

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated January 23, 2023

Preliminary prospectus supplement
(To prospectus dated July 11, 2022)

\$175,000,000



Common stock

We are offering \$175.0 million of our common stock.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "PLRX". On January 20, 2023, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$22.51 per share.

	Per share	Total
Public offering price	\$	\$
Underwriting discounts and commissions(1)	\$	\$
Proceeds to Pliant Therapeutics, Inc., before expenses	\$	\$

(1) See "Underwriting" for a description of the compensation payable to the underwriters.

We have granted the underwriters an option for a period of 30 days to purchase up to \$26.25 million of additional shares of our common stock at the public offering price less the underwriting discounts and commissions.

Investing in our common stock involves a high degree of risk. Please read "[Risk factors](#)" beginning on page S-9 of this prospectus supplement, in the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares to purchasers on or about _____, 2023.

Joint book-running managers

J.P. Morgan

Piper Sandler

RBC Capital Markets

Lead managers

Cantor

Oppenheimer & Co.

H.C. Wainwright & Co.

, 2023

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Prospectus

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Explanatory note

We filed a post-effective amendment no. 2 to our registration statement on Form S-3 (Commission File No. 333-257684) on March 1, 2022, which was declared effective by the Securities and Exchange Commission, or the SEC, on May 31, 2022 and subsequently amended by post-effective amendment no. 3, which became effective upon filing with the SEC on July 11, 2022. Post-effective amendment no. 2 contained (i) a base prospectus covering the offering, issuance and sale by us of up to \$500,000,000 our common stock, preferred stock, debt securities, warrants and/or units from time to time in one or more offerings and (ii) a sales agreement prospectus covering the offering, issuance and sale by us of up to a maximum aggregate offering price of up to \$150,000,000 of our common stock that may be issued and sold from time to time under that certain Controlled Equity OfferingSM sales agreement, dated July 2, 2021, or the Sales Agreement, with Cantor Fitzgerald & Co., or Cantor, which we refer to as the Sales Agreement Prospectus. As of the date of this prospectus supplement, no shares have been sold pursuant to the Sales Agreement or the Sales Agreement Prospectus. On January 23, 2022, we delivered written notice to Cantor that we were suspending and terminating the Sales Agreement Prospectus. We will not make any sales of securities pursuant to the Sales Agreement unless and until a new prospectus or prospectus supplement is filed. Other than the termination of the Sales Agreement Prospectus, the Sales Agreement remains in full force and effect.

About this prospectus supplement

This document is in two parts. The first part is this prospectus supplement, including the documents incorporated by reference herein, which describes the specific terms of this offering and also adds to and updates the information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated July 11, 2022, including the documents incorporated by reference therein, provides more general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both parts combined. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference herein or therein that were filed with the SEC before the date of this prospectus supplement, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference herein and therein. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in any documents incorporated by reference herein that are filed with the SEC after the date of this prospectus supplement, the statements made in such documents incorporated by reference will be deemed to modify or supersede those made in this prospectus supplement. Before deciding to invest in the common stock being offered, we urge you to carefully read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference herein and therein, and any related free writing prospectus that we have authorized for use in connection with this offering, as well as the additional information described in this prospectus supplement under “Where you can find more information.”

Neither we nor the underwriters have authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus that we have authorized for use in connection with this offering. We and the underwriters 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 or in which the person making such offer or solicitation is not qualified to do so or to any person to whom it is unlawful to make such offer or solicitation. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering, or any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates.

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 supplement 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 supplement must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus supplement outside of the United States.

This prospectus supplement contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus supplement and the accompanying prospectus are a part, and you may obtain copies of those documents as described under “Incorporation of certain information by reference.”

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The representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus supplement or the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

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 supplement and the accompanying prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus supplement and the accompanying 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.

Unless otherwise stated or the context indicates otherwise, as used in this prospectus supplement, the terms “us,” “our,” “Pliant,” “we,” the “Company” and similar designations refer to Pliant Therapeutics, Inc.

Prospectus supplement summary

This summary highlights information contained in greater detail elsewhere or incorporated by reference in this prospectus supplement. This summary does not contain all the information you should consider before investing in our common stock. Before investing in our common stock, you should carefully read this entire prospectus supplement and the accompanying prospectus, including the section titled "Risk factors" contained in this prospectus supplement, as well as the information included in any free writing prospectus that we have authorized for use in connection with this offering. You should also carefully read the information incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements, and the related notes incorporated by reference in this prospectus supplement and the accompanying prospectus, before deciding to invest in our common stock.

Overview

We are a clinical stage biopharmaceutical company focused on discovering and developing novel therapies for the treatment of fibrosis and related diseases. Our initial focus is on treating fibrosis by inhibiting integrin-mediated activation of TGF- β and we have developed screening assays for 19 of the 24 known integrins. 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 wholly owned lead product candidate, PLN-74809 (bexotegraft), is an oral, small-molecule, dual selective inhibitor of $\alpha v\beta 6$ and $\alpha v\beta 1$ integrins that we are developing for the treatment of idiopathic pulmonary fibrosis, or IPF, and primary sclerosing cholangitis, or PSC. Bexotegraft has received Fast Track Designation and Orphan Drug Designation from the U.S. Food and Drug Administration, or FDA, in IPF and Orphan Drug Designation from the FDA and European Medicines Agency, or EMA, in PSC.

We have completed several Phase 1 and Phase 2a trials of bexotegraft in IPF, and are currently recruiting a Phase 2a trial in PSC.

Our second product candidate, PLN-1474, is an oral, small-molecule selective inhibitor of $\alpha v\beta 1$ for the treatment of liver fibrosis associated with nonalcoholic steatohepatitis, or NASH, which we have partnered with Novartis Institutes for Biomedical Research, Inc., or Novartis. PLN-1474 successfully completed a Phase 1 single-ascending dose/multiple-ascending dose trial in March 2021, and the Investigational New Drug, or IND, application was transferred to Novartis in the first quarter of 2021. Novartis is responsible for all PLN-1474 development, manufacturing and commercialization activities and we earn research and development services revenue in supporting certain aspects of the development plan.

In December 2022, we submitted an IND for our third clinical program, PLN-101095, a dual selective inhibitor of $\alpha v\beta 8$ and $\alpha v\beta 1$ integrins that we are developing for the treatment of solid tumors. We plan to initiate Phase 1 clinical trials in the first half of 2023.

In addition to our clinical programs, we currently have a preclinical integrin-based program targeting muscular dystrophies.

Recent developments

Recent clinical developments

On January 22, 2023, we announced 12-week interim data from the 320 mg dose group of INTEGRIS-IPF, a multinational, randomized, double-blind, placebo-controlled Phase 2a clinical trial of bexotegraft in patients

with IPF. The 320 mg group met its primary and secondary endpoints demonstrating that bexotegast was well tolerated over a 12-week treatment period and displayed a favorable pharmacokinetic profile. The trial's exploratory efficacy endpoints assessed changes in forced vital capacity, or FVC, Quantitative Lung Fibrosis, or QLF, imaging and biomarkers. Bexotegast at 320 mg demonstrated a statistically significant mean increase in FVC from baseline at all timepoints, surpassing all lower dose cohorts, and showed a strong treatment effect on FVC percent predicted, or FVCpp, QLF and profibrotic biomarkers versus placebo at 12 weeks.

The INTEGRIS-IPF Phase 2a trial is evaluating bexotegast at once-daily doses of 40 mg, 80 mg, 160 mg, 320 mg or placebo for 12 weeks in 119 patients with IPF.

The 320 mg group enrolled 21 patients in the active arm and 8 patients in the placebo arm. Comparable to the lower dose groups, approximately 80% of all enrolled patients were on standard of care and were equally distributed between nintedanib and pirfenidone. The 320 mg group will continue until all patients have been treated for at least 24 weeks, with final data expected in the second quarter of 2023.

Bexotegast 320 mg was well tolerated with no drug-related severe or serious adverse events

The primary endpoint of the INTEGRIS-IPF trial is the evaluation of the safety and tolerability of bexotegast. The secondary endpoint is an assessment of its pharmacokinetics.

Bexotegast was well tolerated at 320 mg over 12 weeks of treatment with no drug-related severe or serious adverse events, or SAEs, reported. All drug-related adverse events were mild or moderate in severity.

Bexotegast exhibited dose-proportional increases in plasma concentrations, consistent with prior studies.

AE, n (%) of Participants Reporting	Bexotegast 40mg (n=22)	Bexotegast 80mg (n=23)	Bexotegast 160mg (n=22)	Bexotegast 320mg (n=21)	Bexotegast All (n=88)	Placebo (n=31)
Any AEs	16 (72.7)	15 (65.2)	15 (68.2)	18 (85.7)	64 (72.7)	21 (67.7)
TEAE	16 (72.7)	15 (65.2)	14 (63.6)	17 (81.0)	62 (70.5)	21 (67.7)
Related to study drug	4 (18.2)	7 (30.4)	4 (18.2)	4 (19.0)	19 (21.6)	10 (32.3)
Serious TEAE	1 (4.5)	0	2 (9.1)	1 (4.8)	4 (4.5)	3 (9.7)
Related to study drug	0	0	0	0	0	0
TEAE of CTCAE Grade 3 or Higher	2 (9.1)	0	2 (9.1)	2 (9.5)	6 (6.8)	2 (6.5)
Related to study drug	0	0	1 (4.5)	0	1 (1.1)	0
TEAE Leading to Interruption of Study Drug	0	0	1 (4.5) ¹	1 (4.8) ²	2 (2.3)	0
TEAE Leading to Withdrawal of Study Drug	0	0	0	3 (14.3) ^{2,3,4}	3 (3.4)	3 (9.7)
TEAE Leading to Early Termination from Study	0	0	0	3 (14.3) ^{2,3,4}	3 (3.4)	2 (6.5)
TEAE Leading to Death	0	0	0	1 (4.8) ²	1 (1.1)	0

