

PROSPECTUS SUPPLEMENT
(To Prospectus dated February 7, 2022)



Up to \$75,000,000

Common Stock

We have entered into an Open Market Sale AgreementSM, or the Sales Agreement, with Jefferies LLC, or Jefferies or the Agent, dated May 11, 2022, relating to our common stock, par value \$0.0001 per share, offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the Sales Agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$75,000,000 from time to time through or to Jefferies, acting as our sales agent.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "XERS". On May 9, 2022, the last reported sale price of our common stock, as reported on The Nasdaq Global Select Market, was \$1.84 per share.

Sales of our common stock, if any, under this prospectus supplement will be made by any method permitted by law deemed to be "at the market offerings" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Jefferies is not required to sell any specific number or dollar amount of securities, but will act as our sales agent using 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 trading and sales practices, on mutually agreed terms between Jefferies and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Jefferies will be entitled to compensation at a commission rate of 3.0% of the gross sales price per share of common stock sold under the Sales Agreement. See "Plan of Distribution" beginning on page S-25 for additional information regarding the compensation to be paid to Jefferies. In connection with the sale of the 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 commissions or discounts. We have also agreed to provide indemnification and contribution to Jefferies against certain liabilities, including liabilities under the Securities Act and the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Investing in our common stock involves risks. You should read this prospectus supplement and the accompanying prospectus carefully before you make an investment decision. See "[Risk Factors](#)" beginning on page S-8 of this prospectus supplement, as well as the documents that are incorporated by reference herein for more information.

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.

Jefferies

The date of this prospectus supplement is May 11, 2022.

TABLE OF CONTENTS

PROSPECTUS SUPPLEMENT

ABOUT THIS PROSPECTUS SUPPLEMENT	S-1
PROSPECTUS SUPPLEMENT SUMMARY	S-3
THE OFFERING	S-6
RISK FACTORS	S-8
CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS	S-15
USE OF PROCEEDS	S-17
DIVIDEND POLICY	S-18
DILUTION	S-19
MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS	S-21
PLAN OF DISTRIBUTION	S-25
LEGAL MATTERS	S-27
EXPERTS	S-27
WHERE YOU CAN FIND MORE INFORMATION	S-28
INCORPORATION BY REFERENCE	S-29

PROSPECTUS

ABOUT THIS PROSPECTUS	ii
RISK FACTORS	1
CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS	2
PROSPECTUS SUMMARY	4
USE OF PROCEEDS	7
SECURITIES WE MAY OFFER	8
DESCRIPTION OF CAPITAL STOCK	9
DESCRIPTION OF DEBT SECURITIES	14
DESCRIPTION OF WARRANTS	22
DESCRIPTION OF UNITS	23
PLAN OF DISTRIBUTION	26
LEGAL MATTERS	29
EXPERTS	29
WHERE YOU CAN FIND MORE INFORMATION	29
INCORPORATION BY REFERENCE	30

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering. The second part is the accompanying base prospectus, which describes more general information about securities we may offer from time to time, some of which does not apply to this offering of common stock. Generally, when we refer to the prospectus, we are referring to both parts of this document combined. If information in this prospectus supplement or any related free writing prospectus differs from information in the accompanying prospectus, you should rely on the information in this prospectus supplement or the related free writing prospectus.

For investors outside of the United States: We have not, and the Agent has not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the shares of common stock in certain jurisdictions may be restricted by law. Persons who come into possession of this prospectus supplement, any related free writing prospectus and the accompanying prospectus should inform themselves about and observe any such restrictions. This prospectus supplement, any related free writing prospectus and the accompanying prospectus do not constitute, and may not be used in connection with, an offer or solicitation by anyone in any jurisdiction in which such offer or solicitation is not authorized 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 not consider any information in this prospectus supplement, any related free writing prospectus or the accompanying prospectus to be investment, legal or tax advice. You should consult your own counsel, accountant and other advisors for legal, tax, business, financial and related advice regarding the purchase of the shares of common stock. We are not making any representation to you regarding the legality of an investment in the shares of common stock by you under applicable investment or similar laws.

You should read and consider all information contained or incorporated by reference in this prospectus supplement, any related free writing prospectus and the accompanying prospectus that we provide or make available to you before making your investment decision. We and the Agent have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus we provide to you. Neither we nor the Agent take any responsibility for, and cannot provide any assurance as to the reliability of, any information other than the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus we provide to you. We and the Agent are not making an offer of the common stock in any jurisdiction where the offer is not permitted.

The information contained in this prospectus supplement, the accompanying prospectus or any free writing prospectus we provide you is accurate only as of its date, regardless of its time of delivery or of any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date. You should not assume that the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus is accurate as of any date other than the date on the front of that document. You should read this prospectus supplement, as well as the documents incorporated by reference herein, the additional information described under the section titled “*Where You Can Find More Information*” and “*Incorporation by Reference*” in this prospectus supplement and any free writing prospectus that we have authorized for use in connection with this offering, before investing in our common stock.

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 were made solely for the benefit of the parties to that agreement, including, in some cases, for the purpose of allocating risk among the parties to those agreements, and should not be deemed to be a representation, warranty or covenant to you.

[Table of Contents](#)

Moreover, those representations, warranties or covenants were accurate only as of the date when made. Accordingly, those representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Currency amounts in this prospectus supplement are stated in U.S. dollars.

We use various trademarks and trade names in our business, including without limitation our corporate name, product names and logo. All other trademarks or trade names referred to in this prospectus supplement are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus supplement 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.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where such offers and sales are permitted. The distribution of this prospectus supplement and the offering of our common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about and observe any restrictions relating to the offering of our common stock and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless the context otherwise indicates, references in this prospectus supplement to the “company,” “we,” “us” and “our” refer to Xeris Biopharma Holdings, Inc., and, where appropriate, our subsidiaries.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. As a result, it does not contain all of the information that may be important to you or that you should consider before making an investment. Before investing in our common stock, you should carefully read this entire prospectus supplement and accompanying prospectus, including the “Risk Factors” section in this prospectus supplement, the accompanying prospectus and our most recently filed Annual Report on Form 10-K, as well as our consolidated financial statements and the related notes thereto and the other documents incorporated by reference in this prospectus supplement and accompanying prospectus, which are described under “Where You Can Find Additional Information” on page S-28.

Company Overview

We are a biopharmaceutical company committed to developing and commercializing innovative solutions to enhance the lives of people with life-threatening diseases. Our primary focus is on therapies for patient populations in endocrinology, neurology, and gastroenterology. We currently have three commercially available products, Gvoke, a ready-to-use liquid glucagon for the treatment of severe hypoglycemia, Keveyis, the first and only U.S. Food and Drug Administration (“FDA”) approved therapy for primary periodic paralysis (“PPP”) and Recorlev, approved by the FDA in December 2021 for the treatment of endogenous hypercortisolemia in adult patients with Cushing’s Syndrome. We also have a pipeline of development programs to extend our current marketed products into new indications and uses or bring new products forward using our proprietary formulation technology platforms, XeriSol and XeriJect.

