $0.03 per share, were not purchased by the award holders as of December 31, 2018. As these shares of the restricted common stock awards were not issued, they are not included in the table above.

The aggregate fair value of restricted stock awards vested during the years ended December 31, 2017 and 2018 was $22,000 and $0.1 million, respectively. Total intrinsic value of outstanding unvested restricted stock awards was $3.6 million as of December 31, 2018.

Incentive Stock Options and Nonqualified Stock Options

Stock options issued under the Plan generally vest over a four-year period and expire ten years from the date of grant. Certain options provide for accelerated vesting if there is a change in control, as defined in the Plan. There were no stock options granted prior to 2018.

The Company used Black-Scholes option pricing model to estimate stock-based compensation expense for stock option awards with the following assumptions for the year ended December 31, 2018:

	2018
Expected volatility	81.80% - 82.50%
Risk-free interest rate	2.78% - 3.07%
Expected dividend	— %
Expected term (in years)	5.78 - 6.06
Underlying common stock fair value	$0.39 - $0.72

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A summary of option activity under the Plan is as follows:

	Number of Options	Weighted-Average Exercise Price per Share	Weighted-Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2017	—	$ —	—	$ —
Granted	809,200	$ 0.29		
Outstanding as of December 31, 2018	809,200	$ 0.29	9.77	$ 348
Exercisable as of December 31, 2018	5,625	$ 0.29	9.66	$ 2
Vested and expected to vest as of December 31, 2018	809,200	$ 0.29	9.77	$ 348

Aggregate intrinsic value represents the difference between the fair value of the underlying common stock and the exercise price as of December 31, 2018. There were no option exercises in 2018. The weighted-average grant date fair value of options granted during the year ended December 31, 2018 was $0.48 per share.

Stock-Based Compensation Expense

The following table presents the components and classification of stock-based compensation expense for the Company's stock-based awards for the years ended December 31, 2017 and 2018 (in thousands):

	Year Ended December 31,	
	2017	2018
Restricted stock awards and founders' common stock awards	$ 33	$ 207
Stock options	—	21
Total stock-based compensation expense	$ 33	$ 228
Research and development expenses	$ 8	$ 114
General and administrative expenses	$ 25	$ 114

As of December 31, 2018, there was $0.7 million and $0.4 million of unrecognized compensation costs that is expected to be recognized over the weighted-average periods of 2.2 years and 3.7 years related to restricted stock awards and stock options, respectively.

12. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2017 and December 31, 2018. The Company has incurred net operating losses only in the United States since its inception. The Company has not reflected any benefit of such net operating loss carryforwards in the financial statements.

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A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2017	2018
Income tax computed at federal statutory rate	34.0%	21.0%
State taxes, net of federal tax benefit	7.1%	9.1%
General business credit—federal	1.3%	2.6%
Stock based compensation	(0.1%)	(0.2%)
Impact of federal rate change	(20.1%)	(0.0%)
Change in valuation allowance	(22.2%)	(32.5%)
Effective income tax rate	— %	— %

Net deferred tax assets and liabilities consisted of the following (in thousands):

	As of December 31,	
	2017	2018
Deferred tax assets:		
Asset basis	$ 392	$ 227
Net operating losses	8,437	16,684
Research and development credits	1,346	3,048
Accrued expenses	248	88
Other	3	147
Deferred rent	—	110
Stock based compensation	—	1
Total deferred tax assets	10,426	20,304
Deferred tax liabilities:		
Prepaid expenses	(18)	(65)
Total deferred tax liabilities	(18)	(65)
Valuation allowance	(10,408)	(20,240)
Net deferred taxes	$ —	$ —

Net operating losses and tax credit carryforwards were as follows (in thousands):

	As of December 31, 2018	Expiration Year
Net operating losses, federal (starting from January 1, 2018)	$ 29,183	Does not expire
Net operating losses, federal (before January 1, 2018)	$ 29,901	2035-2037
Net operating losses, state	$ 59,571	2035-2038
Tax credits, federal	$ 2,288	2036-2038
Tax credits, state	$ 2,086	Does not expire

Utilization of the net operating loss carryforwards and research credit carryforwards may be subject to an annual limitation due to the ownership percentage change limitations provided by the Internal Revenue Code and

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similar state provisions. Annual limitations may result in the expiration of the net operating losses and tax credit carryforwards before they are utilized. The Company does not expect any previous ownership changes to result in a limitation that will reduce the total amount of net operating loss and tax credit carryforwards disclosed that can be utilized. Subsequent ownership changes may affect the limitation in future years.

