

**PUMA BIOTECHNOLOGY, INC.**

**1,792,114 Shares of Common Stock**

The Selling Stockholder (as defined herein) may offer and sell up to 1,792,114 shares of common stock, par value \$0.0001 per share, from time to time in one or more offerings. This prospectus provides you with a general description of the securities. We will not receive any proceeds from the sale of our common stock by the Selling Stockholder.

To the extent necessary when it sells securities, the Selling Stockholder may provide a supplement to this prospectus that contains specific information about the offering and the Selling Stockholder, as well as the amounts, prices and terms of the securities. 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 any applicable prospectus supplement before you invest in any of our securities.

The Selling Stockholder may offer and sell these shares of our common stock from time to time. 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 SECURITIES INVOLVES RISKS. SEE THE “RISK FACTORS” ON PAGE 5 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN ANY APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.**

Our common stock is listed on the Nasdaq Global Select Market (“Nasdaq”) under the symbol “PBYI.” On July 22, 2022, the last reported sale price of our common stock on Nasdaq was \$3.22 per share.

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

**The date of this prospectus is August 1, 2022**

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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, the Selling Stockholder named herein may, from time to time, sell shares of common stock as described in this prospectus. To the extent necessary when it sells securities, the Selling Stockholder may provide a supplement to this prospectus that contains specific information about the offering and the Selling Stockholder, as well as the amounts, prices and terms of the securities. 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.”

Neither we, nor the Selling Stockholder, have 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 and the Selling Stockholder 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 Selling Stockholder 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, 2021, filed with the SEC on [March 3, 2022](#).
- 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 29, 2022](#).
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, filed with the SEC on [May 5, 2022](#).
- Our Current Reports on Form 8-K, filed with the SEC on [March 14, 2022](#) and [June 17, 2022](#).
- Our Registration Statement on Form 8-A, filed with the SEC on [December 30, 2016](#), 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.

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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 (“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 any 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 any 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 will not receive any of the proceeds from the sale of our common stock offered by the Selling Stockholder pursuant to this prospectus.

**DETERMINATION OF OFFERING PRICE**

The prices at which the shares of our common stock covered by this prospectus may actually be sold will be determined by the prevailing public market price for shares of our common stock, by negotiations between the Selling Stockholder and buyers of our common stock in private transactions or as otherwise described in “Plan of Distribution.”

**SELLING SECURITYHOLDER**

On March 8, 2022, we entered into a Securities Purchase Agreement (the “Purchase Agreement”) with Alan Auerbach, our President, Chief Executive Officer and Chairman of the Board, and Athyrium Opportunities IV Co-Invest 2 LP, an affiliate of the administrative agent and a purchaser under our existing note purchase agreement (the “Selling Stockholder” and together with Mr. Auerbach, the “Purchasers”). Pursuant to the Purchase Agreement, among other things, we (i) agreed to sell an aggregate of 3,584,228 shares of our common stock, par value \$0.0001 per share, to the Purchasers, and (ii) agreed to register the resale of such shares. We are registering the securities offered by this prospectus on behalf of the Selling Stockholder.

The Selling Stockholder may from time to time offer and sell pursuant to this prospectus any or all of the shares of common stock registered pursuant to this prospectus. Because the Selling Stockholder is not obligated to sell its securities, we cannot state with certainty the amount of our securities that the Selling Stockholder will hold upon consummation of any such sales. In addition, since the date on which the Selling Stockholder provided this information to us, the Selling Stockholder may have sold, transferred or otherwise disposed of all or a portion of their securities.

	<b>Number of shares owned</b>	<b>Percent of shares owned before the offering</b>	<b>Number of shares offered hereby</b>	<b>Number of shares owned after the completion of the offering<sup>(1)</sup></b>	<b>Percent of shares owned after the offering</b>
Athyrium Opportunities IV Co-Invest 2 LP <sup>(2)</sup>	1,792,114	3.93%	1,792,114	—	—

(1) Assumes the sale of all shares of common stock offered hereby the Selling Stockholder.