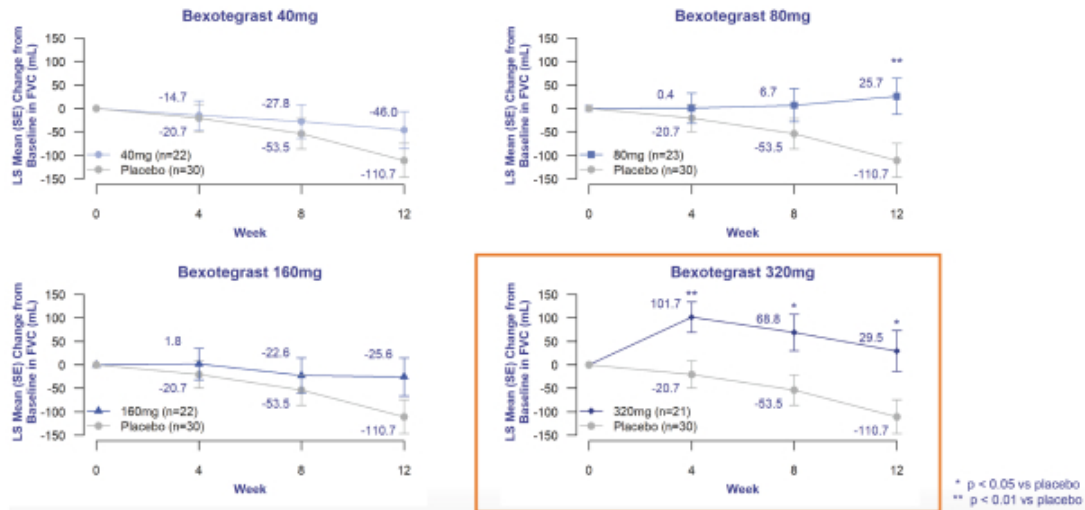
1 – COVID-19; 2 – Abdominal pain/Diarrhea in participant with pre-existing ulcerative colitis; 3 – Acute respiratory failure in a GAP Stage III participant with pre-existing atrial fibrillation 8 days following elective atrioventricular node ablation; 4 – Diarrhea in participant with concomitant use of nintedanib.

AE = Adverse Event; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Events. Adverse events coded using MedDRA v. 24.0. TEAE is defined as any AE starting (or worsening) on or after the date of first dose.

Figure 1. Adverse Events Reported by Participants in INTEGRIS-IPF Trial through 320 mg 12-Week Interim Data Readout.

Bexotegast 320 mg group demonstrated strong treatment effects on FVC, QLF and profibrotic biomarkers versus placebo over 12 weeks

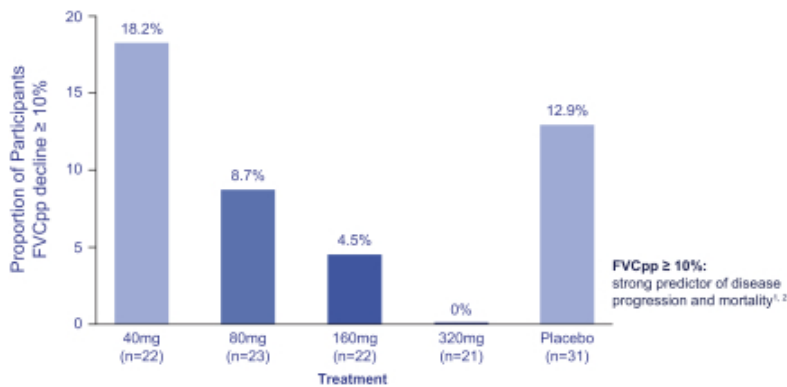
The exploratory efficacy endpoints of the INTEGRIS-IPF trial measured changes in FVC, high-resolution CT-based QLF, and profibrotic biomarkers over 12 weeks of treatment.



FVC = forced vital capacity; mITT = modified intent to treat; 1 participant in the placebo group was identified as a statistical outlier across all treatment groups and excluded from the mITT analysis. Data from the 40, 80 and 160mg groups have been updated to remove this statistical outlier.

Figure 2. Change in FVC from Baseline of Bexotegast Over 12 Weeks in INTEGRIS-IPF; Mixed Model Repeat Measures Analysis – Modified Intent to Treat Population

A strong dose-dependent treatment effect was observed in the bexotegast 320 mg dose group, with and without standard of care therapy. The bexotegast 320 mg group demonstrated mean FVC increase of +29.5 mL relative to baseline at 12 weeks, versus a decline of 110.7 mL in the placebo group resulting in a 140 mL increase compared to placebo. Mean increases in FVC versus placebo reached statistical significance at all timepoints.



FVCpp = Forced vital capacity; percent predicted
¹ Ann Am Thorac Soc. 2017 Sep; 14(9): 1395-1402; ² Am J Respir Crit Care Med. 2022 Apr 15;205(8):936-948

Figure 3. Proportion of Participants with FVCpp Decline ≥ 10% - Intent to Treat Population

A decline of $\geq 10\%$ in FVCpp at 12 weeks has been associated with increased mortality in IPF patients over a two-year period. Over 12 weeks of treatment, no patients in the 320 mg group experienced $\geq 10\%$ decline in FVCpp.

An increase in QLF score has been associated with worsening of pulmonary fibrosis. The mean percentage change in QLF at 12 weeks was 0.20% in the 320 mg group versus 1.46% in the placebo group.

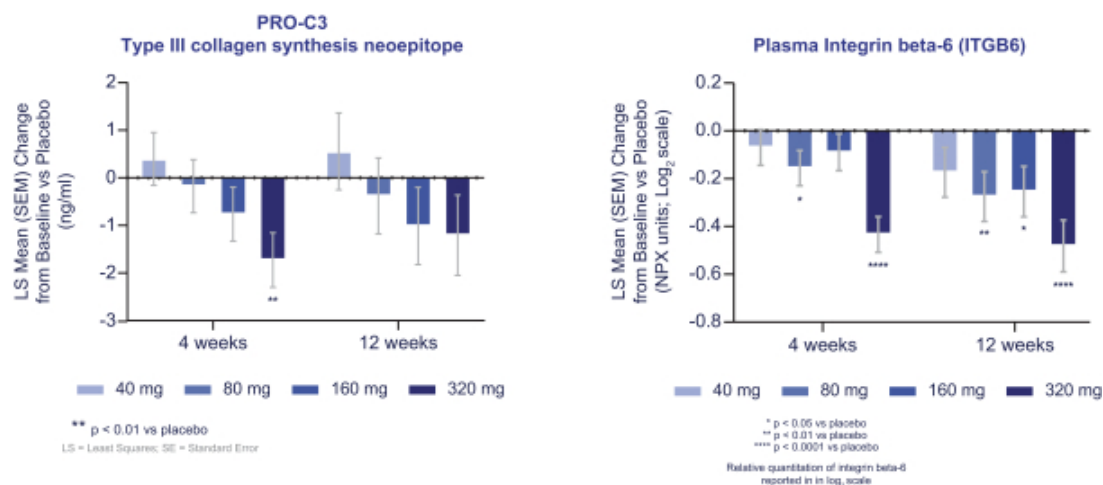


Figure 4. Circulating PRO-C3 and Integrin beta-6 Biomarker Levels– Change from Baseline at 4- and 12-Weeks vs Placebo

PRO-C3, a serum biomarker of type III collagen synthesis, is elevated in patients with IPF and associated with progressive disease. The 320 mg group demonstrated a reduction in PRO-C3 at both 4 ($p < 0.01$) and 12 weeks versus placebo.

Elevated integrin beta-6 plasma levels have been associated with ILD progression as defined by mortality, transplant or $\geq 10\%$ relative reduction in FVC (mL) over 12 months. The 320 mg group demonstrated a reduction in integrin beta-6 at both 4 and 12 weeks ($p < 0.0001$ at both timepoints) versus placebo.

These findings support a potential dose-dependent antifibrotic effect of bexotegast, consistent with its mechanism of action and preclinical findings.

Bexotegast clinical development next steps

Data from the 320 mg group of the INTEGRIS-IPF trial in patients treated for at least 24 weeks are expected in the second quarter of 2023. We are planning to initiate a Phase 2b clinical trial of bexotegast in mid-2023. Trial details will be shared closer to initiation.

Financial update

Our financial statements for the quarter and year ended December 31, 2022 will not be available until after this offering is completed and consequently will not be available to you prior to investing in this offering. Based upon preliminary estimates and information available to us as of the date of this prospectus supplement, we expect to report that we had approximately \$331.2 million of cash, cash equivalents and short-term investments as of December 31, 2022. We have not yet completed our quarter- and year-end financial close processes for the

quarter and year ended December 31, 2022. This estimate of our cash, cash equivalents and short-term investments as of December 31, 2022 is preliminary, has not been audited and is subject to change upon completion of our financial statement closing procedures. Our independent registered public accounting firm has not audited or performed any procedures with respect to this estimate and does not express an opinion or any other form of assurance with respect thereto. Additional information and disclosure would be required for a more complete understanding of our financial position and results of operations as of December 31, 2022.

Sales Agreement update

In connection with this offering, we terminated the Sales Agreement Prospectus related to our Sales Agreement with Cantor. We will not make any sales of securities pursuant to the Sales Agreement unless and until a new prospectus or prospectus supplement is filed. Other than the termination of the Sales Agreement Prospectus, the Sales Agreement remains in full force and effect.

Risks associated with our business

Our business is subject to numerous risks, as more fully described in "Risk factors" beginning on page S-9 of this prospectus supplement, as well as those risk factors that are described in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. In particular, risks associated with our business include, among others:

- We have incurred significant net losses since inception, and we expect to continue to incur significant net losses for the foreseeable future.
- 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.
- Covenants and other provisions in our term loan facility with Oxford Finance LLC, or the Oxford Loan Agreement, restrict our business and operations in many ways, and if we do not effectively manage our covenants, our financial conditions and results of operations could be adversely affected. In addition, our operations may not provide sufficient cash to meet the repayment obligations of our debt incurred under the Oxford Loan Agreement.
- We have a limited operating history, which may make it difficult to evaluate our prospects and likelihood of success.
- Our business is highly dependent on the success of our lead product candidate, bexotegrast, 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.
- Our approach to drug discovery and development in the area of fibrotic diseases is unproven and may not result in marketable products.
- 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 bexotegrast or any other product candidates.

- We may fail to obtain and maintain orphan designations in some jurisdictions and therefore fail to secure orphan exclusivity in those jurisdictions.
- 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.
- 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.
- Our success depends in part on our ability to obtain patent term extensions and 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 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 have entered into a collaboration agreement with Novartis for the development of PLN-1474 and may in the future seek to enter into collaborations with third parties for the development and commercialization of other product candidates. If we fail to enter into such collaborations, or if our collaborations are not successful, we may be unable to continue development of such product candidates, we would not receive any contemplated milestone payments or royalties, and we could fail to capitalize on the market potential of such product candidates.
- We rely on third parties to conduct certain aspects of our preclinical studies and clinical trials and for tissue samples and other materials required for our research and development activities.
- The ongoing COVID-19 pandemic could adversely impact our business, including our preclinical studies and clinical trials.
- Our loss of key management personnel, or our failure to recruit additional highly skilled personnel, will impair our ability to develop current product candidates or identify and develop new product candidates, could result in loss of markets or market share and could make us less competitive.