During the years ended December 31, 2017 and 2018, the Company recorded a full valuation allowance on federal and state deferred balances since management does not forecast the Company to be in a profitable position in the near future. Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2017 and 2018 related primarily to the increases in net operating loss carryforwards and research and development tax credit carryforwards and were as follows (in thousands):

	Year Ended December 31,	
	2017	2018
Valuation allowance at the beginning of the year	$ 6,335	$ 10,408
Increases recorded to income tax provision	4,073	9,832
Valuation allowance at the end of the year	$ 10,408	$ 20,240

The Company's U.S. federal and state income tax returns are generally subject to tax examinations for the tax years ended December 31, 2015 through December 31, 2018. There are currently no pending income tax examinations. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service and state tax authorities to the extent utilized in a future period. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision.

On December 22, 2017, the U.S. government enacted comprehensive tax legislation through the Tax Cuts and Jobs Act (the "Tax Act"). The Tax Act significantly revises the future ongoing U.S. corporate income tax by, among other things, lowering the U.S. corporate income tax rates and implementing a modified territorial tax system. The corporate tax rate was reduced from 34.0% to 21.0% for tax years beginning after December 31, 2017. Changes in tax law are accounted for in the period of enactment. As such, the Company's financial statements as of December 31, 2017 reflect the impact of the Tax Act, which consisted of remeasuring the Company's deferred tax assets, deferred tax liabilities and valuation allowance using the newly enacted U.S. corporate tax rate. This rate change resulted in a $3.7 million reduction in the Company's net deferred tax assets with a corresponding offset to the valuation allowance. Under the Tax Act, net operating losses arising after December 31, 2017 do not expire and cannot be carried back. However, the Tax Act limits the amount of net operating losses that can be used annually to 80.0% of taxable income for periods beginning after December 31, 2017. Existing net operating losses arising in years ending on or before December 31, 2017 are not affected by these provisions.

The entire amount of the unrecognized tax benefits would not impact the Company's effective tax rate if recognized. The Company has elected to include interest and penalties as a component of tax expense. During the years ended December 31, 2017 and 2018, the Company did not recognize accrued interest and penalties related to unrecognized tax benefits. The Company does not anticipate that the amount of existing unrecognized tax benefits will significantly increase or decrease during the next 12 months.

Pliant Therapeutics, Inc.
Notes to Financial Statements
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A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	Year Ended December 31,	
	2017	2018
January 1	$ 169	$ 403
Additions based on tax positions related to current year	234	452
December 31	$ 403	$ 855

13. Commitments and Contingencies

Purchase Commitments

The Company has contractual arrangements with research and development organizations and suppliers; however, these contracts are generally cancelable on 30 days' notice and the obligations under these contracts are largely based on services performed.

License and Collaboration Agreements

Potential payments related to the Company's license and research agreements, including milestone and royalty payments, are detailed in Notes 7 and 8.

Leases

In 2017 and 2018, the Company leased approximately 18,000 square feet of corporate offices and research facilities in Redwood City, California. Rent expense, including common area maintenance expense, was approximately $0.1 million per month. This lease expired on June 28, 2018.

