

**PROSPECTUS SUPPLEMENT**  
(To Prospectus dated July 13, 2021)



We have entered into an Open Market Sale Agreement<sup>SM</sup> (the “Sale Agreement”) with Jefferies LLC (“Jefferies”), relating to shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the Sale Agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$50,000,000 from time to time through Jefferies acting as our sales agent.

Our common stock is traded on the Nasdaq Global Select Market under the symbol “PBYI” On November 3, 2021, the last reported sale price per share of our common stock was \$6.58.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus will be made through sales deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended (the “Securities Act”). Jefferies is not required to sell any specific amount of our common stock but will act as our sales agent and use commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal sales and trading practices, on mutually agreed terms between Jefferies and us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Jefferies will receive from us a commission of 3.0% of the gross proceeds of any shares of common stock sold under the Sale Agreement. In connection with the sale of our common stock on our behalf, Jefferies will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation of Jefferies will be deemed to be underwriting discounts or commissions. We have agreed to indemnify Jefferies against certain liabilities, including liabilities under the Securities Act, or to contribute payments that Jefferies may be required to make because of such liabilities.

**INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD CAREFULLY REVIEW THE RISKS AND UNCERTAINTIES REFERENCED UNDER THE HEADING “RISK FACTORS” BEGINNING ON PAGE S-8 OF THIS PROSPECTUS SUPPLEMENT AND IN THE ACCOMPANYING PROSPECTUS, AND IN THE OTHER DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS SUPPLEMENT.**

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

**Jefferies**

Prospectus Supplement dated November 4, 2021.

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## ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 (File No. 333-257687) that we filed with the U.S. Securities and Exchange Commission (the “SEC”) on July 2, 2021, using a “shelf” registration process. Under this shelf registration, we may, from time to time, sell common stock and other securities, including in this offering.

This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part consists of the accompanying prospectus, which provides more general information, some of which may not apply to this offering. Generally, when we refer only to the “prospectus,” we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. 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, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus, including the documents incorporated by reference therein. Information in any document we subsequently file that is incorporated by reference shall modify or supersede the information in this prospectus supplement, the accompanying prospectus and documents incorporated by reference prior to such subsequent filing. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents we have referred you to in the section entitled “Where You Can Find More Information” below in this prospectus supplement.

We are responsible for the information contained and incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and Jefferies has not, authorized anyone to give you any other information, and neither we, nor Jefferies, take any responsibility for any other information that others may give you. We are not, and Jefferies is not, making offers to sell the securities in any jurisdiction in which an offer or solicitation is not authorized or permitted or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. The information contained and incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering speaks only as of the date of this document, unless the information specifically indicates that another date applies. Neither the delivery of this prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering, nor any sale of securities made under these documents, will, under any circumstances, create any implication that there has been no change in our affairs since the date of this prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering, nor that the information contained or incorporated by reference is correct as of any time subsequent to the date of such information. You should assume that the information contained and incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the date of the documents containing the information, unless the information specifically indicates that another date applies. Our business, financial condition, results of operations and prospects may have changed since those dates.

We further note that 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.

This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the shares of common stock to which it relates, nor do this prospectus supplement and the accompanying prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

Unless otherwise indicated, information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus concerning our industry and the markets in which we operate, including market position and market opportunity, is based on information from our management’s estimates, as well as from industry publications and research, surveys and studies conducted by third parties. Management estimates are derived from publicly available information, our knowledge of our industry and assumptions based on such information and knowledge, which we believe to be reasonable. However, assumptions and estimates of our future performance, and the future performance of our industry, are subject to numerous known and unknown risks and uncertainties, including those described under the heading “Risk Factors” beginning on page S-8 of this prospectus supplement and in the risk factors incorporated by reference into this prospectus supplement and the accompanying prospectus. These and other important factors could result in our estimates and assumptions being materially different from future results. You should read the information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus completely and with the understanding that future results may be materially different and worse from what we expect. See the information included under the heading “Cautionary Note Regarding Forward-Looking Statements.”