Commercial Products

Our number one priority is maximizing the commercial potential of our three commercial products: Gvoke, Keveyis and Recorlev.

- *Gvoke (Gvoke HypoPen, Gvoke PFS, Gvoke Kit)* is the first ready-to-use liquid stable glucagon for severe hypoglycemia. The product is indicated for use in pediatric and adult patients with diabetes age 2 years and above and can be administered in 2 simple steps. The estimated total addressable market for this therapy is approximately \$4.0 billion in the United States.

Throughout this document, unless otherwise noted, references to Gvoke include Gvoke PFS, Gvoke HypoPen, Gvoke Kit and Ogluo.

- *Keveyis* is the first and only therapy approved in the United States to treat hyperkalemic, hypokalemic, and related variants of PPP. PPP is a rare genetic, neuromuscular disorder that can cause extreme muscle weakness and/or paralysis; some forms are also commonly associated with myotonia or muscle stiffness. The estimated total addressable market for this therapy is greater than \$0.5 billion in the United States.
- *Recorlev* is a cortisol synthesis inhibitor proved for the treatment of endogenous hypercortisolemia in adult patients with Cushing’s syndrome for whom surgery is not an option or has not been curative. Endogenous Cushing’s syndrome is a rare but serious and potentially fatal endocrine disease caused by chronic elevated cortisol exposure. The estimated total addressable market for this therapy is approximately \$2.0 billion in the United States. Recorlev was approved by FDA on December 30, 2021 and launched in the United States in January 2022.

[Table of Contents](#)

Our pipeline

The following table summarizes key information about our internal products and product candidates.

Product Candidate	Indication	Development Stage					
		Preclinical	Phase 1	Phase 2	Phase 3	NDA Submitted	Marketed
Gvoke® (US)	Severe Hypoglycemia	Marketed					
Keveylis®	Primary Periodic Paralysis†	Marketed					
Recorlev®	Endogenous Cushing's syndrome†	Marketed					
Ogluo® (EU)	Severe Hypoglycemia	Available in UK*					
Self-Administered Glucagon for prevention	Exercise-Induced Hypoglycemia	Phase 2					
Levothyroxine	Endocrinology: Hypothyroidism	Phase 1					
XP-9164	Gastroenterology	Phase 1					

† Orphan Drug Designation

* Through Tetris Pharma

Company information

Xeris Pharmaceuticals, Inc. (“Xeris Pharma”) was incorporated under the laws of the State of Delaware in 2005. We are the successor corporation to Xeris Pharma and were incorporated under the laws of the State of Delaware in 2021 in connection with our acquisition of Strongbridge Biopharma plc (“Strongbridge”). Upon the closing of the acquisition, each of Xeris Pharma and Strongbridge became our wholly-owned subsidiaries. Our principal offices are located at 180 N. LaSalle Street, Suite 1600, Chicago, Illinois 60601, and our telephone number is (844) 445-5704. Our website address is www.xerispharma.com. We do not incorporate the information on or accessible through our website into this prospectus supplement, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus supplement. You should not rely on any such information in making your decision whether to purchase our common stock. Our common stock trades on The Nasdaq Global Select Market under the symbol “XERS”.

Implications of being an emerging growth company

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, as amended. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- Only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
- Reduced disclosure about our executive compensation arrangements;
- No advisory votes on executive compensation or golden parachute arrangements; and
- Exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.07 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous

[Table of Contents](#)

three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus supplement. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock.

We are also a “smaller reporting company” as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that the value of our voting and non-voting common stock held by non-affiliates is more than \$250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than \$100 million during the most recently completed fiscal year and the value of our voting and non-voting common stock held by non-affiliates is more than \$700 million measured on the last business day of our second fiscal quarter.

THE OFFERING

Common stock offered by us	Shares of our common stock having an aggregate offering price of up to \$75,000,000.
Common stock to be outstanding immediately after this offering	Up to 181,591,581 shares (as more fully described in the notes following this table), assuming sales of 40,760,869 shares of our common stock in this offering at an offering price of \$1.84 per share, which was the last reported sale price of our common stock on The Nasdaq Global Select Market on May 9, 2022. The actual number of shares issued will vary depending on how many shares of our common stock we choose to sell and the prices at which such sales occur.
Plan of distribution	“At the market offering” that may be made from time to time on The Nasdaq Global Select Market or other existing trading market for our common stock through our sales agent, Jefferies. See “Plan of Distribution” on page S-25 of this prospectus supplement.
Use of proceeds	Our management will retain broad discretion regarding the allocation and use of the net proceeds. We currently intend to use the net proceeds from this offering primarily to fund research and development activities relating to the advancement of our product candidates, sales and marketing costs to support commercialization of Gvoke, Keveyis and Recorlev, potential strategic acquisitions of complementary businesses, assets, services or technologies, expansion of our technology or manufacturing infrastructure and capabilities, debt repayment and refinancing, working capital, capital expenditures, and other general corporate purposes. See “Use of Proceeds” on page S-17 of this prospectus supplement.
Risk factors	Investing in our common stock involves significant risks. See “Risk Factors” on page S-8 of this prospectus supplement and page 1 of the accompanying prospectus, and under similar headings in the documents incorporated by reference into this prospectus supplement for a discussion of the factors you should carefully consider before deciding to invest in our common stock.
The Nasdaq Global Select Market symbol	“XERS”

All information in this prospectus supplement related to the number of shares of our common stock to be outstanding immediately after this offering is based on 140,830,712 shares of our common stock outstanding as of March 31, 2022, which includes 5,302,517 shares of unvested restricted stock, and excludes as of that date, unless otherwise indicated:

- 1,784,379 of common stock issuable upon exercise of options issued under Xeris Pharmaceuticals, Inc.’s 2011 Stock Option/Stock Issuance Plan at a weighted-average exercise price of \$4.12 per share;
- 2,913,012 shares of common stock issuable upon exercise of options issued under Xeris Pharmaceuticals, Inc.’s 2018 Stock Option and Incentive Plan at a weighted-average exercise price of \$6.27 per share;