In February 2018, the Company entered into a non-cancelable lease agreement (the "Lease") for premises consisting of approximately 32,974 square feet located in South San Francisco, California (the "Premises"). The Company moved into the Premises in July 2018. The Premises is being used for the Company's corporate headquarters and principal operating facility. The term of the Lease is eighty-four months, which commenced on July 1, 2018. Base rent was abated for the first two months of the lease term and thereafter is $0.2 million per month during the first year of the lease term, with specified annual increases thereafter. The Company paid a refundable security deposit of approximately $0.4 million, which is included in long term assets in the balance sheet at December 31, 2018. The Company has the right to extend the lease term by seven years upon written notice not more than twelve months nor less than nine months prior to the expiration of the original lease term, with monthly payments equal to the "fair rental value" as defined in the Lease.

During the years ended December 31, 2017 and 2018, rent expense, including common area maintenance expense, was $1.3 million and $1.8 million, respectively.

Future minimum lease payments under the Lease as of December 31, 2018 were as follows (in thousands):

Year ending December 31:	Operating Lease
2019	$ 1,892
2020	1,959
2021	2,027
2022	2,098
2023 and beyond	5,562
Total	$ 13,538

Pliant Therapeutics, Inc.
Notes to Financial Statements
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Legal Proceedings

The Company, from time to time, may be party to litigation arising in the ordinary course of business. The Company was not subject to any material legal proceedings during the years ended December 31, 2017 and 2018, and, to the best of its knowledge, no material legal proceedings are currently pending or threatened.

Indemnification

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend an indemnified party for losses suffered or incurred by the indemnified party. Some of the provisions will limit losses to those arising from third party actions. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amount of future payments the Company could be required to make under these provisions is not determinable. The Company has never incurred material costs to defend lawsuits or settle claims related to these indemnification provisions. The Company has also entered into indemnification agreements with its directors and officers that may require the Company to indemnify its directors and officers against liabilities that may arise by reason of their status or service as directors or officers to the fullest extent permitted by Delaware corporate law. The Company currently has directors' and officers' insurance.

14. Related Party Transactions

Certain employees of Third Rock Ventures, a stockholder of the Company, provided consulting services to the Company. Consulting service expenses of $132,000 and $54,000 were recorded for the years ended December 31, 2017 and 2018, respectively.

In 2018, the Company made charitable contributions to the University of California, San Francisco Foundation (the "UCSF Foundation"), which were directed to support research performed in the laboratories of two of the Company's scientific founders. Charitable contributions made to the UCSF Foundation during the year ended December 31, 2018 was $0.5 million.

In February 2017, the Company entered into a consulting agreement with the founder of Healthcare & Humanity Foundation (the "Director") pursuant to which the Director provided consulting services to the Company at a rate of $5,000 per month in 2017 and 2018 years. In addition, the Company granted the Director 45,000 shares of restricted stock at an purchase price of $0.01 per share with quarterly vesting over a one-year period contingent upon the Director providing consulting services during the vesting period. The Director became a director of the Company in December 2017. In February 2018, the agreement with the Director terminated pursuant to its terms. General and administrative services provided while the Director was a director of the Company amounted to $5,000 during the year ended December 31, 2018.

In March 2018, the Company sold 1.0 million shares of Series A Preferred to pH Pharma Co. Ltd. ("pH Pharma"), an entity in which the Director has a majority ownership, for $1.0 million. These shares of Series A Preferred represent 1.0% of the Company's outstanding equity on a fully diluted basis as of December 31, 2018. In May 2018, the Company entered into a research services agreement with pH Pharma. In the year ended December 31, 2018, the Company was reimbursed $51,000 for services performed in connection with the research services agreement, which were recorded as a credit to research and development expenses in the statements of operations. As of December 31, 2018, all services were completed under this agreement.

Pliant Therapeutics, Inc.
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15. Defined Contribution Plan

The Company sponsors a defined contribution plan under Section 401(k) of the Internal Revenue Code covering substantially all full-time U.S. employees. Employee contributions are voluntary and are determined on an individual basis subject to the maximum allowable under federal tax regulations. The Company made contributions to the plan of $0.1 million and $0.2 million for the years ended December 31, 2017 and 2018, respectively.