Unless otherwise mentioned or unless the context requires otherwise, throughout this prospectus supplement, the words “Puma,” “we,” “us,” “our,” the “Company” or similar references refer to Puma Biotechnology, Inc. and its consolidated subsidiaries; and the term “securities” refers to shares of our common stock.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this prospectus supplement are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words, or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the commercialization of NERLYNX® (neratinib);
- our commercialization, marketing, and manufacturing capabilities and strategy;
- the development of our drug candidates, including when we expect to undertake, initiate and complete clinical trials of our product candidates;
- the timing and likelihood of regulatory approvals for our product candidates;
- the regulatory approval of our drug candidates;
- the potential market opportunities for commercializing our products and drug candidates;
- our expectations regarding the potential market size and the size of the patient populations for our drug and product candidates, if approved for commercial use;
- the impact of the global COVID-19 pandemic, and measures to control the spread of COVID-19, on business, financial condition, results of operations and ongoing trials;
- estimates of our expenses, revenue, capital requirements, and our needs for additional financing;
- our ability to develop, acquire, and advance product candidates into, and successfully complete, clinical studies;
- the implementation of our business model and strategic plans for our business, products and product candidates and the integration and performance of any businesses we have acquired or may acquire;
- our ability to secure adequate protection for our intellectual property;
- our ability to find collaborative partners for research, development and commercialization of potential products;
- efforts of our sub-licensees to obtain regulatory approval and commercialize NERLYNX in areas outside the United States;
- our ability to compete against other companies and research institutions;
- our ability to maintain and establish relationships with third parties, such as contract research organizations, contract manufacturing organizations, suppliers, and distributors;
- our financial performance and the expansion of our organization;
- our ability to obtain supply of our products and product candidates;
- the scalability and commercial viability of our manufacturing methods and processes;

- our intention and ability to vigorously defend against any litigation to which we are or may become party;
- our estimates for damages that we may be required to pay in connection with the class action lawsuit or other litigation to which we are a party;
- our ability to attract and retain key personnel;
- developments and projections relating to our competitors and our industry; and
- other risks and uncertainties, including those listed or incorporated by reference in “Risk Factors.”

Any forward-looking statements in this prospectus supplement reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those discussed below under “Risk Factors” and discussed elsewhere and incorporated by reference in this prospectus supplement. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This prospectus supplement also contains or incorporates by reference estimates, projections, and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources.

## PROSPECTUS SUPPLEMENT SUMMARY

*The items in the following summary are described in more detail later in this prospectus supplement and the accompanying prospectus. This summary provides an overview of selected information and does not contain all of the information you should consider before buying our common stock. Therefore, you should read the entire prospectus supplement and the accompanying prospectus carefully, including the information in our filings with the Securities and Exchange Commission (“SEC”) incorporated by reference herein, before deciding to invest in our common stock. Investors should carefully consider the information set forth under “Risk Factors” beginning on page S-8 of this prospectus supplement and page 5 of the accompanying prospectus and those risks identified in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q. In this prospectus supplement, unless the context otherwise requires, references to “the Company,” “we,” “us,” “our,” or “Puma” refer to Puma Biotechnology, Inc. and its consolidated subsidiaries.*

### Overview

We are a biopharmaceutical company with a focus on the development and commercialization of innovative products to enhance cancer care. Our lead product is NERLYNX, an oral version of neratinib, which is a potent irreversible tyrosine kinase inhibitor that blocks signal transduction through the human epidermal growth factor receptors, HER1, HER2 and HER4. In 2017, we obtained approval from the United States Food and Drug Administration, or FDA, to market, and commenced commercialization of NERLYNX in the United States for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer following adjuvant trastuzumab-based therapy. More recently, in February 2020, we received FDA approval to expand the indication for NERLYNX to include its use in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting.

### Corporate History and Information

We were originally incorporated in the State of Delaware in April 2007 under the name Innovative Acquisitions Corp. We were a “shell” company registered under the Exchange Act with no specific business plan or purpose until we acquired Puma Biotechnology, Inc., a privately-held Delaware corporation formed on September 15, 2010, or Former Puma, in October 2011. As a result of this transaction, Former Puma became our wholly-owned subsidiary and subsequently merged with and into us, at which time we adopted Former Puma’s business plan and changed our name to “Puma Biotechnology, Inc.”

Our principal executive offices are located at 10880 Wilshire Boulevard, Suite 2150, Los Angeles, CA 90024, and our telephone number is (424) 248-6500.