Corporate 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 supplement or the accompanying prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus supplement or the accompanying prospectus. Our website address is included in this prospectus supplement as an inactive textual reference only.

The offering

Common stock offered by us	\$175.0 million of shares.
Option to purchase additional shares	The underwriters have been granted the option to purchase up to an additional \$26.25 million of shares of our common stock, which they may exercise, in whole or in part, for a period of 30 days from the date of this prospectus supplement.
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	<p>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, in each case after deducting underwriting discounts and commissions and estimated offering expenses payable by us.</p> <p>We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, to develop our ongoing and future preclinical and clinical programs including bexotegrast and PLN-101095, further develop our integrin targeting platform, and the remainder, if any, to fund working capital, operating expenses and capital expenditures, and for other general corporate purposes. See "Use of proceeds" on page S-12 of this prospectus supplement for additional information.</p>
Risk factors	Investing in our common stock involves significant risks. You should carefully read the section titled "Risk factors" in this prospectus supplement beginning on page S-9 as well as those risk factors described in the documents that are incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors that you should consider before deciding to invest in our common stock.
Nasdaq Global Select Market symbol	"PLRX"

The number of shares of our common stock to be outstanding after this offering is based on 48,749,842 shares of common stock outstanding as of September 30, 2022, and excludes:

- 5,474,346 shares of our common stock issuable upon the exercise of options outstanding as of September 30, 2022, with a weighted-average exercise price of \$13.05 per share;
- 523,475 shares of our common stock issuable upon the vesting and settlement of restricted stock units outstanding as of September 30, 2022;
- 709,064 shares of our common stock issuable upon the vesting and settlement of performance stock units outstanding as of September 30, 2022, considering satisfaction of the underlying performance conditions at

100% (target) achievement, plus an additional 709,064 shares of common stock may be issued upon satisfaction of the underlying performance conditions at 200% (maximum) achievement;

- 307,800 shares of common stock issuable upon the exercise of options granted after September 30, 2022, with a weighted-average exercise price of \$21.60 per share;
- 3,090,672 shares of our common stock reserved for future issuance under our 2020 Stock Option and Incentive Plan, or the 2020 Plan, as of September 30, 2022; and
- 888,184 shares of our common stock reserved for future issuance under our 2020 Employee Stock Purchase Plan, or the 2020 ESPP, as of September 30, 2022.

Unless otherwise indicated, all information in this prospectus supplement assumes:

- no exercise by the underwriters of their option to purchase additional shares of common stock; and
- no exercise, vesting or settlement of the outstanding options, restricted stock units or performance stock units described above.

The number of shares of common stock to be outstanding immediately following this offering as shown above does not reflect any automatic (or other) increases in the number of shares of common stock reserved for future issuance under the 2020 Plan or the 2020 ESPP, including the 2,447,067 shares of common stock automatically added to the 2020 Plan on January 1, 2023 in accordance with the terms of the 2020 Plan. In addition, the number of shares of common stock to be outstanding immediately following this offering as shown above does not include up to \$150.0 million of our common stock that remained available for sale at September 30, 2022 pursuant to the Sales Agreement. As of the date of this prospectus supplement, no shares have been sold pursuant to the Sales Agreement. In connection with this offering, we terminated the Sales Agreement Prospectus. We will not make any sales of securities pursuant to the Sales Agreement unless and until a new prospectus or prospectus supplement is filed. Other than the termination of the Sales Agreement Prospectus, the Sales Agreement remains in full force and effect.

Risk factors

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should carefully consider the risks and uncertainties described below and those described in the section titled "Risk Factors" in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC that are incorporated herein by reference, together with other information in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering. The risks described in these documents are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be materially adversely affected. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also carefully read the section titled "Special note regarding forward-looking statements."

Risks related to this offering

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

You will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of \$ per share, purchasers of common stock in this offering will experience immediate dilution of \$ per share in net tangible book value of our common stock. In the past, we issued options and other securities to acquire common stock at prices significantly below the public offering price. To the extent these outstanding securities are ultimately exercised, investors purchasing common stock in this offering will sustain further dilution. See the section titled "Dilution" for a more detailed description of the dilution to new investors in this offering.

We will have broad discretion in how we use the net proceeds of this offering and may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We will have considerable discretion in the application of the net proceeds of this offering, including for any of the purposes described in the section titled "Use of proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. As a result, investors will be relying upon our management's judgment with only limited information about our specific intentions for the use of the net proceeds of this offering. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value. The failure by our management to apply the net proceeds effectively could result in financial losses that could harm our business, cause the price of our common stock to decline and delay the development or commercialization of our product candidates.

Special note regarding forward-looking statements

This prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, contain 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 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, bexotegrast, including statements regarding the safety, tolerability, pharmacodynamics and therapeutic potential of bexotegrast, as well as PLN-1474, PLN-101095 and our other product candidates;
- our estimates regarding the impact of the COVID-19 pandemic on our business and operations, and our ability to manage such impacts;
- our or our current or future collaborators' 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 and fast track designations for bexotegrast;
- 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 dependence on current and future collaborators for developing, obtaining regulatory approval for and commercializing product candidates in the collaboration;
- our receipt and timing of any milestone payments or royalties under any current or future research collaboration or license agreements or arrangements;
- our plans and strategy regarding the commercialization of any products that are approved for marketing and our ability to establish adequate pricing in the U.S. and international markets;
- 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;

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- our ability to attract and retain qualified employees and key personnel;
- our expectations regarding government and third-party payor coverage and reimbursement; and
- our expected use of the net proceeds from this offering and our existing cash, cash equivalents and short-term investments.

In some cases, you can identify forward-looking statements by terminology such as “anticipates,” “believes,” “continue,” “estimates,” “expects,” “intends,” “may,” “plans,” “potential,” “predicts,” “should,” “will” 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 titled “Risk factors” and elsewhere in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus we have authorized for use in connection with this offering.

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 carefully and completely read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus we have authorized for use in connection with this offering, 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 supplement and the accompanying prospectus represent our views as of the date of this prospectus supplement. 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 supplement.

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 supplement, 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.

Use of proceeds

We estimate that the net proceeds to us from the sale of the 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, in each case after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, to develop our ongoing and future preclinical and clinical programs including bexotegrast and PLN-101095, further develop our integrin targeting platform, and the remainder, if any, to fund working capital, operating expenses and capital expenditures, and for other general corporate purposes.

Our expected use of net proceeds from this offering represents our intentions based upon our present plans and business conditions. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds from 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, cash equivalents and short-term investments 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, the timing of regulatory submissions and unforeseen cash needs. Accordingly, our management will have broad discretion in using the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of the net proceeds.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation instruments, including short-term and immediate-term, interest-bearing instruments, investment-grade securities, certificates of deposit or direct or guaranteed obligations of the U.S. government. We cannot predict whether the proceeds invested will yield a favorable return.

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 price per share of common stock in this offering and the as adjusted net tangible book value per share of common stock immediately after this offering.

Our net tangible book value as of September 30, 2022 was approximately \$337.0 million, or \$6.91 per share. Net tangible book value is the amount of our total tangible assets less our total liabilities. Net tangible book value per share is net tangible book value divided by the total number of shares of common stock outstanding as of September 30, 2022.

After giving effect to the sale of shares of our common stock in this offering at the public offering price of \$ per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2022 would have been approximately \$ million, or \$ per share. This represents an immediate increase in net tangible book value of \$ per share to our existing stockholders and an immediate dilution of \$ per share to investors participating in this offering.

The following table illustrates this dilution on a per share basis.

Public offering price per share	\$
Historical net tangible book value per share as of September 30, 2022	\$6.91
Increase in net tangible book value per share attributable to new investors purchasing our common stock in this offering	_____
As adjusted net tangible book value per share after giving effect to this offering	\$
Dilution per share to investors purchasing our common stock in this offering	\$

If the underwriters exercise in full their option to purchase additional shares of common stock in this offering at the public offering price of \$ per share, the as adjusted net tangible book value after this offering would be \$ per share, the increase in the net tangible book value to existing stockholders would be \$ per share, and the dilution to new investors purchasing our common stock in this offering would be \$ per share.

The foregoing table and calculations (other than the historical net tangible book value calculation) are based on 48,749,842 shares of common stock outstanding as of September 30, 2022, and excludes:

- 5,474,346 shares of our common stock issuable upon the exercise of options outstanding as of September 30, 2022, with a weighted-average exercise price of \$13.05 per share;
- 523,475 shares of our common stock issuable upon the vesting and settlement of restricted stock units outstanding as of September 30, 2022;
- 709,064 shares of our common stock issuable upon the vesting and settlement of performance stock units outstanding as of September 30, 2022, considering satisfaction of the underlying performance conditions at 100% (target) achievement, plus an additional 709,064 shares of common stock may be issued upon satisfaction of the underlying performance conditions at 200% (maximum) achievement;
- 307,800 shares of common stock issuable upon the exercise of options granted after September 30, 2022, with a weighted-average exercise price of \$21.60 per share;

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- 3,090,672 shares of our common stock reserved for future issuance under our 2020 Plan as of September 30, 2022; and
- 888,184 shares of our common stock reserved for future issuance under our 2020 ESPP as of September 30, 2022.

The number of shares of common stock to be outstanding immediately following this offering as shown above does not reflect any automatic (or other) increases in the number of shares of common stock reserved for future issuance under the 2020 Plan or the 2020 ESPP, including the 2,447,067 shares of common stock automatically added to the 2020 Plan on January 1, 2023 in accordance with the terms of the 2020 Plan. In addition, the number of shares of common stock to be outstanding immediately following this offering as shown above does not include up to \$150.0 million of our common stock that remained available for sale at September 30, 2022 pursuant to the Sales Agreement. As of the date of this prospectus supplement, no shares have been sold pursuant to the Sales Agreement. In connection with this offering, we terminated the Sales Agreement Prospectus. We will not make any sales of securities pursuant to the Sales Agreement unless and until a new prospectus or prospectus supplement is filed. Other than the termination of the Sales Agreement Prospectus, the Sales Agreement remains in full force and effect.