16. Net Loss Per Share Attributable to Common Stockholders

The following outstanding shares of potentially dilutive securities were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods presented, because including them would have been antidilutive:

	Year Ended December 31,	
	2017	2018
Redeemable convertible preferred stock (on an as-converted basis)	36,500,000	105,501,221
Options to purchase common stock	—	809,200
Restricted stock awards granted and not purchased	30,000	32,600
Unvested restricted shares	4,603,275	5,027,800
Unvested shares of founders' common stock	1,403,855	333,729
Total	42,537,130	111,704,548

A reconciliation of the numerator and denominator used in the calculation of the basic and diluted net loss per share attributable to common stockholders is as follows (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2017	2018
Net loss per share:		
Numerator		
Net loss and comprehensive loss	$ (18,333)	$ (30,276)
Add: accretion to redemption value and cumulative dividends on redeemable convertible preferred stock	(2,289)	(4,876)
Net loss attributable to common stockholders	$ (20,622)	$ (35,152)
Denominator		
Weighted-average common shares outstanding used to calculate net loss per share attributable to common stockholders, basic and diluted	5,745	8,333
Net loss per share attributable to common stockholders, basic and diluted	$ (3.59)	$ (4.22)

Pliant Therapeutics, Inc.
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The following table sets forth the computation of the Company's unaudited pro forma basic and diluted net loss per share attributable to common stockholders (in thousands, except share and per share data) assuming the automatic conversion of the redeemable convertible preferred stock based on the mid-point of the IPO price range of $, upon consummation of an IPO as if such event had occurred as of the beginning of the respective period:

	Year Ended December 31, 2018 (unaudited)
Unaudited Pro Forma Net Loss Per Share	
Net loss	$
Pro forma adjustment to accretion to redemption value and cumulative dividends on redeemable convertible preferred stock	
Pro forma net loss attributable to common stockholders, basic and diluted	
Weighted-average shares used to calculate net loss per share attributable to common stockholders, basic and diluted	
Pro forma adjustment to reflect assumed conversion of all redeemable convertible preferred stock	
Weighted-average shares used to calculate pro forma net loss per share attributable to common stockholders, basic and diluted	
Pro forma net loss per share attributable to common stockholders, basic and diluted	$

17. Subsequent Events

In January 2019, the Company's board of directors and shareholders voted to increase the number of shares reserved for issuance under the 2015 Equity Incentive Plan by 3.0 million shares.

In January 2019 and March 2019, the Company granted stock options to purchase an aggregate of 6.7 million shares of common stock.

The Company has evaluated subsequent events for financial statement purposes occurring through May 10, 2019, the date these financial statements were issued, and determined that no additional subsequent events had occurred that would require recognition in these financial statements and that all subsequent events that required disclosure have been disclosed.

Shares

Pliant Therapeutics, Inc.

Common Stock

PRELIMINARY PROSPECTUS

, 2019

Joint Book-Running Managers

Citigroup
Cowen
Piper Jaffray

Lead Manager

Needham & Company

Through and including , 2019 (25 days after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

Part II

Information Not Required in Prospectus

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the fees and expenses, other than underwriting discounts and commissions, payable in connection with the registration of the common stock hereunder. All amounts are estimates except the SEC registration fee, the FINRA filing fee and the Nasdaq Global Market listing fee.

	Amount Paid or to Be Paid
SEC registration fee	$ *
FINRA filing fee	*
Nasdaq Global Market listing fee	*
Printing and mailing	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer agent and registrar fees and expenses	*
Miscellaneous	*
Total	$ *

* To be completed by amendment.

Item 14. Indemnification of Directors and Officers.

Section 145 of the Delaware General Corporation Law, or the DGCL, authorizes a corporation to indemnify its directors and officers against liabilities arising out of actions, suits and proceedings to which they are made or threatened to be made a party by reason of the fact that they have served or are currently serving as a director or officer to a corporation. The indemnity may cover expenses (including attorneys' fees) judgments, fines and amounts paid in settlement actually and reasonably incurred by the director or officer in connection with any such action, suit or proceeding. Section 145 permits corporations to pay expenses (including attorneys' fees) incurred by directors and officers in advance of the final disposition of such action, suit or proceeding. In addition, Section 145 provides that a corporation has the power to purchase and maintain insurance on behalf of its directors and officers against any liability asserted against them and incurred by them in their capacity as a director or officer, or arising out of their status as such, whether or not the corporation would have the power to indemnify the director or officer against such liability under Section 145.