## THE OFFERING

Common stock offered by us pursuant to this prospectus supplement	Shares of our common stock having an aggregate offering price of up to \$50,000,000.
Common stock to be outstanding immediately after this offering	Up to 48,459,626 shares of our common stock, assuming sales of 7,598,784 shares of our common stock in this offering at a public offering price of \$6.58 per share, which was the last reported sale price per share of our common stock on the Nasdaq Global Select Market on November 3, 2021. The actual number of shares of our common stock issued will vary depending on the sales price under this offering.
Plan of distribution	“At the market offering” that may be made from time to time through Jefferies acting as our sales agent. See “Plan of Distribution” for additional information.
Use of proceeds	Our management will retain broad discretion regarding the allocation and use of the net proceeds. We intend to use the net proceeds, if any, from this offering for general corporate purposes. See “Use of Proceeds” on page S-10 for additional information.
Risk factors	You should read and consider the information set forth under the heading “Risk Factors” in this prospectus supplement and in the accompanying prospectus, together with the risk factors and cautionary statements described in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, incorporated by reference herein, before deciding to invest in shares of our common stock.
Nasdaq Global Select Market Symbol	“PBYI”

The number of shares of common stock to be outstanding after this offering is based on 40,860,842 shares of common stock outstanding as of September 30, 2021 and excludes:

- 4,757,783 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2021 having a weighted-average exercise price of \$63.13 per share;
- 1,887,458 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2021;
- 4,500 shares of common stock issuable upon the vesting of performance stock units outstanding as of September 30, 2021;
- 3,919,963 shares of common stock reserved for issuance pursuant to future equity awards under our Puma Biotechnology, Inc. 2011 Incentive Award Plan (“2011 Plan”) as of September 30, 2021, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2011 Plan;

- 1,341,851 shares of common stock reserved for future issuance under our Puma Biotechnology, Inc. 2017 Employment Inducement Incentive Award (“2017 Plan”) as of September 30, 2021, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2017 Plan; and
- 2,116,250 shares of our common stock issuable upon the exercise of a warrant held by Alan H. Auerbach, our President and Chief Executive Officer, at \$16.00 per share.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding stock options or vesting of restricted stock units or performance stock units as of September 30, 2021.

## RISK FACTORS

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks described below, together with the other information contained in this prospectus supplement or incorporated by reference in this prospectus supplement, including the risks and uncertainties discussed under “Risk Factors” in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference herein in their entirety. If any of the risks incorporated by reference herein or set forth below occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

### **Risks Relating to this Offering**

#### ***Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.***

If we or our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline. Based upon the number of shares of common stock outstanding as of September 30, 2021, and assuming sales of 7,598,784 shares of our common stock in this offering at a public offering price of \$6.58 per share, which was the last reported sale price per share of our common stock on the Nasdaq Global Select Market on November 3, 2021, as a result of this offering we would have outstanding a total of approximately 48,459,626 shares of common stock, all of which would be freely tradable (subject to the restrictions in Rule 144 for shares of common stock held by our affiliates). Any shares sold in this offering will be freely tradable, without restriction, in the public market.

#### ***We have broad discretion as to the use of proceeds from this offering and may not use the proceeds effectively.***

Our management will retain broad discretion as to the allocation of the proceeds and may spend these proceeds in ways in which you may not agree. Because of the number and variability of factors that will determine our use of our existing cash, cash equivalents and short-term investments and the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure of our management to apply these funds effectively could result in unfavorable returns and uncertainty about our prospects, each of which could cause the price of our common stock to decline.

#### ***If you purchase shares of our common stock in this offering, you may incur immediate and substantial dilution.***

Some or all of the public offering prices per share in this offering may exceed the as-adjusted net tangible book value per share of our outstanding common stock. After giving effect to an assumed sale of shares of common stock in the aggregate amount of \$50,000,000 at an assumed public offering price of \$6.58 per share, which was the last reported sale price per share of our common stock on the Nasdaq Global Select Market on November 3, 2021, and after deducting the commissions and estimated offering expenses payable by us, you would incur immediate and substantial dilution in the amount of \$7.21 per share. In addition, you may also experience additional dilution after this offering on any future equity issuances, including the issuance of common stock under the 2011 Plan. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial additional dilution. See “Dilution” for additional information.