To the extent that outstanding options, restricted stock units or performance stock units outstanding as of September 30, 2022 have been or may be exercised or settled or other shares issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

Material U.S. federal income tax consequences to non-U.S. holders of our common stock

The following is a summary of material U.S. federal income tax consequences of the ownership and disposition of shares of our common stock as of the date hereof. Except where noted, this summary deals only with common stock that is held as a capital asset by a non-U.S. holder (as defined below). This summary is based upon provisions of the Code and regulations, rulings and judicial decisions as of the date hereof. Those authorities may be changed, perhaps retroactively, so as to result in U.S. federal income tax consequences different from those summarized below. We cannot assure you that a change in law will not alter significantly the tax considerations that we describe in this summary.

A “non-U.S. holder” means a beneficial owner of shares of our common stock (other than an entity treated as a partnership for U.S. federal income tax purposes) that is not, for U.S. federal income tax purposes, any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation (or any other entity treated as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if it (1) is subject to the primary supervision of a court within the United States and one or more U.S. persons (as defined under the Code) have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

This summary does not address all aspects of U.S. federal income taxation that may be relevant to non-U.S. holders in light of their particular circumstances. In addition, this summary does not address the Medicare tax on certain net investment income, U.S. federal gift or estate tax laws, any state, local or non-U.S. tax laws or any tax treaties. This summary also does not address the U.S. federal income tax consequences applicable to non-U.S. holders that are subject to special treatment under the U.S. federal income tax laws, including (without limitation) former citizens or long-term residents of the United States, foreign pension funds, “controlled foreign corporations,” “passive foreign investment companies,” financial institutions, insurance companies, regulated investment companies, real estate investment trusts, mutual funds, broker-dealers, traders in securities or other persons that elect to use a mark-to-market method of accounting for their holdings in our common stock, persons who hold our common stock as “qualified small business stock” within the meaning of Section 1202 of the Code, persons who hold our common stock as a position in a hedging transaction, “straddle,” “conversion transaction,” or other risk reduction transaction or integrated investment, persons subject to the alternative minimum tax, persons who acquired our common stock through stock options or in other compensatory transactions or partnerships or other pass-through entities for U.S. federal income tax purposes.

If a partnership (or other entity or arrangement treated as a partnership for U.S. federal income tax purposes) holds shares of our common stock, the tax treatment of a partner will generally depend upon the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partners in partnerships (including entities or arrangements treated as partnerships for U.S. federal income tax purposes) considering the purchase of our common stock should consult their tax advisors regarding the U.S. federal income tax considerations of the purchase, ownership and disposition of our common stock by such partnership.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT TAX ADVICE. PROSPECTIVE INVESTORS ARE ENCOURAGED TO CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATION, AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL GIFT OR ESTATE TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL, NON-U.S. OR OTHER TAXING JURISDICTION OR UNDER ANY APPLICABLE TAX TREATY.

Distributions

Distributions of cash or property 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. To the extent those distributions exceed our current and accumulated earnings and profits, the distributions will be treated as a nontaxable return of capital to the extent of the non-U.S. holder's tax basis in our common stock and thereafter as capital gain from the sale or exchange of such common stock. Please read "—Sales or other taxable dispositions." Subject to the withholding rules discussed below under "—Backup withholding and information reporting" and "—Additional withholding requirements under FATCA" and except for effectively connected dividends, any distribution made to a non-U.S. holder on our common stock generally will be subject to U.S. withholding tax at a rate of 30% of the gross amount of the distribution unless an applicable income tax treaty provides for a lower rate. To receive the benefit of a reduced treaty rate, a non-U.S. holder must provide the applicable withholding agent with a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E (or other applicable or successor form) certifying qualification for the reduced rate, and the non-U.S. holder will be required to update such forms and certifications from time to time as required by law. A non-U.S. holder eligible for a reduced rate of U.S. federal withholding tax pursuant to an applicable income tax treaty may be eligible to obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. If the non-U.S. holder holds our common stock through a financial institution or other agent acting on the non-U.S. holder's behalf, the non-U.S. holder will be required to provide appropriate documentation to the agent, which then will be required to provide certification to us or our paying agent, either directly or through other intermediaries. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under an applicable income tax treaty.

If dividends paid to a non-U.S. holder are effectively connected with a trade or business conducted by the non-U.S. holder in the United States (and, if required by an applicable income tax treaty, are treated as attributable to a permanent establishment maintained by the non-U.S. holder in the United States), the non-U.S. holder will be exempt from the U.S. withholding tax described above, provided the non-U.S. holder satisfies certain certification requirements by providing the applicable withholding agent a properly executed IRS Form W-8ECI certifying eligibility for exemption, and the non-U.S. holder will be required to update such forms and certifications from time to time as required by law. Any such effectively connected dividends generally will be taxed on a net income basis at the rates and in the manner generally applicable to U.S. persons (as defined under the Code). If the non-U.S. holder is a corporation for U.S. federal income tax purposes, it may also be subject to a branch profits tax at a 30% rate (or such lower rate as specified by an applicable income tax treaty) on its effectively connected earnings and profits (as adjusted for certain items), which will include effectively connected dividends. Non-U.S. holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

Sales or other taxable dispositions

Subject to the discussion below under "—Backup withholding and information reporting", any gain realized by a non-U.S. holder on the sale or other disposition of our common stock generally will not be subject to U.S. federal income tax unless:

- the gain is effectively connected with a trade or business of the non-U.S. holder in the United States (and, if required by an applicable income tax treaty, is attributable to a U.S. permanent establishment of the non-U.S. holder);

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- the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of that disposition, and certain other conditions are met; or
- we are or have been a “United States real property holding corporation” for U.S. federal income tax purposes and certain other conditions are met.

A non-U.S. holder described in the first bullet point immediately above will be subject to tax on the gain derived from the sale or other disposition on a net income tax basis at the U.S. federal income tax rates applicable to U.S. citizens and residents or domestic corporations, as applicable. In addition, if any non-U.S. holder described in the first bullet point immediately above is a foreign corporation, the gain realized by such non-U.S. holder may 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). An individual non-U.S. holder described in the second bullet point immediately above will be subject to a 30% (or such lower rate as may be specified by an applicable income tax treaty) tax on the gain derived from the sale or other disposition, which gain may be offset by U.S. source capital losses even though the individual is not considered a resident of the United States.

Generally, a corporation is a “United States real property holding corporation” (“USRPHC”) 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 and its other assets used or held for use in a trade or business (all as determined for U.S. federal income tax purposes). We believe that we are not currently and will not become a USRPHC, and the remainder of this discussion assumes this is the case. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our other business assets, there can be no assurance that we will not become a USRPHC in the future. If we are or become a USRPHC, however, so long as our common stock is regularly traded on an established securities market during the calendar year in which the sale or other disposition occurs, only a non-U.S. holder who actually or constructively holds or held (at any time during the shorter of the five-year period preceding the date of disposition or the holder’s holding period) more than 5% of our common stock will be subject to U.S. federal income tax on the sale or other disposition of our common stock.

Backup withholding and information reporting

Any dividends paid to a non-U.S. holder must be reported annually to the IRS and to the non-U.S. holder. Copies of these information returns may be made available to the tax authorities in the country in which the non-U.S. holder resides or is established. Payments of dividends to a non-U.S. holder generally will not be subject to backup withholding if the non-U.S. holder establishes an exemption by properly certifying its non-U.S. status on an IRS Form W-8BEN, IRS Form W-8BEN-E or other applicable or successor form.

Payments of the proceeds from a sale or other disposition by a non-U.S. holder of our common stock effected by or through the U.S. office of a broker generally will be subject to information reporting and backup withholding (currently at the rate of 24%) unless the non-U.S. holder establishes an exemption by properly certifying its non-U.S. status on an IRS Form W-8BEN, IRS Form W-8BEN-E or other applicable or successor form and certain other conditions are met. Information reporting and backup withholding generally will not apply to any payment of the proceeds from a sale or other disposition of our common stock effected outside the United States by a non-U.S. office of a broker. However, unless such broker has documentary evidence in its records that the holder is not a U.S. person and certain other conditions are met, or the non-U.S. holder otherwise establishes an exemption, information reporting will apply to a payment of the proceeds of the disposition of our common stock effected outside the United States by such a broker if it has certain relationships within the United States. Notwithstanding the foregoing, backup withholding and information reporting may apply if either we or our paying agent has actual knowledge, or reason to know, that the non-U.S. holder is a U.S. person who is not an exempt recipient under the Code and applicable Treasury regulations.

Backup withholding is not an additional tax. Rather, the U.S. income tax liability (if any) of persons subject to backup withholding will be reduced by the amount of tax withheld. If backup withholding results in an overpayment of taxes, a refund may be obtained, provided that the required information is timely furnished to the IRS.

Additional withholding requirements under FATCA

Sections 1471 through 1474 of the Code, and the Treasury regulations and administrative guidance issued thereunder ("FATCA"), impose a 30% withholding tax on any dividends paid on our common stock if paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code) (including, in some cases, when such foreign financial institution or non-financial foreign entity is acting as an intermediary), unless (1) in the case of a foreign financial institution, such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are non-U.S. entities with U.S. owners); (2) in the case of a non-financial foreign entity, such entity certifies that it does not have any "substantial United States owners" (as defined in the Code) or provides the applicable withholding agent with a certification identifying the direct and indirect substantial United States owners of the entity (in either case, generally on an IRS Form W-8BEN-E) and provides certain information with respect to such United States owners; or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules and provides appropriate documentation (such as an IRS Form W-8BEN-E). The Treasury Secretary has issued proposed regulations providing that the withholding provisions under FATCA do not apply with respect to gross proceeds from a sale or other disposition of our common stock, which may be relied upon by taxpayers until final regulations are issued. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing these rules may be subject to different rules. Under certain circumstances, a holder might be eligible for refunds or credits of such taxes.

INVESTORS CONSIDERING THE PURCHASE OF OUR COMMON STOCK SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AND THE APPLICABILITY AND EFFECT OF U.S. FEDERAL GIFT AND ESTATE TAX LAWS AND ANY STATE, LOCAL OR NON-U.S. TAX LAWS AND TAX TREATIES.