Table of Contents

- 179,989 shares of common stock issuable upon exercise of options issued under Xeris Pharmaceuticals, Inc.'s Inducement Equity Plan at a weighted-average exercise price of \$6.25 per share;
- 4,024,846 shares of common stock issuable upon exercise of options issued under Strongbridge Biopharma plc's 2015 Equity Compensation Plan at a weighted-average exercise price of \$4.76 per share;
- 810,301 shares of common stock issuable upon exercise of options issued under Strongbridge Biopharma plc's 2017 Inducement Plan at a weighted-average exercise price of \$5.53 per share;
- 744,074 shares of common stock issuable upon exercise of options issued under Strongbridge Biopharma plc's Non-Employee Director Equity Compensation Plan and Written Stock Option Agreements (outside of the 2015 Plan and the Non-Employee Director Plan) at a weighted-average exercise price of \$12.21 per share;
- 12,808,695 shares of common stock issuable upon the exercise of warrants to purchase common stock at a weighted-average exercise price of \$3.96 per share;
- 3,308,937 shares of common stock reserved for issuance under Xeris Pharmaceuticals, Inc.'s 2018 Stock Option and Incentive Plan;
- 863,727 shares of common stock reserved for future issuance under Xeris Pharmaceuticals, Inc.'s 2018 Employee Stock Purchase Plan;
- 221,674 shares of common stock reserved for future issuance under Xeris Pharmaceuticals, Inc.'s Inducement Equity Plan;
- 1,820,963 shares of common stock reserved for future issuance under Strongbridge Biopharma plc's 2015 Equity Compensation Plan; and
- 1,244,386 shares of Common Stock reserved for future issuance under Strongbridge Biopharma plc's 2017 Inducement Plan.

Unless otherwise stated, all information contained in this prospectus supplement assumes no exercise of stock options after March 31, 2022 and reflects an assumed public offering price of \$1.84, which was the last reported sale price of our common stock on The Nasdaq Global Select Market on May 9, 2022.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below and in the accompanying prospectus, 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, as well as any amendments thereto reflected in subsequent filings with the SEC, each of which are incorporated by reference in this prospectus supplement, and all of the other information in this prospectus supplement, including our financial statements and related notes incorporated by reference herein. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our common stock could decline due to the materialization of any of these risks, and you may lose all or part of your investment. Additional risks and uncertainties that are not yet identified or that we currently believe to be immaterial may also materially harm our business, financial condition or results of operations and could result in a complete loss of your investment.

Risks Related to this Offering and our Common Stock

Our stock price has been and will likely continue to be volatile, and you may not be able to resell shares of our common stock at or above the price you paid.

The trading price of our common stock historically has been highly volatile and could continue to be subject to large fluctuations in response to various factors. The market price of our common stock has varied between a high price of \$27.98 on September 12, 2018 and a low price of \$1.42 on March 19, 2020. This volatility may affect the price at which you could sell the shares of our common stock, and the sale of substantial amounts of our common stock could adversely affect the price of our common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including:

- our ability to successfully commercialize Gvoke, Keveyis and Recorlev;
- regulatory actions with respect to our products and product candidates;
- regulatory actions with respect to our competitors' products and product candidates;
- the success of existing or new competitive products or technologies;
- results of clinical trials of product candidates of our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- the timing and results of clinical trials of our pipeline product candidates;
- commencement or termination of collaborations for our development programs;
- the results of our efforts to develop additional product candidates or products;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure or discontinuation of any of our development programs;
- the pricing and reimbursement of Gvoke, Keveyis or any of our product candidates that may be approved;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- actual or anticipated changes in estimates as to financial results or development timelines;

Table of Contents

- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions;
- global health concerns, such as the ongoing COVID-19 pandemic; and
- the other factors described in this “Risk Factors” section.

In recent years, the stock markets, and particularly the stock of smaller pharmaceutical and biotechnology companies, at times have experienced price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of affected companies. Broad market and industry factors may significantly affect the market price of our common stock unrelated to our actual operating performance. Since shares of our common stock were sold in our IPO in June 2018 at a price of \$15.00 per share, our stock price has fluctuated significantly.

In addition, in the past, class action litigation has often been instituted against companies whose securities have experienced periods of volatility in market price. Securities litigation brought against us following volatility in our stock price, regardless of the merit or ultimate results of such litigation, could result in substantial costs, which would hurt our financial condition and operating results and divert management’s attention and resources from our business.

We have broad discretion in the use of the net proceeds from this offering and may invest or spend the proceeds in ways with which you do not agree and in ways that may not yield a return on your investment.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section titled “Use of Proceeds,” as well as our existing cash and you will be relying on the judgment of our management regarding such application. You will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used effectively. Our management might not apply the net proceeds or our existing cash in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering or our existing cash in ways that enhance stockholder value, we may fail to achieve expected results, which could cause our stock price to decline. Pending their use, we may invest the net proceeds from this offering in short-term U.S. Treasury securities with insignificant rates of return. These investments may not yield a favorable return to our stockholders.

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

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior at the time of sale. Assuming that an aggregate of 40,760,869 shares of our common stock are sold at a price of \$1.84 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on May 9, 2022, for aggregate gross proceeds of \$75,000,000, after deducting commissions and estimated aggregate offering expenses payable by us, investors in this offering would experience immediate dilution of \$1.73 per share, representing the difference between our as-adjusted net tangible book value per share as of March 31, 2022, after giving effect to this offering, and the assumed offering price.

Table of Contents

This dilution is due to the substantially lower price paid by some of our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering and the exercise of stock options granted to our employees, directors and consultants. In addition, we have a significant number of stock options and restricted stock units outstanding. The exercise of any of these outstanding options and the settlement of these restricted stock units would result in further dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. Further, because we expect we will need to raise additional capital to fund our future activities, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock.

Future issuances of common stock or common stock-related securities, together with the exercise of outstanding stock options, if any, may result in further dilution. For a further description of the dilution that you will experience immediately after this offering, see the section titled “*Dilution.*”

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

Additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

In addition, sales of a substantial number of shares of our outstanding common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Persons who were our stockholders prior to our IPO continue to hold a substantial number of shares of our common stock that many of them are now able to sell in the public market. Significant portions of these shares are held by a relatively small number of stockholders. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

In addition, certain holders of shares of our common stock are entitled, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

We have registered the shares of common stock issuable upon exercise or settlement of all equity awards issued or reserved for issuance under Xeris Pharmaceuticals, Inc.’s 2018 Stock Option and Incentive Plan, Xeris Pharmaceuticals, Inc.’s 2018 Employee Stock Purchase Plan and Xeris Pharmaceuticals, Inc.’s Inducement Equity Plan under a Registration Statement on Form S-8. These shares can be freely sold in the public market upon issuance and once vested, subject to the lock-up agreements described above and Rule 144 in the case of our affiliates.

Securities analysts may publish inaccurate or unfavorable research or reports about our business or may publish no information at all, which could cause our stock price or trading volume to decline.

The trading market for our common stock is influenced by the research and reports that industry or financial analysts publish about us and our business. We do not control these analysts. Analysts who publish information about our common stock may have relatively little experience with our company, which could affect their ability to accurately forecast our results and could make it more likely that we fail to meet their estimates. If any of the

[Table of Contents](#)

analysts who cover us provide inaccurate or unfavorable research or issue an adverse opinion regarding our stock price, our stock price could decline. If one or more of these analysts cease coverage of our company or fail to publish reports covering us regularly, we could lose visibility in the market, which in turn could cause our stock price or trading volume to decline.