#### ***It is not possible to predict the aggregate proceeds resulting from sales made under the Sale Agreement.***

Subject to certain limitations in the Sale Agreement and compliance with applicable law, we have the discretion to deliver an issuance notice to Jefferies at any time throughout the term of the Sale Agreement. The number of shares that are sold through Jefferies after delivering an issuance notice, if any, will fluctuate based on a number of factors, including the market price of shares of our common stock during the sales period, the limits we set with Jefferies in any applicable issuance notice and the demand for shares of our common stock during the sales period. Because the price per share of each share of common stock sold pursuant to the Sale Agreement will fluctuate during this offering, it is not currently possible to predict the number of shares of common stock that will be sold or the aggregate proceeds we will raise in connection with those sales under the Sale Agreement, and we may not sell any shares of common stock.

***If securities or industry analysts either do not publish research about us or publish inaccurate or unfavorable research about us, our business or our market, or if they change their recommendations regarding our common stock adversely, the trading price or trading volume of our common stock could decline.***

The trading market for our common stock will be influenced in part by the research and reports that securities or industry analysts may publish about us, our business, our market, or our competitors. If one or more of these analysts initiate research with an unfavorable rating or downgrade our common stock, provide a more favorable recommendation about our competitors or publish inaccurate or unfavorable research about our business, our common stock price would likely decline. If any analyst who may cover us were to cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause the trading price or trading volume of our common stock to decline.

***The common stock offered hereby will be sold in “at the market offerings,” and investors who buy shares at different times will likely pay different prices.***

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

## USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$50,000,000 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the Sale Agreement with Jefferies as a source of financing.

We intend to use the net proceeds, if any, from this offering for general corporate purposes. Any remaining proceeds will be used for other ongoing research and development, working capital and other general corporate purposes. The expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures will depend on numerous factors, the accompanying base prospectus and the documents incorporated by reference herein and therein, as well as the amount of cash used in our operations. We may find it necessary or advisable to use the net proceeds for other purposes, and management will have broad discretion in the timing and application of the net proceeds.

Pending the use of the net proceeds, we may invest the proceeds in interest-bearing, investment-grade securities, certificates of deposit or government securities.

## **DIVIDEND POLICY**

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings to fund the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future. In addition, any future financing instruments could preclude us from paying dividends. Any future determination to pay dividends will be made at the discretion of our board of directors subject to applicable laws, and will depend upon, among other factors, our results of operations, financial condition, contractual restrictions and capital requirements. Investors should not purchase our common stock with the expectation of receiving cash dividends.

## DILUTION

Dilution represents the difference between the amount per share of common stock paid by purchasers of shares of common stock in this offering and the as-adjusted net tangible book value per share of our common stock immediately after this offering. The data in this section are derived from our balance sheet as of September 30, 2021. Net tangible book value per share of common stock is equal to our total tangible assets less the amount of our total liabilities, divided by the sum of the number of shares of common stock outstanding as of September 30, 2021, excluding shares of common stock underlying outstanding options and unvested restricted stock units and performance stock units as of September 30, 2021. Our historical net tangible book value as of September 30, 2021 was approximately \$(79.1) million, or \$(1.93) per share.

After giving effect to the assumed sale of shares of common stock in the aggregate amount of \$50,000,000 at an assumed public offering price of \$6.58 per share, which was the last reported sale price per share of our common stock on the Nasdaq Global Select Market on November 3, 2021, and after deducting the commissions and estimated offering expenses payable by us, our as-adjusted net tangible book value as of September 30, 2021 would have been \$(30.8) million, or \$(0.63) per share of common stock. This represents an immediate increase in net tangible book value to existing stockholders of \$1.30 per share of common stock and immediate dilution in net tangible book value to purchasers of shares of common stock in this offering of \$7.21 per share of common stock. The following table illustrates this dilution per share of common stock:

Assumed public offering price per share		\$	6.58
Historical net tangible book value per share as of September 30, 2021	\$	(1.93)	
Increase in as-adjusted net tangible book value per share of common stock attributable to new investors	\$	1.30	
As-adjusted net tangible book value per share after this offering		\$	(0.63)
Dilution per share to investors participating in this offering		\$	7.21

The table above illustrates that an aggregate of 7,598,784 shares of our common stock are sold at a price of \$6.58 per share, the last reported sale price of our common stock on the Nasdaq Global Select Market on November 3, 2021. The shares of common stock sold in this offering, if any, will be sold from time to time at various prices. An increase of \$1.00 per share in the assumed price at which the shares of common stock are sold would increase the dilution in net tangible book value per share to purchasers of shares of common stock in this offering to \$8.06 per share, after deducting the commissions and estimated offering expenses payable by us. A decrease of \$1.00 per share in the assumed price at which the shares of common stock are sold would decrease the dilution in net tangible book value per share to purchasers of shares of common stock in this offering to \$6.37 per share, after deducting the commissions and estimated offering expenses payable by us. This information is supplied for illustrative purposes only.