Underwriting

We are offering shares of common stock described in this prospectus supplement through a number of underwriters. J.P. Morgan Securities LLC and Piper Sandler & Co. are acting as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	
Piper Sandler & Co.	
RBC Capital Markets, LLC	
Cantor Fitzgerald & Co.	
Oppenheimer & Co. Inc.	
H.C. Wainwright & Co., LLC	
Total	

The underwriters are committed to purchase all the shares of common stock offered by us if they purchase any shares of common stock. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the shares of common stock directly to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of \$ per share of common stock. After the offering of the shares of common stock to the public, if all of the shares of common stock are not sold at the public offering price set forth on the cover page of this prospectus supplement, the underwriters may change the offering price and the other selling terms. Sales of any shares of common stock made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus supplement to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$ per share of common stock. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without option to purchase additional shares	With option to purchase additional shares
Per share of common stock	\$	\$
Total	\$	\$

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We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$. We have agreed to reimburse the underwriters for expenses relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc. in an amount up to \$20,000.

A prospectus supplement and the accompanying prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, sell, contract to sell, pledge, hedge, or otherwise dispose of, (or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition (whether by actual disposition or effective economic disposition due to cash settlement or otherwise) by us or any of our affiliates or any person in privity with us or any of our affiliates), directly or indirectly, including the submission or filing (or participation in the submission or filing) of a registration statement with the SEC in respect of, or establish or increase a put equivalent position or liquidate or decrease a call equivalent position within the meaning of Section 16 of the Exchange Act, any other shares of our common stock or any securities convertible into, or exercisable, or exchangeable for, shares of our common stock; or publicly announce an intention to effect any such transaction; in each case, without the prior written consent of the representatives for a period of 60 days after the date of this prospectus supplement.

The restrictions described in the immediately preceding paragraph do not apply to:

- (i) the transactions contemplated by the underwriting agreement;
- (ii) the grant of options or issuance of shares of common stock to our employees, officers, directors, advisors or consultants pursuant to employee benefit plans, provided, that each recipient of such securities that is a newly appointed director or executive officer pursuant to this clause (ii) agrees to restrictions on the resale of securities that are consistent with the provisions set forth in the lock-up agreement;
- (iii) the filing of one or more registration statements on Form S-8 relating to stock options or our employee benefit plans; or
- (iv) the offer, issuance and sale of our common stock or securities convertible into or exercisable or exchangeable for Common Stock in connection with any (1) mergers, (2) acquisition of securities, businesses, property or other assets, (3) joint ventures, (4) strategic alliances, (5) partnerships with experts or other talent to develop or provide content or (6) equipment leasing arrangements, provided, that the aggregate number of shares of our common stock or securities convertible into or exercisable for our common stock (on an as-converted or as-exercised basis, as the case may be) that we may issue or agree to issue pursuant to this clause (iv) shall not exceed 5% of the total number of shares of our common stock issued and outstanding immediately following the completion of the transactions contemplated by the underwriting agreement, and provided, further, that each recipient of such securities that is a newly appointed director or executive officer agrees to restrictions on the resale of securities that are consistent with the provisions set forth in the lock-up agreement.

Our directors, executive officers and certain of our stockholders (each, a "lockup party") have entered into lockup agreements with the underwriters prior to the commencement of this offering pursuant to which each of these lockup parties, subject to specified limited exceptions, for a period of 60 days after the date of this prospectus supplement (such period, the "restricted period"), will not, (i) offer, sell, contract to sell, pledge,

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hedge or otherwise dispose of (or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition (whether by actual disposition or effective economic disposition due to cash settlement or otherwise) by any of these persons or entities or any of their respective affiliates or any person in privity with any of the lockup parties or any of their respective affiliates), directly or indirectly, including the submission or filing (or participation in the submission or filing) of a registration statement with the SEC in respect of, or establish or increase a put equivalent position or liquidate or decrease a call equivalent position within the meaning of Section 16 of the Exchange Act, and the rules and regulations of the SEC promulgated thereunder with respect to, any shares of our capital stock or any securities convertible into, or exercisable or exchangeable for such capital stock (the "Lock-Up Securities"), (ii) engage in any hedging or other transactions designed or intended, or which could reasonably be expected to lead to or result in, a sale or disposition of any shares of our common stock, or securities convertible into exercisable or exchangeable for our common stock, even if any such sale or disposition transaction or transactions would be made or executed by or on behalf of someone other than any of the lockup parties, or (iii) publicly announce an intention to effect any such transaction described in clause (i) or (ii) above.

The restrictions described in the immediately preceding paragraph do not apply to, among other items and subject to certain limited exceptions:

- (i) transactions relating to shares of our common stock or other securities acquired in the transactions contemplated pursuant to the underwriting agreement or in open market transactions after the completion of the transactions contemplated pursuant to the underwriting agreement;
- (ii) transfers of Lock-Up Securities as a bona fide gift or charitable contribution;
- (iii) exercise of stock options or warrants to purchase shares of our common stock or the vesting of stock awards of our common stock and any related transfer of shares of our common stock in connection therewith (x) deemed to occur upon the "cashless" or "net" exercise of such options or warrants or (y) for the purpose of paying the exercise price of such options or warrants or for paying taxes due as a result of the exercise of such options or warrants, the vesting of such options, warrants or stock awards, or as a result of the vesting of such shares of our common stock, it being understood that all shares of our common stock received upon such exercise, vesting or transfer will remain subject to the restrictions of this lock-up agreement during the restricted period, and provided if the lockup party is required to file a report under the Exchange Act reporting a reduction in beneficial ownership of shares of our common stock during the restricted period, the lockup party shall clearly indicate in the footnotes thereto that the filing relates to the circumstances described in this paragraph and no other filing or public announcement shall be made voluntarily during the restricted period in connection with such exercise, vesting or transfer;
- (iv) transfers of Lock-Up Securities to us pursuant to any contractual arrangement that provides us with an option to repurchase such shares of our common stock in the event the lockup party ceases to provide services to us, provided that such contractual arrangement is disclosed in the final prospectus supplement relating to this offering or our filings with the SEC, and provided further that if each of the lockup parties is required to file a report under the Exchange Act reporting a reduction in beneficial ownership of shares of our common stock during the restricted period, such lockup party shall clearly indicate in the footnotes thereto that the filing relates to the termination of the lockup party's employment or other services and no other filing or public announcement shall be made voluntarily during the restricted period in connection with such transfer;
- (v) transfers to the spouse, domestic partner, parent, child (including stepchild or adopted child) or grandchild or first cousin of the lockup party (each, an "Immediate Family Member") or to a trust formed for the direct or indirect benefit of the lockup party or an Immediate Family Member;

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- (vi) transfers by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary, trustee or Immediate Family Member of the lockup party;
- (vii) transfers pursuant to a divorce settlement agreement or decree or a qualified domestic relations order;
- (viii) transfers of Lock-Up Securities to any affiliate (as such term is defined in Rule 405 of the Securities Act), limited partners, general partners, limited liability company members or stockholders of the lockup party, or if the lockup party is a corporation to any wholly owned subsidiary of such corporation; or
- (ix) transfer of Lock-Up Securities pursuant to a bona fide third-party tender offer for our securities, merger, consolidation or other similar transaction that is approved by our Board of Directors, made to all holders of our common stock involving a transaction or a series of related transactions, the result of which is that any "person" (as defined in Section 13(d)(3) of the Exchange Act), or group of persons, other than us, becomes the beneficial owner (as defined in Rules 13d-3 and 13d-5 of the Exchange Act) of 75% or more of the total voting power of our voting stock (or the surviving entity), provided that in the event that such tender offer, merger, consolidation or other such transaction is not completed, the Lock-Up Securities shall remain subject to the provisions of this lock-up agreement;

provided, that, in the case of clause (i) above, no filing under the Exchange Act reporting a reduction in beneficial ownership of shares of our common stock shall be required or voluntarily made during the restricted period, other than Forms 5 and Schedule 13F; provided further that in the case of any transfer or distribution pursuant to clauses (ii), (v), (vi), (vii) and (viii), (a) the recipient agrees to be bound in writing by the same restrictions set forth herein for the duration of the restricted period, (b) no filing under the Exchange Act reporting a reduction in beneficial ownership of shares of our common stock shall be required or voluntarily made during the restricted period, other than Forms 5 and Schedule 13F, and (c) any such transfer shall not involve a disposition for value.

In addition, none of the lockup parties is prohibited from entering into any plan designed to satisfy the requirements of Rule 10b5-1 under the Exchange Act (a "10b5-1 Plan"); provided, however, that (i) no sale of Lock-Up Securities may be made under such 10b5-1 Plan during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required by or on behalf of the lockup party or us regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of our common stock may be made under such plan during the restricted period and no filings or public announcement shall be made voluntarily during the restricted period regarding the establishment of such plan. Additionally, the foregoing restrictions shall not apply to sales of Lock-Up Securities made pursuant to a 10b5-1 Plan that has been entered into and disclosed to the Representatives by the undersigned prior to the date of this lock-up agreement, provided that if the undersigned reports any such transfer on a Form 4 filed with the SEC pursuant to Section 16 of the Exchange Act, such Form 4 shall clearly indicate in the footnotes thereto that such transfer was effected pursuant to a trading plan designed to satisfy the requirements of Rule 10b5-1 under the Exchange Act and no other filing or public announcement shall be made voluntarily during the restricted period in connection with such transfer.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "PLRX."

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of common stock, which involves the sale by the underwriters of a

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greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be “covered” shorts, which are short positions in an amount not greater than the underwriters’ option to purchase additional shares referred to above, or may be “naked” shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. 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 common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discounts and commissions received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The Nasdaq Global Market, in the over-the-counter market or otherwise.

Other relationships

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future. For example, in the third quarter of 2021, we entered into the Sales Agreement with Cantor, one of the underwriters.