We do not anticipate paying any cash dividends in the foreseeable future, and accordingly, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.

We do not anticipate declaring any cash dividends to holders of our common stock in the foreseeable future. In addition, under our Credit Agreement and Guaranty dated March 8, 2022, among ourselves, Xeris Pharma, the subsidiary guarantors from time to time parties thereto, the lenders from time to time parties thereto and Hayfin Services LLP, as the administrative agent, we are restricted from paying any dividends or making any distributions on account of our capital stock. Our ability to pay cash dividends also may be prohibited by future loan agreements. Consequently, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investment. Investors seeking cash dividends should not invest in our common stock.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we face this type of litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Changes in tax law may adversely affect us or our investors.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. It cannot be predicted whether, when, in what form or with what effective dates tax laws, regulations and rulings may be enacted, promulgated or issued, which could result in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law.

We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to "emerging growth companies" and "smaller reporting companies" may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we have elected to take advantage of certain exemptions and relief from various reporting requirements that are applicable to other public companies that are not "emerging growth companies." In particular, while we are an "emerging growth company," (i) we will not be required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, (ii) we will be exempt from any rules that may be adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotations or a supplement to the auditor's report on financial statements, (iii) we will be subject to reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (iv) we will not be required to hold nonbinding advisory votes on executive compensation or stockholder approval of any golden parachute payments not previously approved.

As a result, our public filings may not be comparable to companies that are not "emerging growth companies". We may remain an "emerging growth company" until the fiscal year-end following the fifth

Table of Contents

anniversary of the completion of our IPO, though we may cease to be an “emerging growth company” earlier under certain circumstances, including (i) if the market value of our common stock that is held by nonaffiliates exceeds \$700 million as of any June 30, in which case we would cease to be an “emerging growth company” as of the following January 1, or (ii) if our gross revenue exceeds \$1.07 billion in any fiscal year.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. In addition, we qualify as a “smaller reporting company,” which allows us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. Even after we no longer qualify as an “emerging growth company,” we may still qualify as a “smaller reporting company” if the market value of our common stock that is held by non-affiliates is below \$250 million (or \$700 million if our annual revenue is less than \$100 million) as of June 30 in any given year, which would allow us to continue to take advantage of these exemptions.

Investors may find our common stock less attractive if we rely on these exemptions and relief granted by the JOBS Act. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may decline and/or become more volatile.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2021, we had federal net operating loss carryforwards of \$475.7 million and various state net operating loss carryforwards of \$309.7 million. If not utilized, the federal net operating losses generated in taxable years beginning on or before December 31, 2017 will expire at various dates between 2025 and 2037, and these net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Federal net operating losses generated in taxable years beginning after December 31, 2017 can be carried forward indefinitely; however, such net operating losses may only offset up to 80% of taxable income in taxable years beginning after December 31, 2021. As of December 31, 2021, we had \$5.4 million and \$2.5 million of federal and state income tax credits, respectively, to reduce future tax liabilities. If not utilized, the \$5.4 million in federal income tax credits will begin to expire in 2025, and the \$2.5 million of state research and development credits will begin to expire in 2022, and these tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (“Code”) and corresponding provisions of state law, if a corporation undergoes an “ownership change,” which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. Our existing net operating losses or credits may be subject to limitations arising from previous ownership changes, and if we undergo future ownership changes, many of which may be outside of our control, our ability to utilize our net operating losses or credits could be further limited by Sections 382 and 383 of the Code. Accordingly, we may not be able to utilize a material portion of our net operating losses or credits.

Provisions in our corporate charter documents and under Delaware law, as well as in the base indenture for senior debt securities dated June 30, 2020 (the “Base Indenture”), as supplemented by the first supplemental indenture thereto dated June 30, 2020 and the second supplemental indenture thereto dated October 5, 2021 (“the Supplemental Indentures” and together with the Base Indenture, the “Indenture”) for our 5.00% Convertible Senior Notes due 2025 (the “Convertible Notes”), may prevent or frustrate attempts by our stockholders to change our management or hinder efforts to acquire a controlling interest in us.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you

Table of Contents

might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of the board are not elected at one time; allow the authorized number of our directors to be changed only by resolution of our board of directors; and limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholders;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors;
- require the approval of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws; and
- provide that the Court of Chancery of the State of Delaware will be the exclusive forum for any state law derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty by one or more of our directors, officers or employees, any action asserting a claim against us pursuant to the Delaware General Corporation Law, or any action asserting a claim against us that is governed by the internal affairs doctrine, and that the United States District Court for the District of Illinois will be the exclusive forum for claims arising under the Securities Act of 1933, as amended (the “Securities Act”).

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders. This could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in our stockholders’ best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

In addition, certain provisions in the Indenture governing our Convertible Notes could make a third-party attempt to acquire us more difficult or expensive. For example, if a takeover constitutes a fundamental change, then noteholders will have the right to require us to repurchase their notes for cash. In addition, if a takeover constitutes a make-whole fundamental change, then we may be required to temporarily increase the conversion rate. In either case, and in other cases, our obligations under the notes and the indenture could increase the cost of acquiring us or otherwise discourage a third party from acquiring us or removing incumbent management, including in a transaction that noteholders or holders of our common stock may view as favorable.

[Table of Contents](#)

Our bylaws designate certain courts as the sole and exclusive forums for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees and may discourage such lawsuits with respect to such claims.

Our amended and restated bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claim for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of or based on a fiduciary duty owed by any of our current or former directors, officers and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein (the "Delaware Forum Provision"). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Securities Exchange Act of 1934, as amended. In addition, our amended and restated bylaws further provide that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the "Federal Forum Provision").

This forum selection provision may limit a shareholder's ability to bring a claim in a judicial forum that it finds favorable or cost-efficient for disputes with us or any of our directors, officers, employees or agents, which may discourage such lawsuits, or increase the costs to a shareholder of bringing such lawsuits, against us and such persons.

The enforceability of forum selection provisions in other companies' articles of incorporation, bylaws or similar governing documents has been challenged in legal proceedings, and it is possible that in connection with any action a court could find the forum selection provisions contained in our bylaws to be inapplicable or unenforceable in such action. If a court were to find these forum selection provisions inapplicable or unenforceable, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely impact our operating or financial condition or performance.

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 levels of dilution and different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold in this offering. Investors may experience a decline in the value of the shares they purchase in this offering as a result of sales made at prices lower than the prices they paid.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the information and documents that we incorporate by reference herein contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “may,” “will,” “should,” “expects,” “plans,” “anticipates,” “could,” “intends,” “target,” “projects,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these words or other similar terms or expressions that concern our expectations, strategy, plans or intentions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus supplement and the documents incorporated by reference herein, and in particular those factors referenced in the section titled “Risk Factors.”