We have adopted provisions in our amended and restated certificate of incorporation and amended and restated bylaws to be in effect immediately prior to the completion of this offering that limit or eliminate the personal liability of our directors to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders; any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law; any unlawful payments related to dividends or unlawful stock purchases, redemptions or other distributions; or any transaction from which the director derived an improper personal benefit.

These limitations of liability do not alter director liability under the federal securities laws and do not affect the availability of equitable remedies such as an injunction or rescission.

In addition, our bylaws provide that:

- we will indemnify our directors, officers and, in the discretion of our board of directors, certain employees to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended; and

- we will advance reasonable expenses, including attorneys' fees, to our directors and, in the discretion of our board of directors, to our officers and certain employees, in connection with legal proceedings relating to their service for or on behalf of us, subject to limited exceptions.

We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements will provide that we will indemnify each of our directors, certain of our executive officers and, at times, their affiliates to the fullest extent permitted by Delaware law. We will advance expenses, including attorneys' fees (but excluding judgments, fines and settlement amounts), to each indemnified director, executive officer or affiliate in connection with any proceeding in which indemnification is available and we will indemnify our directors and officers for any action or proceeding arising out of that person's services as a director or officer brought on behalf of us or in furtherance of our rights. Additionally, certain of our directors or officers may have certain rights to indemnification, advancement of expenses or insurance provided by their affiliates or other third parties, which indemnification relates to and might apply to the same proceedings arising out of such director's or officer's services as a director referenced herein. Nonetheless, we will agree in the indemnification agreements that our obligations to those same directors or officers are primary and any obligation of such affiliates or other third parties to advance expenses or to provide indemnification for the expenses or liabilities incurred by those directors are secondary.

We will maintain general liability insurance which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the Securities Act of 1933, as amended, or the Securities Act.

The underwriting agreement filed as Exhibit 1.1 to this registration statement provides for indemnification of us and our directors and officers by the underwriters against certain liabilities under the Securities Act and the Securities Exchange Act of 1934.

Item 15. Recent Sales of Unregistered Securities.

In the three years preceding the filing of this registration statement, we have issued the following securities that were not registered under the Securities Act. No underwriters were involved in the sales and the certificates representing the securities sold and issued contain legends restricting transfer of the securities without registration under the Securities Act or an applicable exemption from registration.

(a) Issuances of Capital Stock

In April 2016, we sold an aggregate of 5,000,000 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share for an aggregate purchase price of approximately $5.0 million.

In September 2016, we sold an aggregate of 5,000,000 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share for an aggregate purchase price of approximately $5.0 million.

In February 2017, we sold an aggregate of 8,000,000 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share for an aggregate purchase price of approximately $8.0 million.

In July 2017, we sold an aggregate of 12,000,000 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share for an aggregate purchase price of approximately $12.0 million.

In January 2018, we sold an aggregate of 8,500,000 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share for an aggregate purchase price of approximately $8.5 million.

In March 2018, we sold an aggregate of 11,000,000 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.00 per share for an aggregate purchase price of approximately $11.0 million.

In July 2018, we sold an aggregate of 45,142,960 shares of our Series B redeemable convertible preferred stock at a purchase price of $1.3767 per share for an aggregate purchase price of approximately $62 million.

In November 2018, we sold an aggregate of 4,358,261 shares of our Series B redeemable convertible preferred stock at a purchase price of $1.3767 per share for an aggregate purchase price of approximately $6 million.