Selling restrictions

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement and the accompanying prospectus may not be offered or sold, directly or indirectly, nor may this prospectus supplement and the accompanying prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement and the accompanying prospectus come are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying

prospectus do not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Notice to Prospective Investors in the European Economic Area

None of this prospectus supplement, the accompanying prospectus and any related free writing prospectus is a prospectus for the purposes of Regulation (EU) 2017/1129 (the "Prospectus Regulation"). This prospectus supplement, the accompanying prospectus and any related free writing prospectus have been prepared on the basis that any offer of shares of our common stock in any Member State of the European Economic Area will be made pursuant to an exemption under the Prospectus Regulation from the requirement to publish a prospectus for offers of shares of our common stock. Accordingly any person making or intending to make an offer in that Member State of shares of our common stock which are the subject of the offering contemplated in this prospectus supplement, the accompanying prospectus and any related free writing prospectus may only do so in circumstances in which no obligation arises for the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Regulation in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares of our common stock in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

In relation to each Member State of the European Economic Area (each a "Relevant State"), no shares of our common stock have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares of our common stock which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that the shares of our common stock may be made to the public in that Relevant State at any time:

- (a) to any legal entity which is a qualified investor as defined under Article 2 of the Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of representatives for any such offer; or
- (c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation;

provided that no such offer of the shares of our common stock shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation and each person who initially acquires any shares of our common stock or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the representatives and the Company that it is a "qualified investor" within the meaning of Article 2(e) of the Prospectus Regulation. In the case of any shares of our common stock being offered to a financial intermediary as that term is used in Article 5 of the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares of our common stock acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares of our common stock to the public other than their offer or resale in a Relevant State to qualified investors as so defined or in circumstances in which the prior consent of the representatives have been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an "offer to the public" in relation to the shares of our common stock in any Relevant State means the communication in any form and by any means of sufficient

information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase or subscribe for any shares of our common stock.

This European Economic Area selling restriction is in addition to any other selling restrictions set out below.

Notice to Prospective Investors in the United Kingdom

In the United Kingdom, none of this prospectus supplement, the accompanying prospectus and any related free writing prospectus is a prospectus for the purposes of Regulation (EU) 2017/1129 as it forms part of domestic law in the United Kingdom by virtue of the European Union (Withdrawal) Act 2018, as amended by the European Union (Withdrawal Agreement) Act 2020 (the "EUWA") (the "UK Prospectus Regulation"). This prospectus supplement, the accompanying prospectus and any related free writing prospectus have been prepared on the basis that any offer of shares of our common stock in the United Kingdom will be made pursuant to an exemption under the UK Prospectus Regulation from the requirement to publish a prospectus for offers of shares of our common stock. Accordingly any person making or intending to make an offer in the United Kingdom of shares of our common stock which are the subject of the offering contemplated in this prospectus supplement, the accompanying prospectus and any related free writing prospectus may only do so in circumstances in which no obligation arises for the Company or any of the underwriters to publish a prospectus pursuant to Section 85 of the United Kingdom's Financial Services and Markets Act 2000, as amended (the "FSMA") in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares of our common stock in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

No shares of our common stock have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the shares of our common stock which has been approved by the Financial Conduct Authority, except that the shares of our common stock may be offered to the public in the United Kingdom at any time:

- (i) to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;
- (ii) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- (iii) in any other circumstances falling within Section 86 of the FSMA,

provided that no such offer of the shares of our common stock shall require the Company or any underwriter to publish a prospectus pursuant to Section 85 of the FSMA and each person who initially acquires any shares of our common stock or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the representatives and the Company that it is a "qualified investor" within the meaning of Article 2(e) of the UK Prospectus Regulation. In the case of any shares of our common stock being offered to a financial intermediary as that term is used in Article 5 of the UK Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares of our common stock acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares of our common stock to the public other than their offer or resale in the United Kingdom to qualified investors as so defined or in circumstances in which the prior consent of the representatives have been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an "offer to the public" in relation to the shares of our common stock in the United Kingdom means the communication in any form and by any means of sufficient

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information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase or subscribe for any shares of our common stock.

The communication of this prospectus supplement, the accompanying prospectus, any related free writing prospectus and any other document or materials relating to the issue of the shares of our common stock offered hereby is not being made, and such documents and/or materials have not been approved, by an authorized person for the purposes of section 21 of the FSMA. Accordingly, such documents and/or materials are not being distributed to, and must not be passed on to, the general public in the United Kingdom. This document and such other documents and/or materials are for distribution only to persons who (i) have professional experience in matters relating to investments and who fall within the definition of investment professionals (as defined in Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Financial Promotion Order")), (ii) fall within Article 49(2)(a) to (d) of the Financial Promotion Order, (iii) are outside the United Kingdom or (iv) are any other persons to whom it may otherwise lawfully be made under the Financial Promotion Order (all such persons together being referred to as "relevant persons"). This document is directed only at relevant persons and must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this prospectus supplement, the accompanying prospectus and any related free writing prospectus relates will be engaged in only with, relevant persons. Any person in the United Kingdom that is not a relevant person should not act or rely on this prospectus supplement, the accompanying prospectus or any related free writing prospectus or any of their contents.

Any invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) in connection with the issue or sale of the shares of our common stock may only be communicated or caused to be communicated in circumstances in which Section 21(1) of the FSMA does not apply to the Company.

All applicable provisions of the FSMA must be complied with in respect to anything done by any person in relation to the shares of our common stock in, from or otherwise involving the United Kingdom.

Notice to Prospective Investors in France

Neither this prospectus nor any other offering material relating to the shares of our common stock 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 of our common stock 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 of our common stock 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 of our common stock 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

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- 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 of our common stock 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

The shares of our common stock have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (the “SFO”) and any rules made thereunder; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) (the “C(WUMP)O”) or which do not constitute an offer to the public within the meaning of the C(WUMP)O. No advertisement, invitation or document relating to the shares of our common stock has been or will be issued or has been or will be in the possession of any person for the purposes of issue, 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 to do so under the securities laws of Hong Kong) other than with respect to the shares of our common stock 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 thereunder.

Notice to Prospective Investors in Japan

The shares of our common stock have not been and will not be registered pursuant to Article 4, Paragraph 1 of the Financial Instruments and Exchange Act. Accordingly, none of the shares of our common stock nor any interest therein may be offered or sold, directly or indirectly, in Japan or to, or for the account or 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 account or benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan in effect at the relevant time.

Notice to Prospective Investors in Singapore

This prospectus supplement has not been and will not be registered as a prospectus under the Securities and Futures Act 2001 (the “SFA”) by the Monetary Authority of Singapore, and the offer of the shares of our common stock in Singapore is made primarily pursuant to the exemptions under Section 274 and 275 of the SFA. Accordingly, this Offering Memorandum and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares of our common stock may not be circulated or distributed, nor may the shares of our common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to any person in Singapore other than:

- (a) to an institutional investor as defined in Section 4A of the SFA (an “Institutional Investor”) pursuant to Section 274 of the SFA;
- (b) to an accredited investor as defined in Section 4A of the SFA (an “Accredited Investor”) or other relevant person as defined in Section 275(2) of the SFA (a “Relevant Person”) and pursuant to Section 275(1) of the SFA, or to any person pursuant to an offer referred to in Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA and (where applicable) Regulation 3 of the Securities and Futures (Classes of Investors) Regulations 2018; or

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(c) otherwise pursuant to, and in accordance with, the conditions of any other applicable exemption or provision of the SFA.

It is a condition of the offer that where the shares of our common stock are subscribed for or acquired pursuant to an offer made in reliance on Section 275 of the SFA by a Relevant Person which is:

- (a) a corporation (which is not an Accredited Investor), 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
- (b) a trust (where the trustee is not an Accredited Investor), the sole purpose of which is to hold investments and each beneficiary of the trust is an individual who is an Accredited Investor,

securities or securities-based derivatives contracts (each term as defined in Section 2(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 subscribed for or acquired the shares of our common stock except:

- (i) to an Institutional Investor, an Accredited Investor, a Relevant Person, or which arises from an offer referred to in Section 275(1A) of the SFA (in the case of that corporation) or Section 276(4) of the SFA (in the case of that trust);
- (ii) where no consideration is or will be given for the transfer;
- (iii) where the transfer is by operation of law;
- (iv) as specified in Section 276(7) of the SFA; or
- (v) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

Notice to Prospective Investors in Australia

This prospectus supplement:

- does not constitute a disclosure document or a prospectus under Chapter 6D.2 of the Corporations Act 2001 (Cth), or the "Corporations Act";
- has not been, and will not be, lodged with the Australian Securities and Investments Commission, or the ASIC, as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document for the purposes of the Corporations Act; and
- may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, available under section 708 of the Corporations Act, or the Exempt Investors.

The shares of our common stock may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the shares of our common stock may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any shares of our common stock may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the shares of our common stock, you represent and warrant to us that you are an Exempt Investor.

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As any offer of shares of our common stock under this prospectus supplement will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the shares of our common stock, you undertake to us that you will not, for a period of 12 months from the date of issue of the shares, offer, transfer, assign or otherwise alienate those shares of our common stock to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

Notice to Prospective Investors in Canada

The shares of our common stock 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 of our common stock 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.

Notice to Prospective Investors in Israel

This prospectus supplement does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus supplement is being distributed only to, and is directed only at, and any offer of the shares of our common stock is directed only at, (i) a limited number of persons in accordance with the Israeli Securities Law and (ii) investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and "qualified individuals," each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case, purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

Legal matters

Sidley Austin LLP is serving as our counsel in this offering. Cooley LLP is representing the underwriters in this offering.

Experts

The financial statements of the Company as of December 31, 2021 and 2020, and for each of the three years in the period ended December 31, 2021, incorporated by reference in this Prospectus, and the effectiveness of the Company's internal control over financial reporting have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their reports. Such financial statements are incorporated by reference in reliance upon the reports of such firm given their authority as experts in accounting and auditing.

Where you can find more information

This prospectus supplement and the accompanying prospectus are part of a registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth or incorporated by reference in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus supplement or the accompanying prospectus for a copy of such contract, agreement or other document. You may obtain copies of the registration statement and its exhibits via the SEC's EDGAR database.

We file annual, quarterly and current reports, proxy statements and other information with the SEC under the Exchange Act. The SEC maintains a website that contains reports, proxy and information statements and other information regarding issuers, including us, that file electronically with the SEC. You may obtain documents that we file with the SEC at www.sec.gov.

Our website address is <https://pliantrx.com>. We do not incorporate the information on or accessible through our website into this prospectus supplement or the accompanying prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus supplement or the accompanying prospectus. Our website address is included herein as an inactive textual reference only.