This prospectus supplement, any related free writing prospectus and the information and documents incorporated by reference herein contain forward-looking statements 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 future events or our future operational or 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. Forward-looking statements include, but are not limited to, statements about:

- the rate and degree of market acceptance and clinical utility of Gvoke, Keveyis and Recorlev;
- the pricing and reimbursement of Gvoke, Keveyis and Recorlev or any of our product candidates, if approved;
- the effect of uncertainties related to the current coronavirus pandemic, or any other health epidemic, on U.S. and global markets, our business, financial condition, operations, third-party suppliers or the global economy as a whole;
- our estimates regarding the market opportunities for Gvoke, Keveyis and Recorlev and our product candidates;
- the commercialization, marketing and manufacturing of Gvoke, Keveyis and Recorlev and our product candidates, if approved;
- our ability to manufacture, or the ability of third parties to deliver, sufficient quantities of components and drug product for commercialization of Gvoke, Keveyis and Recorlev or any of our product candidates, if approved;
- our expectations related to the anticipated launch of Ogluo in certain European countries;
- the rate and degree of market acceptance and clinical utility of any of our product candidates for which we receive marketing approval in the future;
- the initiation, timing, progress and results of our research and development programs and future preclinical and clinical studies;
- our ability to advance any other product candidates into, and successfully complete, clinical studies and obtain regulatory approval for them;
- our ability to identify additional product candidates;
- the implementation of our strategic plans for our business, product candidates and technology;

Table of Contents

- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to use the proceeds of this offering and our borrowings in ways that increase the value of your investment;
- our expectations related to the use of proceeds from our public offerings and borrowings and estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- our ability to maintain and establish collaborations;
- our financial performance;
- our ability to effectively manage our anticipated growth;
- developments relating to our competitors and our industry, including the impact of government regulation; and
- other risks and uncertainties, including those listed under the caption “Risk Factors.”

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation, the risk factors and cautionary statements described in other documents that we file from time to time with the SEC, specifically under “Item 1A. Risk Factors” and elsewhere in 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 the section of this prospectus supplement titled “*Risk Factors*.”

The forward-looking statements in this prospectus supplement, any related free writing prospectus and the documents incorporated by reference represent our views as of their respective dates. We anticipate that subsequent events and developments will cause our views to change. While we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so 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 dates on which they were made.

This prospectus supplement, any related free writing prospectus and the documents incorporated by reference also contain estimates, projections and other information concerning our industry, our business, and the markets for certain Gvoke, Keveyis and Recorlev and our product candidates. 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 that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from our own internal estimates and research as well as 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.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$75,000,000 from time to time. The amount of proceeds from this offering will depend upon the number of shares of our common stock sold and the market price at which they are sold. There can be no assurance that we will be able to sell any shares under or fully utilize the Sales Agreement with Jefferies as a source of financing. Therefore, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time.

We intend to use any net proceeds from this offering to fund research and development activities including clinical development relating to the advancement of our product candidates and the expansion of our product pipeline; sales and marketing costs to support commercialization of our products including of Gvoke, Keveyis and Recorlev; potential strategic acquisitions of complementary businesses, assets, services or technologies; expansion of our technology and manufacturing infrastructure and capabilities; repayment and refinancing of debt; working capital; capital expenditures; and other general corporate purposes. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including investment grade, interest bearing instruments and U.S. government securities, until they are used for their stated purpose. 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.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future.

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 public offering price per share of our common stock in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering. Our net tangible book value as of March 31, 2022 was approximately \$(55) million, or approximately \$(0.39) per share of common stock. Net tangible book value per share represents the amount of total tangible assets (total assets less intangible assets and goodwill) less total liabilities, divided by the number of shares of our common stock outstanding as of March 31, 2022.

Dilution in net tangible book value per share to new investors participating in this offering represents the difference between the amount per share paid by purchasers in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering. After giving effect to the assumed sale of 40,760,869 shares of our common stock in the aggregate amount of approximately \$75,000,000 at an assumed offering price of \$1.84 per share, the last reported sale price of our common stock on May 9, 2022, and after deduction of commissions and estimated aggregate offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2022 would have been approximately \$20 million, or approximately \$0.11 per share of common stock. This represents an immediate increase in net tangible book value of \$0.50 per share of common stock to our existing stockholders and an immediate dilution in net tangible book value of \$1.73 per share of common stock to investors participating in this offering at the assumed offering price.

Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the assumed public offering price per share paid by new investors. The following table illustrates this per share dilution:

Assumed offering price per share		\$1.84
Net tangible book value per share as of March 31, 2022	\$(0.39)	
Increase in net tangible book value per share attributable to new investors attributable to this offering	\$ 0.50	
As adjusted net tangible book value per share as of March 31, 2022, after giving effect to this offering		\$0.11
Dilution in net tangible book value per share to new investors participating in this offering		\$1.73

The table above assumes for illustrative purposes that an aggregate of 40,760,869 shares of our common stock are sold at a price of \$1.84 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on May 9, 2022, for aggregate gross proceeds of approximately \$75,000,000. The shares 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 price at which the shares are sold from the assumed offering price of \$1.84 per share shown in the table above, assuming all of our common stock in the aggregate amount of approximately \$75,000,000 is sold at that price, would result in an increase to our adjusted net tangible book value per share after the offering to \$0.01 and an increase in the dilution in net tangible book value per share to new investors in this offering to \$0.99, after deducting commissions payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$1.84 per share shown in the table above, assuming all of our common stock in the aggregate amount of approximately \$75,000,000 is sold at that price, would result in a decrease to our adjusted net tangible book value per share after the offering to \$0.02 and a decrease in the dilution in net tangible book value per share to new investors in this offering to \$0.98, after deducting commissions payable by us. This information is supplied for illustrative purposes only, and will adjust based on the actual offering prices, the actual number of shares that we offer and sell in this offering and other terms of each sale of shares in this offering.