Except as noted above, the foregoing excludes, in each case as of September 30, 2021:

- 4,757,783 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2021 having a weighted-average exercise price of \$63.13 per share;
- 1,887,458 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2021;
- 4,500 shares of common stock issuable upon the vesting of performance stock units outstanding as of September 30, 2021;
- 3,919,963 shares of common stock reserved for issuance pursuant to future equity awards under our 2011 Plan as of September 30, 2021, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2011 Plan;

- 1,341,851 shares of common stock reserved for future issuance under our 2017 Plan as of September 30, 2021, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2017 Plan; and
- 2,116,250 shares of our common stock issuable upon the exercise of a warrant held by Alan H. Auerbach, our President and Chief Executive Officer, at \$16.00 per share.

Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. New investors may experience further dilution if any of our outstanding options are exercised, new options are issued and exercised under our equity incentive plans or we issue additional shares of common stock, other equity securities or convertible debt securities in the future.

## PLAN OF DISTRIBUTION

We have entered into a Sale Agreement with Jefferies, under which we may offer and sell up to \$50 million of our shares of common stock from time to time through Jefferies acting as agent. Sales of our shares of common stock, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act.

Each time we wish to issue and sell our shares of common stock under the Sale Agreement, we will notify Jefferies of the number of shares to be issued, the dates on which such sales are anticipated to be made, any limitation on the number of shares to be sold in any one day and any minimum price below which sales may not be made. Once we have so instructed Jefferies, unless Jefferies declines to accept the terms of such notice, Jefferies has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Jefferies under the Sale Agreement to sell our shares of common stock are subject to a number of conditions that we must meet.

The settlement of sales of shares between us and Jefferies is generally anticipated to occur on the second trading day following the date on which the sale was made. Sales of our shares of common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Jefferies may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay Jefferies a commission equal to 3% of the aggregate gross proceeds we receive from each sale of our shares of common stock. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. In addition, we have agreed to reimburse Jefferies for the fees and disbursements of its counsel, payable upon execution of the sales agreement, in an amount not to exceed \$75,000, in addition to certain ongoing disbursements of its legal counsel. We estimate that the total expenses for the offering, excluding any commissions or expense reimbursement payable to Jefferies under the terms of the Sale Agreement, will be approximately \$210,000. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

Jefferies will provide written confirmation to us before the open on the Nasdaq Global Select Market on the day following each day on which our shares of common stock are sold under the Sale Agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross proceeds of such sales and the proceeds to us.

In connection with the sale of our shares of common stock on our behalf, Jefferies may be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Jefferies against certain civil liabilities, including liabilities under the Securities Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities.

The offering of our shares of common stock pursuant to the Sale Agreement will terminate upon the earlier of (i) the sale of all shares of common stock subject to the Sale Agreement and (ii) the termination of the Sale Agreement as permitted therein. We and Jefferies may each terminate the Sale Agreement at any time upon ten days’ prior notice.

This summary of the material provisions of the Sale Agreement does not purport to be a complete statement of its terms and conditions. A copy of the Sale Agreement is filed as an exhibit to a current report on Form 8-K filed under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and incorporated by reference in this prospectus supplement.

Jefferies and its affiliates may in the future provide various investment banking, commercial banking, financial advisory and other financial services for us and our affiliates, for which services they may in the future receive customary fees. In the course of its business, Jefferies may actively trade our securities for its own account or for the accounts of customers, and accordingly, Jefferies may at any time hold long or short positions in such securities.

A prospectus supplement and the accompanying prospectus in electronic format may be made available on a website maintained by Jefferies, and Jefferies may distribute the prospectus supplement and the accompanying prospectus electronically.