Incorporation of certain information by reference

SEC rules permit us to incorporate information by reference into this prospectus supplement and the accompanying prospectus. This means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus supplement, except for information superseded by information contained in this prospectus supplement or in any subsequently filed incorporated document. This prospectus supplement incorporates by reference the documents set forth below that we have previously filed with the SEC, other than information in such documents that is deemed to be furnished and not filed. These documents contain important information about us, our business and financial condition. Any report or information within any of the documents referenced below that is furnished, but not filed, shall not be incorporated by reference into this prospectus:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 1, 2022, as amended by the Form 10-K/A filed with the SEC on [March 1, 2022](#) and the Form 10-K/A filed with the SEC on [May 27, 2022](#);

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- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2021 from our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on April 29, 2022;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022, June 30, 2022 and September 30, 2022, filed with the SEC on [May 9, 2022](#), [August 8, 2022](#) and [November 8, 2022](#), respectively;
- our Current Reports on Form 8-K, filed with the SEC on [May 5, 2022](#), [June 17, 2022](#), [July 11, 2022](#), [July 14, 2022](#) (only as to information therein explicitly filed with the SEC), [September 16, 2022](#), [November 18, 2022](#), [January 23, 2023](#) and [January 23, 2023](#); and
- the description of our common stock contained in our registration statement on [Form 8-A](#), filed with the SEC on May 29, 2020, including all amendments and reports filed for the purpose of updating such description, including [Exhibit 4.3](#) to our Annual Report on Form 10-K for the year ended December 31, 2020.

All documents that we file (but not documents or parts of documents that we furnish) pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus supplement and prior to the termination of this offering shall be deemed to be incorporated by reference into this prospectus supplement and will automatically update and supersede the information in this prospectus supplement, the accompanying prospectus and any previously filed documents.

We will furnish without charge to each person to whom this prospectus is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. Any such request may be made by writing or calling us at the following address or phone number:

Pliant Therapeutics, Inc.
260 Littlefield Avenue
South San Francisco, California 94080
Attention: General Counsel and Corporate Secretary
(650) 481-6770

PROSPECTUS



Pliant Therapeutics, Inc.

\$500,000,000

**Common Stock
Preferred Stock
Debt Securities
Warrants
Units**

From time to time, we may offer and sell our common stock, preferred stock, debt securities, warrants and/or units consisting of some or all of these securities, in any combination, together or separately, in one or more offerings, in amounts, at prices and on terms that will be determined at the time of the offering, of up to \$500,000,000 and which will be set forth in a prospectus supplement. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus.

The securities may be sold directly to investors, through agents designated from time to time or to or through underwriters or dealers. If any agents, underwriters or dealers are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents, underwriters or dealers and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement.

You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as the documents incorporated or deemed incorporated by reference in this prospectus, before you invest.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "PLRX." On February 25, 2022, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$9.65 per share.

Our principal executive office is located at 260 Littlefield Avenue, South San Francisco, California 94080, and our telephone number is (650) 481-6770.

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading "[Risk Factors](#)" contained in this prospectus beginning on page 2, the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is July 11, 2022.

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ABOUT THIS PROSPECTUS

This prospectus is part of a shelf registration statement that we filed with the Securities and Exchange Commission, or the SEC using a “shelf” registration process. Under this shelf registration process, we may offer and sell shares of our common stock, preferred stock, debt securities, warrants and/or units, either individually or in combination with other securities, in one or more offerings, for an aggregate offering amount of up to \$500,000,000 in amounts, at prices, and on terms that will be determined at the time of the offering. This prospectus provides you with a general description of the securities we may offer.

Each time we offer securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus. You should carefully read this prospectus, any applicable prospectus supplement and any free writing prospectuses we have authorized for use in connection with a specific offering, together with the information incorporated herein by reference as described under the section titled “Incorporation of Certain Information by Reference,” before buying any of the securities in this offering.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

You should rely only on the information contained in, or incorporated by reference into, this prospectus and the applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We have not authorized anyone to provide you with different or additional information. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so.

The information appearing in this prospectus, any applicable prospectus supplement and any related free writing prospectus is accurate only as of the date on the front of the document and any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, the applicable prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the section titled “Where You Can Find More Information.”

Unless the context indicates otherwise, as used in this prospectus, the terms “us,” “our,” “Pliant,” “we,” the “Company” and similar designations refer to Pliant Therapeutics, Inc.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should carefully consider the risks and uncertainties described under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and described under the section titled “Risk Factors” contained in our most recent annual report on Form 10-K and in our most recent quarterly reports on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with a specific offering. The risks described in these documents are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be materially adversely affected. This could cause the trading price of our securities to decline, resulting in a loss of all or part of your investment. Please also carefully read the section titled “Special Note Regarding Forward-Looking Statements.”

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents incorporated by reference in this prospectus, contain 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 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, as well as PLN-1474 and our other product candidates;
- Our estimates regarding the impact of the COVID-19 pandemic on our business and operations, and our ability to manage such impacts;
- Our or our current or future collaborators 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;
- 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 dependence on current and future collaborators for developing, obtaining regulatory approval for and commercializing product candidates in the collaboration;
- Our receipt and timing of any milestone payments or royalties under any current or future research collaboration or license agreements or arrangements;
- Our plans and strategy regarding the commercialization of any products that are approved for marketing and our ability to establish adequate pricing in the U.S. and international markets;
- 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 ability to attract and retain qualified employees and key personnel; and
- Our expectations regarding government and third-party payor coverage and reimbursement.

In some cases, you can identify forward-looking statements by terminology such as “anticipates,” “believes,” “continue,” “estimates,” “expects,” “intends,” “may,” “plans,” “potential,” “predicts,” “should,” “will” or the

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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, the applicable prospectus supplement, any free writing prospectus we may authorize for use in connection with a specific offering, our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC.

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 carefully and completely read this prospectus, the applicable prospectus supplement, the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus we may authorize for use in connection with a specific offering, 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.

THE COMPANY

We are a clinical stage biopharmaceutical company focused on discovering and developing novel therapies for the treatment of fibrosis and related diseases. Our initial focus is on treating fibrosis by inhibiting integrin-mediated activation of TGF- β . 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 wholly-owned lead product candidate, PLN-74809, is an oral small molecule, dual selective inhibitor of $\alpha\beta 6$ and $\alpha\beta 1$ 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 a Phase 1b proof-of-mechanism trial of PLN-74809 in IPF and are currently conducting three Phase 2a trials in our lead indications: two in IPF and one in PSC. We announced interim data from our first Phase 2a IPF trial in September 2021. Our Phase 2a INTEGRIS-IPF trial has completed enrollment and we expect to release data mid-2022. Our Phase 2a INTEGRIS-PSC trial is currently enrolling with full enrollment expected in mid-2022, with data readout expected by late 2022 or early 2023. We have also developed a second product candidate, PLN-1474, a Phase 2-ready small molecule selective inhibitor of $\alpha\beta 1$ for the treatment of liver fibrosis associated with nonalcoholic steatohepatitis, or NASH, for which we have partnered with Novartis. In addition to our clinical programs, we currently have preclinical integrin-based programs targeting oncology and muscular dystrophies.

In September 2021, we announced positive interim results from a Phase 2a positron emission tomography, or PET, imaging trial evaluating target engagement of PLN-74809 in the lungs of IPF patients. Each patient across the four dose cohorts tested achieved target engagement levels greater than 50% in the most fibrotic portions of their lungs after only one dose of PLN-74809. Target engagement of 50% was previously established in a Phase 1b trial as the threshold for predicted clinical anti-fibrotic effect. In addition, there was a dose- and plasma concentration-dependent response with the two highest doses approaching target saturation. PLN-74809 was well tolerated in the trial with no serious adverse events, or SAEs, reported. The interim data confirm that PLN-74809 penetrates the highly fibrotic lung tissue of IPF patients, and potently binds to its target. These interim data allow us to construct a full exposure-target engagement curve model, decoding our ongoing Phase 2a trials and guiding future clinical development of PLN-74809.

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- β may hold the key to successfully treating fibrosis. In normal tissues, TGF- β 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- β signaling becomes dysregulated, with TGF- β being continuously activated, leading to excess collagen deposition, even in the absence of acute tissue injury. TGF- β , 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- β cannot be blocked systemically without disrupting these homeostatic functions and causing significant toxicities. To treat fibrosis more precisely in specific tissues, we believe it is crucial to discover and treat the underlying mechanism causing excess TGF- β 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- β . While the role of integrins in TGF- β 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 bioavailability. We believe that we have addressed these challenges with our platform. We have built a library of compounds that

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includes bioavailable, selective and potent inhibitors of multiple integrins that may be used to target a range of fibrotic diseases across different tissues.

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://plianrx.com>. We do not incorporate the information on or accessible through our website into this prospectus or any prospectus supplement, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus or any prospectus supplement. Our website address is included in this prospectus as an inactive textual reference only.

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we intend to use the net proceeds from the sale of the securities under this prospectus for working capital and other general corporate purposes. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds. We will set forth in the applicable prospectus supplement our intended use for the net proceeds received from the sale of any securities. Pending the use of the net proceeds, we may temporarily invest the net proceeds in a variety of capital preservation instruments, including investment grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government, or may hold such proceeds as cash, until they are used for their stated purpose.

DESCRIPTION OF CAPITAL STOCK

As of the date of the filing of the registration statement of which this prospectus forms a part, our authorized capital stock consists of 300,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share, all of which preferred stock are undesignated.

As of December 31, 2021, 36,083,301 shares of our common stock were outstanding.

The following description of our common stock and preferred stock, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common stock and preferred stock that we may offer under this prospectus. The following description of our capital stock does not purport to be complete and is subject to, and qualified in its entirety by, our certificate of incorporation and bylaws, which are exhibits to the registration statement of which this prospectus forms a part, and by applicable law. The terms of our common stock and preferred stock may also be affected by Delaware law.

Common Stock

We are 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 Certificate of Incorporation and Bylaws” below, a majority vote of the holders of common stock is generally required to take action under our certificate of incorporation and bylaws. Our certificate of incorporation establishes a classified board of directors, divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. 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

Our board of directors is authorized, without action by our stockholders (except as may be required by applicable securities exchange rules), to designate and issue up to the authorized amount 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. No shares of preferred stock are outstanding as of the date of the filing of the registration statement of which this prospectus forms a part, and we have no present plans to issue any shares of preferred stock.

Anti-Takeover Effects of Delaware Law and Provisions of Our Certificate of Incorporation and Bylaws

Our certificate of incorporation and bylaws 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

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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 certificate of incorporation, our board is divided into three classes serving staggered three-year terms, with one class being elected each year. Our 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 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 office 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 General Corporation Law of the State of Delaware, or the DGCL, any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our 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 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 two-thirds of the outstanding shares entitled to vote on the amendment, voting together as a single class.
- *Undesignated preferred stock.* Our 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 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 our control.