[Table of Contents](#)

The information above and in the foregoing table is based upon 140,830,712 shares of our common stock outstanding as of March 31, 2022, which includes 5,302,517 shares of unvested restricted stock, and excludes as of that date, unless otherwise indicated:

- 1,784,379 of common stock issuable upon exercise of options issued under Xeris Pharmaceuticals, Inc.'s 2011 Stock Option/Stock Issuance Plan at a weighted-average exercise price of \$4.12 per share
- 2,913,012 shares of common stock issuable upon exercise of options issued under Xeris Pharmaceuticals, Inc.'s 2018 Stock Option and Incentive Plan at a weighted-average exercise price of \$6.27 per share;
- 179,989 shares of common stock issuable upon exercise of options issued under Xeris Pharmaceuticals, Inc.'s Inducement Equity Plan at a weighted-average exercise price of \$6.25 per share;
- 4,024,846 shares of common stock issuable upon exercise of options issued under Strongbridge Biopharma plc's 2015 Equity Compensation Plan at a weighted-average exercise price of \$4.76 per share;
- 810,301 shares of common issuable upon exercise of options issued under Strongbridge Biopharma plc's 2017 Inducement Plan at a weighted-average exercise price of \$5.53 per share;
- 744,074 shares of common issuable upon exercise of options issued under Strongbridge Biopharma plc's Non-Employee Director Equity Compensation Plan and Written Stock Option Agreements (outside of the 2015 Plan and the Non-Employee Director Plan) at a weighted-average exercise price of \$12.21 per share;
- 12,808,695 shares of common issuable upon the exercise of warrants to purchase common stock at a weighted-average exercise price of \$3.96 per share;
- 3,308,937 shares of common stock reserved for issuance under Xeris Pharmaceuticals, Inc.'s 2018 Stock Option and Incentive Plan;
- 863,727 shares of common stock reserved for future issuance under Xeris Pharmaceuticals, Inc.'s 2018 Employee Stock Purchase Plan;
- 221,674 shares of common stock reserved for future issuance under Xeris Pharmaceuticals, Inc.'s Inducement Equity Plan;
- 1,820,963 shares of common stock reserved for future issuance under Strongbridge Biopharma plc's 2015 Equity Compensation Plan; and
- 1,244,386 shares of Common Stock reserved for future issuance under Strongbridge Biopharma plc's 2017 Inducement Plan.

In addition, we may choose to raise additional capital in the future 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. To the extent that any of our outstanding options are exercised, new options are issued under our equity incentive plans or we issue additional shares of common stock or other equity or convertible debt securities in the future, there will be further dilution to investors participating in this offering.

CERTAIN MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

- a non-resident alien individual;
- a corporation or other organization taxable as a corporation for U.S. federal income tax purposes that is created or organized in or under laws other than the laws of the United States, any state thereof, or the District of Columbia;
- an estate the income of which is not subject to U.S. federal income tax on a net income basis; or
- a trust the income of which is not subject to U.S. federal income tax on a net income basis and that (1) is not subject to the primary supervision of a court within the United States or over which no U.S. persons have authority to control all substantial decisions and (2) has not made an election to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, and current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus supplement and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus supplement. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code, generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any U.S. state, local or non-U.S. taxes, the alternative minimum tax, the Medicare tax on net investment income, the rules regarding qualified small business stock within the meaning of Section 1202 of the Code, or any other aspect of any U.S. federal tax other than the income tax. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt or governmental organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;

Table of Contents

- “qualified foreign pension funds,” or entities wholly owned by a “qualified foreign pension fund”;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and
- certain U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on Our Common Stock

Distributions, if any, on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder’s investment, up to such holder’s tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in “Gain on Sale or Other Taxable Disposition of Our Common Stock.” Any such distributions will also be subject to the discussions below under the sections titled “Backup Withholding and Information Reporting” and “Withholding and Information Reporting Requirements—FATCA.”

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional “branch profits tax” at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder’s country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) to the applicable withholding agent and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing a U.S. tax return with the IRS.

Gain on Sale or Other Taxable Disposition of Our Common Stock

Subject to the discussions below under “Backup Withholding and Information Reporting” and “Withholding and Information Reporting Requirements—FATCA,” a non-U.S. holder generally will not be subject to any U.S. federal income tax on any gain realized upon such holder’s sale or other taxable disposition of shares of our common stock unless:

- the gain is effectively connected with the non-U.S. holder’s conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base

maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in “Distributions on Our Common Stock” also may apply;

- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or
- we are, or have been, at any time during the five-year period preceding such sale or other taxable disposition (or the non-U.S. holder’s holding period, if shorter) a “U.S. real property holding corporation,” unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in “Distributions on Our Common Stock,” generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker.

Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder’s U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and Information Reporting Requirements—FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, generally impose a U.S. federal withholding tax at a rate of 30% on payments of dividends on our common stock paid to a foreign entity unless (i) if the foreign entity is a “foreign financial institution,” such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a “foreign financial institution,” such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Such withholding may also apply to payments of proceeds from sales or other dispositions of our common stock, although under recently proposed U.S. Treasury Regulations no withholding would apply to payments of gross proceeds. The preamble to the proposed regulations specifies that taxpayers (including withholding agents) are permitted to rely on the proposed regulations pending finalization. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Jefferies, under which we may offer and sell up to \$75,000,000 of our shares of common stock from time to time through the Agent acting as sales 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 Sales Agreement, we will notify the Agent 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 the Agent, unless the Agent declines to accept the terms of such notice, the Agent 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 the Agent under the Sales 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 the Agent 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 the Agent may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay the Agent a commission equal to 3% of the 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 the Agent 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 the Agent under the terms of the sales agreement, will be approximately \$0.3 million. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

The Agent 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 Sales 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, the Agent may be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation of the Agent will be deemed to be underwriting commissions or discounts. We have agreed to indemnify the Agent against certain civil liabilities, including liabilities under the Securities Act and the Exchange Act. We have also agreed to contribute to payments the Agent may be required to make in respect of such liabilities.

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

This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. A copy of the Sales Agreement is filed as an exhibit to a current report on Form 8-K filed under the Exchange Act and incorporated by reference in this prospectus supplement.

The Agent 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

[Table of Contents](#)

receive customary fees. In the course of its business, the Agent may actively trade our securities for its own account or for the accounts of customers, and, accordingly, the Agent 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 the Agent, and the Agent may distribute the prospectus supplement and the accompanying prospectus electronically.

LEGAL MATTERS

Certain legal matters in connection with this offering and the validity of the securities offered by this prospectus will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Jefferies, LLC is being represented in connection with this offering by Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York.

EXPERTS

The consolidated financial statements of Xeris Biopharma Holdings, Inc. as of December 31, 2021 and 2020, and for each of the years in the two-year period ended December 31, 2021, have been incorporated by reference herein and in the registration statement 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.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement is part of a registration statement on Form S-3 that we have filed with the SEC. This prospectus supplement, filed as part of the registration statement, does not contain all the information set forth in the registration statement and its exhibits and schedules, portions of which have been omitted as permitted by the rules and regulations of the SEC. For further information about us, we refer you to the registration statement and to its exhibits and schedules. Certain information in the registration statement has been omitted from this prospectus supplement in accordance with the rules of the SEC.

We are subject to the reporting and information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. These documents also may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (www.sec.gov). Written requests for such copies should be directed to Investor Relations Department, Xeris Biopharma Holdings, Inc., 180 N. LaSalle Street, Suite 1600, Chicago, IL 60601, and our website is located at www.xerispharma.com.