(2) Athyrium Opportunities Associates IV Co-Invest LLC is the general partner of Athyrium Opportunities IV Co-Invest 2 LP. Jeffrey A. Ferrell is the Managing Member of Athyrium Funds GP Holdings LLC, which is the Managing Member of Athyrium Opportunities Associates IV Co-Invest LLC, and in his capacity as such may be deemed to exercise shared voting and investment power over the shares owned by Athyrium Opportunities IV Co-Invest 2 LP. The business address of each of the foregoing is c/o Athyrium Capital Management, LP is 505 Fifth Avenue, Floor 18, New York, New York 10017.

## PLAN OF DISTRIBUTION

The Selling Stockholder and any of its pledgees, donees, transferees, assignees or other successors-in-interest may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices. The Selling Stockholder may use one or more of the following methods when disposing of the shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- through brokers, dealers or underwriters that may act solely as agents;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- through the writing or settlement of options or other hedging transactions entered into after the effective date of the registration statement of which this prospectus is a part, whether through an options exchange or otherwise;
- through agreements between broker-dealers and the Selling Stockholder to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of disposition; and
- any other method permitted pursuant to applicable law.

The Selling Stockholder may also sell shares under Rule 144 or Rule 904 under the Securities Act of 1933, as amended, or Securities Act, if available, or Section 4(a)(1) under the Securities Act, rather than under this prospectus.

Broker-dealers engaged by the Selling Stockholder may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the Selling Stockholder (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The Selling Stockholder does not expect these commissions and discounts to exceed what is customary in the types of transactions involved.

The Selling Stockholder may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell shares of common stock from time to time under this prospectus, or under a supplement or amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

Upon being notified in writing by the Selling Stockholder that any material arrangement has been entered into with a broker-dealer for the sale of common stock through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, we will file a supplement to this prospectus, if required, pursuant to Rule 424(b) under the Securities Act, disclosing (i) the participating broker-dealer(s), (ii) the number of shares involved, (iii) the price at which such shares of common stock were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable, (v) that such broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus, and (vi) other facts material to the transaction. In addition, upon being notified in writing by the Selling Stockholder that a donee or pledgee intends to sell more than 500 shares of common stock, we will file a supplement to this prospectus if then required in accordance with applicable securities law.

The Selling Stockholder also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of the shares of common stock or interests in shares of common stock, the Selling Stockholder may enter into hedging transactions after the effective date of the registration statement of which this prospectus is a part with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The Selling Stockholder may also sell shares of common stock short after the effective date of the registration statement of which this prospectus is a part and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The Selling Stockholder may also enter into option or other transactions after the effective date of the registration statement of which this prospectus is a part with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The Selling Stockholder and any broker-dealers or agents that are involved in selling the shares may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. The maximum commission or discount to be received by any member of the Financial Industry Regulatory Authority (FINRA) or independent broker-dealer will not be greater than 8% of the initial gross proceeds from the sale of any security being sold.

We have advised the Selling Stockholder that they are required to comply with Regulation M promulgated under the Securities Exchange Act of 1934, as amended, during such time as they may be engaged in a distribution of the shares. The foregoing may affect the marketability of the common stock.

The aggregate proceeds to the Selling Stockholder from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. The Selling Stockholder reserves the right to accept and, together with its agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

We are required to pay all fees and expenses incident to the registration of the shares. We have agreed to indemnify the Selling Stockholder against certain losses, claims, damages and liabilities, including liabilities under the Securities Act or otherwise.

We have agreed with the Selling Stockholder to keep the registration statement of which this prospectus constitutes a part effective until the earliest of (a) the date as of which the Selling Stockholder may sell all of the shares of common stock covered by this prospectus under Rule 144 of the Securities Act without volume or manner-of-sale restrictions and without the requirement for us to be in compliance with the current public information requirements under Rule 144(c)(1) (or any successor thereto) promulgated under the Securities Act, (b) March 10, 2024 or, if the Selling Stockholder is an affiliate (for purposes of Rule 144 under the Securities Act) as of such date, then March 10, 2027, or (c) the date on which the Selling Stockholder shall have sold, pursuant to the registration statement of which this prospectus is a part, all of the shares of common stock purchased by it pursuant to the Purchase Agreement.

**LEGAL MATTERS**

The validity of the shares of common stock offered hereby has been passed upon for us by Latham & Watkins LLP.

**EXPERTS**

The consolidated financial statements of Puma Biotechnology, Inc. as of December 31, 2021 and 2020, and for each of the years in the three-year period ended December 31, 2021, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2021 have been incorporated by reference herein in reliance upon the report 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.