- *Exclusive forum.* Our bylaws provide that the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for: (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 DGCL 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. Unless we consent in writing to the selection of an alternate forum, the federal district courts of the United States of America shall be the sole and exclusive forum for resolving any action asserting a claim arising under the Securities Act. Although our bylaws contain the choice of forum provision described above, it is possible that a court could rule that such provisions are inapplicable for a particular claim or action or that such provisions are unenforceable.

Delaware Takeover Statute

We are subject to the provisions of Section 203 of the DGCL. 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, the board of directors of the corporation 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 the board of directors of the corporation 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

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- 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.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar's address is 150 Royall Street, Canton, MA 02021.

Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol "PLRX."

DESCRIPTION OF DEBT SECURITIES

This section describes the general terms and provisions of our debt securities that we may issue from time to time. We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, the applicable prospectus supplement or free writing prospectus will describe the specific terms of any debt securities offered through that prospectus supplement or free writing prospectus. The terms of any debt securities we offer under a prospectus supplement or free writing prospectus may differ from the terms we describe below. Unless the context requires otherwise, whenever we refer to the “indentures,” we are also referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue any senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue any subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The indentures will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We use the term “trustee” to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplement or free writing prospectus and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete applicable indenture that contains the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

We will describe in the applicable prospectus supplement or free writing prospectus the terms of the series of debt securities being offered, including:

- the title;
- the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;
- any limit on the amount that may be issued;
- whether or not we will issue the series of debt securities in global form, and, if so, the terms and who the depository will be;
- the maturity date;
- whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;
- the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

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- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- the terms of the subordination of any series of subordinated debt;
- the place where payments will be payable;
- restrictions on transfer, sale or other assignment, if any;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, the conditions upon which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option, to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- whether the indenture will restrict our ability or the ability of our subsidiaries, if any at such time, to:
 - incur additional indebtedness;
 - issue additional securities;
 - create liens;
 - pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;
 - redeem capital stock;
 - place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;
 - make investments or other restricted payments;
 - sell or otherwise dispose of assets;
 - enter into sale-leaseback transactions;
 - engage in transactions with stockholders or affiliates;
 - issue or sell stock of our subsidiaries; or
 - effect a consolidation or merger;
- whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;
- a discussion of certain material U.S. federal income tax considerations applicable to the debt securities;
- information describing any book-entry features;
- provisions for a sinking fund purchase or other analogous fund, if any;
- the applicability of the provisions in the indenture on discharge;
- whether the debt securities are to be offered at a price such that they will be deemed to be offered at an "original issue discount" as defined in paragraph (a) of Section 1273 of the Internal Revenue Code, as amended;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and

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- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations or advisable in connection with the marketing of the debt securities.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement or free writing prospectus the terms on which a series of debt securities may be convertible into or exchangeable for our common stock, our preferred stock or other securities (including securities of a third party). We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock, our preferred stock or other securities (including securities of a third-party) that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for other securities of ours or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default Under the Indenture

Unless we provide otherwise in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, the following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended;
- if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable at maturity, upon redemption or repurchase or otherwise, and the time for payment has not been extended;
- if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

We will describe in each applicable prospectus supplement or free writing prospectus any additional events of default relating to the relevant series of debt securities.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the unpaid principal, premium, if any, and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

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The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity or security satisfactory to it against any loss, liability or expense. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the trustee or security satisfactory to it against any loss, liability or expense or to be incurred in compliance with instituting the proceeding as trustee; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities, or other defaults that may be specified in the applicable prospectus supplement or free writing prospectus.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indentures.

Modification of Indenture; Waiver

Subject to the terms of the indenture for any series of debt securities that we may issue, we and the trustee may change an indenture without the consent of any holders with respect to the following specific matters:

- to fix any ambiguity, defect or inconsistency in the indenture;
- to comply with the provisions described above under “—Consolidation, Merger or Sale;”
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under “Description of Our Debt Securities—General,” to establish the form of

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any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

- to evidence and provide for the acceptance of appointment hereunder by a successor trustee;
- to provide for uncertificated debt securities and to make all appropriate changes for such purpose;
- to add to our covenants such new covenants, restrictions, conditions or provisions for the benefit of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred to us in the indenture; or
- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, subject to the terms of the indenture for any series of debt securities that we may issue or as otherwise provided in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the stated maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that, subject to the terms of the indenture and any limitation otherwise provided in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement or free writing prospectus, in denominations of \$1,000

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and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement or free writing prospectus with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement or free writing prospectus, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement or free writing prospectus, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement or free writing prospectus the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series. If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus

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supplement or free writing prospectus, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement or free writing prospectus any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Ranking of Debt Securities

The subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement or free writing prospectus. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

The senior debt securities will rank equally in right of payment to all our other senior unsecured debt. The senior indenture does not limit the amount of senior debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement, which includes this prospectus.

General

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities.

We plan to evidence each series of warrants by warrant certificates that we will issue under a separate warrant agreement. We will enter into the warrant agreement with a warrant agent. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the periods during which, and places at which, the warrants are exercisable;
- the manner of exercise;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreement and warrants may be modified;
- if applicable, a discussion of certain material U.S. federal income tax considerations of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

DESCRIPTION OF UNITS

We may issue units comprised of shares of common stock, shares of preferred stock, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement;
- the price or prices at which such units will be issued;
- the applicable U.S. federal income tax considerations relating to the units;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Capital Stock,” “Description of Debt Securities” and “Description of Warrants” will apply to the securities included in each unit, to the extent relevant and as may be updated in any prospectus supplements. We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of a particular series of units will be described in the applicable prospectus supplement.

Unit Agreements

We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

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The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement:

Modification Without Consent

We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

- to cure any ambiguity in any provisions of the governing unit agreement that differ from those described below;
- to correct or supplement any defective or inconsistent provision; or
- to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification With Consent

We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

- impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or
- reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

- if the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or
- if the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document.

In each case, the required approval must be given by written consent.

Unit Agreements Will Not be Qualified Under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

Mergers and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or

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sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Form, Exchange and Transfer

We will issue each unit in global (i.e., book-entry) form only. Units in book-entry form will be represented by a global security registered in the name of a depository, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depository's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depository and its participants. We will describe book-entry securities, and other terms regarding the issuance and registration of the units in the applicable prospectus supplement.

Each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them:

- The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.
- Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.
- Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with the holder's proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.
- If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depository will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

Payments and Notices

In making payments and giving notices with respect to our units, we will follow the procedures as described in the applicable prospectus supplement.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, “at-the-market” offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through one or more underwriters or dealers (acting as principal or agent), through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of the underwriters, dealers or agents, if any;
- the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;
- any over-allotment or other options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents’ or underwriters’ compensation;
- any public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement. Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and compensation received by them on resale of the securities may be deemed to be underwriting discounts. If such dealers or agents were deemed to be underwriters, they may be subject to statutory liabilities under the Securities Act.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. If a dealer is used in the sale of securities, we or an underwriter will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. To the extent required, we will set forth in the prospectus supplement the name of the dealer and the terms of the transaction. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time.

We may use underwriters, dealers or agents with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, dealer or agent, the nature of any such relationship.

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We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions payable to the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, the agent will act on a best-efforts basis for the period of its appointment.

We may provide agents, underwriters and dealers with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents, underwriters or dealers may make with respect to these liabilities. Agents, underwriters and dealers, or their affiliates, may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters that are qualified market makers on the Nasdaq Global Select Market may engage in passive market making transactions in the common stock on the Nasdaq Global Select Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon for us by Sidley Austin LLP, San Francisco, California. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements of the Company incorporated by reference in this Prospectus, and the effectiveness of the Company's internal control over financial reporting have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report. Such financial statements are incorporated by reference in reliance upon the report of such firm, given their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth or incorporated by reference in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. You may obtain copies of the registration statement and its exhibits via the SEC's EDGAR database.

We file annual, quarterly and current reports, proxy statements and other information with the SEC under the Exchange Act. The SEC maintains a website that contains reports, proxy and information statements and other information regarding issuers, including us, that file electronically with the SEC. You may obtain documents that we file with the SEC at www.sec.gov.

Our website address is <https://pliantrx.com>. We do not incorporate the information on or accessible through our website into this prospectus or any prospectus supplement, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus or any prospectus supplement. Our website address is included in this prospectus as an inactive textual reference only.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

SEC rules permit us to incorporate information by reference into this prospectus and any applicable prospectus supplement. This means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus and any applicable prospectus supplement, except for information superseded by information contained in this prospectus or the applicable prospectus supplement itself or in any subsequently filed incorporated document. This prospectus and any applicable prospectus supplement incorporate by reference the documents set forth below that we have previously filed with the SEC, other than information in such documents that is deemed to be furnished and not filed. These documents contain important information about us and our business and financial condition. Any report or information within any of the documents referenced below that is furnished, but not filed, shall not be incorporated by reference into this prospectus.

- Our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 1, 2022;
- The information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the year ended December 31, 2020 from our [Definitive Proxy Statement](#) on Schedule 14A, filed with the SEC on April 30, 2021; and
- The description of our common stock contained in our registration statement on [Form 8-A](#), filed with the SEC on May 29, 2020, including all amendments and reports filed for the purpose of updating such description, including [Exhibit 4.3](#) to our Annual Report on Form 10-K for the year ended December 31, 2020.

All documents that we file (but not documents or parts of documents that we furnish) pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus and prior to the termination of the offering of any of the securities covered under this prospectus shall be deemed to be incorporated by reference into this prospectus and will automatically update and supersede the information in this prospectus, the applicable prospectus supplement and any previously filed documents.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this prospectus or the applicable prospectus supplement shall be deemed to be modified or superseded for purposes of this prospectus and such applicable prospectus supplement to the extent that a statement contained in this prospectus or such applicable prospectus supplement, or in any other subsequently filed document which also is or is deemed to be incorporated by reference into this prospectus and such applicable prospectus supplement, modifies or supersedes such earlier statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus or such applicable prospectus supplement.

We will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. Any such request may be made by writing or calling us at the following address or phone number:

Pliant Therapeutics, Inc.
260 Littlefield Avenue
South San Francisco, CA 94080
(650) 481-6770
Attention: General Counsel and Corporate Secretary

\$175,000,000



Common Stock

Prospectus supplement

Joint book-running managers

J.P. Morgan

Piper Sandler

RBC Capital Markets

Lead managers

Cantor

Oppenheimer & Co.

H.C. Wainwright & Co.