We have the authority to designate and issue more than one class or series of stock having various preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications, and terms and conditions of redemption. See "Description of Capital Stock" in the base prospectus. We will furnish a full statement of the relative rights and preferences of each class or series of our stock which has been so designated and any restrictions on the ownership or transfer of our stock to any shareholder upon request and without charge. Information contained on our website is not incorporated by reference into this prospectus supplement and, therefore, is not part of this prospectus supplement or any accompanying prospectus supplement.

INCORPORATION 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 considered to be a part of this prospectus supplement, and the information that we file later with the SEC will automatically update and, where applicable, supersede the information already incorporated by reference. We incorporate by reference the documents listed below that we filed with the SEC:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2021 filed with the SEC on March 11, 2022;
- our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2022 filed with the SEC on May 11, 2022;
- 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](#) (other than information furnished rather than filed) filed with the SEC on April 28, 2022;
- our Current Reports on Form 8-K filed with the SEC on [January 3, 2022](#), [January 28, 2022](#) and [March 10, 2022](#);
- the description of our common stock, par value \$0.0001 per share, contained in our Current Report on Form 8-K filed with the SEC on [October 5, 2021](#); and
- all future documents filed by us with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, including all filings made after the date of the filing of this registration statement and prior to the effectiveness of this registration statement, prior to the termination of the offering of the underlying securities; provided, however, that we are not incorporating by reference any additional documents or information furnished and not filed with the SEC.

Notwithstanding the foregoing, unless specifically stated to the contrary, information that we furnish (and that is not deemed “filed” with the SEC) under Items 2.02 and 7.01 of any Current Report on Form 8-K, including the related exhibits under Item 9.01, is not incorporated by reference into this prospectus supplement or the registration statement of which this prospectus supplement is a part.

Any statement contained in a document that is incorporated by reference will be modified or superseded for all purposes to the extent that a statement contained in this prospectus supplement or in any other document that is subsequently filed with the SEC and incorporated by reference into this prospectus supplement modifies or is contrary to that previous statement. Any statement so modified or superseded will not be deemed a part of this prospectus supplement, except as so modified or superseded. Since information that we later file with the SEC will update and supersede previously incorporated information, you should look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or in any documents previously incorporated by reference have been modified or superseded.

Upon request, either orally or in writing, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus supplement is delivered, a copy of the documents incorporated by reference into this prospectus supplement but not delivered with the prospectus supplement. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus supplement, at no cost by writing us at the following address: Xeris Biopharma Holdings, Inc., 180 N. LaSalle Street, Suite 1600, Chicago, IL 60601.

You may also access these documents, free of charge on the SEC’s website at www.sec.gov or on our website at <http://www.xerispharma.com>. Information contained on our website is not incorporated by reference into this prospectus supplement, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus supplement.

[Table of Contents](#)

This prospectus supplement is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus supplement or those documents.

PROSPECTUS

\$250,000,000



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

We may from time to time issue, in one or more series or classes, up to \$250.0 million in aggregate principal amount of our common stock, preferred stock, debt securities, warrants and/or units, in any combination, together or separately, in one or more offerings in amounts, at prices and on the terms that we will determine at the time of the offering and which will be set forth in a prospectus supplement and any related free writing prospectus.

We may offer these securities separately or together in units. Each time we sell securities described herein, we will provide prospective investors with a supplement to this prospectus that will specify the terms of the securities being offered. We may sell these securities to or through underwriters or dealers and also to other purchasers or through agents. We will set forth the names of any underwriters or agents, and any fees, conversions, or discount arrangements, in the accompanying prospectus supplement. We may not sell any securities under this prospectus without delivery of the applicable prospectus supplement. You should read this document and any prospectus supplement or amendment carefully before you invest in our securities.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "XERS." On January 25, 2022, the closing price for our common stock, as reported on The Nasdaq Global Select Market, was \$2.10 per share. Our principal executive offices are located at 180 N. LaSalle Street, Suite 1600, Chicago, IL 60601.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "[Risk Factors](#)" contained in this prospectus beginning on page 1 and any applicable prospectus supplement, and under similar headings in the other 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 February 7, 2022.

TABLE OF CONTENTS

	Page
ABOUT THIS PROSPECTUS	ii
RISK FACTORS	1
CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS	2
PROSPECTUS SUMMARY	4
USE OF PROCEEDS	7
SECURITIES WE MAY OFFER	8
DESCRIPTION OF CAPITAL STOCK	9
DESCRIPTION OF DEBT SECURITIES	14
DESCRIPTION OF WARRANTS	22
DESCRIPTION OF UNITS	23
PLAN OF DISTRIBUTION	26
LEGAL MATTERS	29
EXPERTS	29
WHERE YOU CAN FIND MORE INFORMATION	29
INCORPORATION BY REFERENCE	30

ABOUT THIS PROSPECTUS

This prospectus is part of a 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 from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to \$250.0 million.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities described herein, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading “Where You Can Find More Information” and “Incorporation By Reference.”

You should rely only on the information contained in or incorporated by reference in this prospectus or any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

THIS PROSPECTUS MAY NOT BE USED TO OFFER AND SELL SECURITIES UNLESS IT IS ACCOMPANIED BY AN ADDITIONAL PROSPECTUS OR A PROSPECTUS SUPPLEMENT.

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

As used in this prospectus, unless the context otherwise requires, references to the “company,” “we,” “us” and “our” refer to Xeris Biopharma Holdings, Inc., and, where appropriate, our subsidiaries.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks described in the documents incorporated by reference in this prospectus and any prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described in the documents incorporated herein by reference, including (i) our quarterly report on Form 10-Q for the fiscal quarter ended September 30, 2021, which is on file with the SEC and is incorporated herein by reference and (ii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “may,” “will,” “could,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “projects,” “seeks,” “endeavor,” “potential,” “continue,” and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus, and in particular those factors referenced in the section “Risk Factors.”

This prospectus contains forward-looking statements that are based on our management’s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, 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:

- the rate and degree of market acceptance and clinical utility of Gvoke, Keveyis, Recorlev or any other of our product candidates for which we receive marketing approval;
- our estimates regarding the market opportunities for Gvoke, Keveyis, Recorlev and our product candidates;
- the commercialization, marketing and manufacturing of Gvoke, Keveyis, Recorlev and our product candidates, if approved;
- the pricing and reimbursement of Gvoke, Keveyis, Recorlev or any other of our product candidates, if approved;
- the initiation, timing, progress and results of our research and development programs and future preclinical and clinical studies;
- our ability to successfully integrate and combine the businesses of Xeris Pharmaceuticals, Inc. and Strongbridge Biopharma Limited (f/k/a Strongbridge Biopharma plc) and realize the anticipated benefits from the merger;
- our ability to advance any other product candidates into, and successfully complete, clinical studies and obtain regulatory approval for them;
- our ability to identify additional product candidates;
- the implementation of our strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to use the proceeds of this offering in ways that increase the value of your investment;
- our expectations related to the use of proceeds from this offering, and estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- our ability to manufacture, or the ability of third parties to deliver, sufficient quantities of components and drug product for commercialization of Gvoke, Keveyis, Recorlev or any other of our product candidates;

Table of Contents

- our ability to maintain and establish collaborations;
- our financial performance;
- our ability to effectively manage our anticipated growth;
- developments relating to our competitors and our industry, including the impact of government regulation;
- our ability to avoid any findings of material weakness or significant deficiencies we may find in the future;
- the effect of COVID-19 on the foregoing; and
- other risks and uncertainties, including those listed under the caption “Risk Factors.”