The offers and sales of the securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act, including Regulation D and Rule 506 promulgated thereunder, as transactions by an issuer not involving a public offering. All of the purchasers in these transactions represented to us in connection with their purchase that they were acquiring the securities for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. Such purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

(b) Grants and Exercises of Stock Options and Restricted Stock

Since January 1, 2016, we granted stock options to purchase 7,527,947 shares of our common stock to our employees, directors and consultants at a weighted average exercise price of $0.29 per share under the 2015 Plan. We also granted the right to purchase an aggregate of 11,653,916 shares of restricted stock to our employees, directors and consultants at a purchase price of $0.01 per share under the 2015 Plan.

The issuances of the securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act or Rule 701 promulgated under the Securities Act as transactions pursuant to compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of such securities were the registrant's employees, consultants or directors and received the securities under the registrant's 2015 Equity Incentive Plan. The shares of common stock issued upon the exercise of options are deemed to be restricted securities for purposes of the Securities Act.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

Exhibit No.	Description
1.1*	Form of Underwriting Agreement.
3.1*	Amended and Restated Certificate of Incorporation, as amended, of the Registrant, as currently in effect.
3.2*	Form of Amended and Restated Certificate of Incorporation of the Registrant, to be in effect immediately prior to completion of the offering.
3.3*	Bylaws of the Registrant and the amendments thereto, as currently in effect.
3.4*	Form of Amended and Restated Bylaws of the Registrant, to be in effect immediately prior to the completion of the offering.
4.1*	Specimen Common Stock Certificate of the Registrant.
4.2*	Amended and Restated Investors' Rights Agreement by and among the Registrant and certain of its stockholders, dated July 10, 2018.

Exhibit No.	Description
5.1*	Opinion of Goodwin Procter LLP.
10.1*#	2015 Equity Incentive Plan and forms of award agreements thereunder.
10.2*#	2019 Stock Option and Incentive Plan and forms of award agreements thereunder.
10.3*#	2019 Employee Stock Purchase Plan.
10.4*#	Senior Executive Cash Incentive Bonus Plan.
10.5*#	Non-Employee Director Compensation Policy.
10.6*#	Executive Severance Plan.
10.7*#	Offer Letter, by and between the Registrant and Bernard Coulie, M.D., Ph.D., dated November 21, 2018.
10.8*#	Offer Letter, by and between the Registrant and Hans Hull, dated February 9, 2016.
10.9*#	Offer Letter, by and between the Registrant and Keith Cummings, M.D., MBA, dated October 7, 2015.
10.10*#	Offer Letter, by and between the Registrant and Éric Lefebvre, M.D., dated February 27, 2018.
10.11*	Form of Indemnification Agreement, by and between the Registrant and each of its directors and officers.
10.12*	Office Lease, by and between the Registrant and 260 Littlefield Avenue South San Francisco, California 94080, dated February 6, 2018.
23.1*	Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm.
23.2*	Consent of Goodwin Procter LLP (included in Exhibit 5.1).
24.1*	Power of Attorney (included on signature page).

* To be filed by amendment.
† Certain confidential portions (indicated by brackets and asterisks) have been omitted from this exhibit.
# Represents management compensation plan, contract or arrangement.

(b) Financial statement schedules.

None.

Signatures

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Francisco, California, on the day of , 2019.

PLIANT THERAPEUTICS, INC.

By: _____
Bernard Coulie, M.D., Ph.D.
President, Chief Executive Officer and Director

Power of Attorney

Each person whose individual signature appears below hereby authorizes and appoints Bernard Coulie and Keith Cummings and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney in fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Registration Statement, including any and all post effective amendments and amendments thereto, and any registration statement relating to the same offering as this Registration Statement that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys in fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys in fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated below.

Signature	Title	Date
Bernard Coulie, M.D., Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	, 2019
Keith Cummings, M.D., MBA	Chief Financial Officer (Principal Financial and Accounting Officer)	, 2019
Hoyoung Huh, M.D., Ph.D.	Lead Director	, 2019
Suzanne Bruhn, Ph.D.	Director	, 2019
John Curnutte, M.D.	Director	, 2019
Neil Exter	Director	, 2019
Charles Homcy, M.D.	Director	, 2019

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Signature	Title	Date
_____ Kevin Raidy	Director	, 2019
_____ Smital Shah	Director	, 2019