**EXPERTS**

The consolidated financial statements of Puma Biotechnologies, Inc. as of December 31, 2020 and 2019, and for each of the years in the three-year period ended December 31, 2020, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2020 have been incorporated by reference herein in reliance upon the reports of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing. The audit report covering the December 31, 2020 consolidated financial statements refers to a change in the method of accounting for Leases as of January 1, 2019, due to the adoption of Financial Accounting Standards Boards Accounting Standards Codification Topic 842, *Leases*.

**LEGAL MATTERS**

The validity of the common stock being offered in this prospectus supplement will be passed on by Latham & Watkins LLP. Certain legal matters in connection with this offering will be passed upon for Jefferies by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

**WHERE YOU CAN FIND MORE INFORMATION**

We are subject to the informational requirements of the Exchange Act, and in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. The SEC maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the SEC. The address of that site is [www.sec.gov](http://www.sec.gov). Statements contained in this prospectus supplement as to the contents of any contract or other document are not necessarily complete, and in each instance, we refer you to the copy of the contract or document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference.

## INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below:

- Our Annual Report on [Form 10-K](#) for the year ended December 31, 2020, filed with the SEC on March 1, 2021.
- The information specifically incorporated by reference into our Annual Report on Form 10-K from our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on April 26, 2021.
- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021, June 30, 2021 and September 30, 2021, filed with the SEC on [May 6, 2021](#), [August 5, 2021](#) and [November 4, 2021](#), respectively.
- Our Current Reports on Form 8-K filed with the SEC on [February 11, 2021](#), [February 23, 2021](#), [March 29, 2021](#), [June 17, 2021](#), [June 25, 2021](#), [July 14, 2021](#) and [July 29, 2021](#).
- Our Registration Statement on [Form 8-A12B](#) filed with the SEC on December 30, 2016.
- Our Description of the Company's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934 filed as [Exhibit 4.3](#) to our Annual Report on [Form 10-K](#) filed with the SEC on February 28, 2020 and any amendment or report filed with the SEC for the purpose of updating the description.

All documents we file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act shall be deemed incorporated by reference in this prospectus supplement and to be a part of this prospectus supplement from the date of filing of those documents, with the exception of any portion of any report or document that is not deemed "filed" under such provisions on or after the date of this prospectus supplement, until the earlier of the date on which: (1) all of the securities registered hereunder have been sold; or (2) the registration statement of which this prospectus supplement is a part has been withdrawn.

Under no circumstances will any information filed under current items 2.02 or 7.01 of Form 8-K be deemed incorporated herein by reference unless such Form 8-K expressly provides to the contrary.

Upon written or oral request, we will provide without charge to each person to whom a copy of the prospectus supplement is delivered a copy of the documents incorporated by reference herein (other than exhibits to such documents unless such exhibits are specifically incorporated by reference herein). You may request a copy of these filings, at no cost, by writing, calling or emailing us at the contact information set forth below. We have authorized no one to provide you with any information that differs from that contained in this prospectus supplement. Accordingly, we take no responsibility for any other information that others may give you. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date of the front cover of this prospectus supplement.

Puma Biotechnology, Inc.  
10880 Wilshire Boulevard, Suite 2150  
Los Angeles, CA 90024  
Attention: Corporate Secretary  
(424) 248-6500

PROSPECTUS

# PUMA BIOTECHNOLOGY, INC.

## \$50,000,000

### Common Stock

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We may offer and sell up to \$50,000,000 in the aggregate of common stock from time to time in one or more offerings.

Each time we offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the shares being offered and sold. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled “About this Prospectus” and “Plan of Distribution” for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

**INVESTING IN OUR COMMON STOCK INVOLVES RISKS. SEE THE “RISK FACTORS” ON PAGE 5 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR COMMON STOCK.**

Our common stock is listed on the Nasdaq Global Select Market, or Nasdaq, under the symbol “PBYI.” On July 1, 2021, the last reported sale price of our common stock on Nasdaq was \$9.39 per share.

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

**The date of this prospectus is July 13, 2021.**

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## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC using a “shelf” registration process. By using a shelf registration statement, we may sell common stock from time to time and in one or more offerings up to a total dollar amount of \$50,000,000 as described in this prospectus. Each time that we offer and sell such shares, we will provide a prospectus supplement to this prospectus that contains specific information about the shares being offered and sold and the specific 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 or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement (and any applicable free writing prospectuses), together with the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.”

We have not authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover, that the information appearing in any applicable free writing prospectus is accurate only as of the date of that free writing prospectus, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. In addition, the market and industry data and forecasts that may be included or incorporated by reference in this prospectus, any prospectus supplement or any applicable free writing prospectus may involve estimates, assumptions and other risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “Risk Factors” contained in this prospectus, the applicable prospectus supplement and any applicable free writing prospectus, and under similar headings in other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

When we refer to “Puma,” “we,” “our,” “us” and the “Company” in this prospectus, we mean Puma Biotechnology, Inc. and its consolidated subsidiaries, unless otherwise specified. When we refer to “you,” we mean the potential holders of the applicable series of securities.

## WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

### Available Information

We file reports, proxy statements and other information with the SEC. The SEC maintains a web site that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

Our web site address is [www.pumabiotechnology.com](http://www.pumabiotechnology.com). The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

### Incorporation by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus, which 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 deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

- Our Annual Report on [Form 10-K](#) for the year ended December 31, 2020, filed with the SEC on March 1, 2021.
- The information specifically incorporated by reference into our Annual Report on Form 10-K from our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on April 26, 2021.
- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2021, June 30, 2021 and September 30, 2021, filed with the SEC on [May 6, 2021](#), [August 5, 2021](#) and [November 4, 2021](#), respectively.
- Our Current Reports on Form 8-K filed with the SEC on [February 11, 2021](#), [February 23, 2021](#), [March 29, 2021](#), [June 17, 2021](#), and [June 25, 2021](#).
- Our Registration Statement on [Form 8-A12B](#) filed with the SEC on December 30, 2016.
- Our Description of the Company's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934 filed as [Exhibit 4.3](#) to our Annual Report on [Form 10-K](#) filed with the SEC on February 28, 2020 and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus, prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus by writing or telephoning us at the following address:

Puma Biotechnology, Inc.  
10880 Wilshire Boulevard, Suite 2150  
Los Angeles, CA 90024  
Attention: Corporate Secretary  
(424) 248-6500

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus or any accompanying prospectus supplement.

## THE COMPANY

We are a biopharmaceutical company with a focus on the development and commercialization of innovative products to enhance cancer care. Our lead product is NERLYNX, an oral version of neratinib, which is a potent irreversible tyrosine kinase inhibitor that blocks signal transduction through the human epidermal growth factor receptors, HER1, HER2 and HER4. In 2017, we obtained approval from the United States Food and Drug Administration, or FDA, to market, and commenced commercialization of NERLYNX in the United States for the extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer following adjuvant trastuzumab-based therapy. More recently, in February 2020, we received FDA approval to expand the indication for NERLYNX to include its use in combination with capecitabine for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting.

We were originally incorporated in the State of Delaware in April 2007 under the name Innovative Acquisitions Corp. We were a “shell” company registered under the Exchange Act with no specific business plan or purpose until we acquired Puma Biotechnology, Inc., a privately-held Delaware corporation formed on September 15, 2010, or Former Puma, in October 2011. As a result of this transaction, Former Puma became our wholly-owned subsidiary and subsequently merged with and into us, at which time we adopted Former Puma’s business plan and changed our name to “Puma Biotechnology, Inc.”

Our principal executive offices are located at 10880 Wilshire Boulevard, Suite 2150, Los Angeles, CA 90024, and our telephone number is (424) 248-6500.

## **RISK FACTORS**

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. You should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement and any applicable free writing prospectus before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

**USE OF PROCEEDS**

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

## PLAN OF DISTRIBUTION

We may sell the securities covered by this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed 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.

Each time that we sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold 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.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

Our common stock is listed on the Nasdaq Global Select Market. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

## LEGAL MATTERS

Latham & Watkins LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Puma Biotechnology, Inc. 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 consolidated financial statements of Puma Biotechnology, Inc. as of December 31, 2020 and 2019, and for each of the years in the three-year period ended December 31, 2020, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2020 have been incorporated by reference herein in reliance upon the reports of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing. The audit report covering the December 31, 2020 consolidated financial statements refers to a change in the method of accounting for Leases as of January 1, 2019, due to the adoption of Financial Accounting Standards Boards Accounting Standards Codification Topic 842, *Leases*.

**\$50,000,000**



**Common Stock**

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**PROSPECTUS SUPPLEMENT**

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**Jefferies**

November 4, 2021

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