This prospectus and the documents incorporated by reference also contain 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.

You should read this prospectus and the documents that we incorporate by reference in this prospectus completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements in this prospectus and the documents we incorporate by reference herein represent our views as of their respective dates. 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 have no current intention of doing so 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.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus and in the documents we incorporate by reference. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus, including the documents incorporated by reference herein and therein, carefully, especially the risks of investing in our common stock discussed under “Risk Factors” beginning on page 1 of this prospectus and other periodic reports incorporated herein and therein by reference, along with our consolidated financial statements and notes to those consolidated financial statements, before making an investment decision..

Overview

We are a biopharmaceutical company developing and commercializing unique therapies for patient populations in endocrinology, neurology, and gastroenterology. We have three commercially available products, Gvoke, a ready-to-use liquid glucagon for the treatment of severe hypoglycemia, Keveyis, the first and only U.S. Food and Drug Administration (“FDA”) approved therapy for primary periodic paralysis and Recorlev, which was approved by the FDA in December 2021 for the treatment of endogenous hypercortisolemia in adult patients with Cushing’s Syndrome. We also have a robust pipeline of development programs to extend our current marketed products into important new indications and uses and bring new products forward using our proprietary formulation technology platforms, XeriSol and XeriJect.

With novel technology platforms, XeriSol and XeriJect, that enable ready-to-use, room-temperature stable formulations of injectable and infusible therapies, we are advancing a portfolio of solutions in various therapeutic categories. Gvoke, delivers ready-to-use glucagon via a pre-filled syringe (“Gvoke PFS”) or auto-injector (“Gvoke HypoPen”) for the treatment of severe hypoglycemia, a potentially life-threatening condition, in people with diabetes. Gvoke was approved in September 2019 by the FDA for the treatment of severe hypoglycemia in pediatric and adult patients with diabetes ages two years and older. We began the field launches of Gvoke PFS and Gvoke HypoPen in January 2020 and July 2020, respectively, and each is available in two doses: a 0.5 mg/0.1 mL dose for pediatric patients and a 1 mg/0.2 mL dose for adolescent and adult patients. In February 2021, the European Commission (“EC”) granted a marketing authorization for and in April 2021 the United Kingdom’s Medicines and Healthcare products Regulatory Agency (“MHRA”) approved Ogluo for the treatment of severe hypoglycemia in adults, adolescents, and children aged two years and over with diabetes mellitus. On July 19, 2021, we announced that we had entered into an exclusive agreement with Tetris Pharma Limited (“Tetris”) for the commercialization of Ogluo in the European Economic Area, United Kingdom, and Switzerland (the “Territory”). Under the terms of the applicable agreements, Xeris will be responsible for product supply and Tetris will be responsible for commercialization of Ogluo in the Territory. Subject to the terms and conditions set forth in the agreements, Xeris will receive compensation over the contract tied to the first commercial sale and other time-, launch- and sales-related milestones and collect a royalty on sales. Tetris launched Ogluo in the United Kingdom in late December 2021. We are also continuing to evaluate additional applications of our ready-to-use glucagon formulation to address needs in hypoglycemia and related conditions. In addition, we have applied our technology platforms to other commercially available drugs to enable more convenient and patient-friendly subcutaneous (“SC”) and intramuscular (“IM”) routes of administration and continue to seek partners to further develop and commercialize products to address unmet needs in both diabetes and epilepsy. We own the rights to our proprietary formulation technology platforms, Gvoke, Ogluo, and our product candidates domestically and internationally.

Through the acquisition of Strongbridge Biopharma plc (now Strongbridge Biopharma Limited, “Strongbridge”), we added Keveyis (dichlorphenamide) to our commercial product portfolio. Keveyis is the first and only treatment approved by FDA for hyperkalemic, hypokalemic, and related variants of primary periodic paralysis (“PPP”), a group of rare hereditary disorders that cause episodes of muscle weakness or paralysis. In

addition, we added Recorlev (levoketoconazole), the pure 2S,4R enantiomer of the enantiomeric pair comprising ketoconazole, is a next-generation steroidogenesis inhibitor, which was approved by the FDA in December 2021 for the treatment of endogenous hypercortisolemia in adult patients with Cushing's Syndrome. Levoketoconazole has received orphan designation from the FDA and the European Medicines Agency.

Xeris Pharmaceuticals ("Xeris Pharma") owns 140 patents issued globally, including a composition of matter patent covering our ready-to-use glucagon formulation that expires in 2036. Upon completion of the acquisition of Strongbridge, we control the patents of Xeris Pharma and those of Strongbridge Dublin Limited, the latter of which has 53 granted patents globally including those related to proprietary formulations of levoketoconazole (the active pharmaceutical ingredient in Recorlev[®]) and the uses of such formulations in treating certain endocrine-related diseases and syndromes. This includes US Patent No. 11,020,393, which was granted on June 1, 2021, and which provides patent protection through 2040 for the use of Recorlev in the treatment of certain patients with persistent or recurrent Cushing's syndrome.

Strongbridge Biopharma Acquisition

On October 5, 2021, pursuant to the transaction agreement, dated May 24, 2021, by and between us, Strongbridge, Xeris Pharma, and Wells MergerSub, Inc. a Delaware corporation, we completed our acquisition of Strongbridge. Upon completion of the acquisition, (a) we acquired Strongbridge by means of a scheme of arrangement under Irish law pursuant to which we acquired all of the outstanding ordinary shares of Strongbridge ("Strongbridge Shares") in exchange for (i) 0.7840 of a share of our common stock ("Shares") and cash in lieu of fractions of our Shares in exchange for each Strongbridge Share held by such Strongbridge Shareholders and (ii) one (1) non-tradeable contingent value right ("CVR"), worth up to a maximum of \$1.00 per Strongbridge Share settleable in cash, additional Shares, or a combination of cash and additional Shares, at our sole election and (b) MergerSub merged with and into Xeris Pharma, with Xeris Pharma, as the surviving corporation in the merger.

Company information

Xeris Pharma was incorporated under the laws of the State of Delaware in 2005. We were incorporated under the laws of the State of Delaware in 2021 in connection with our acquisition of Xeris Pharma and Strongbridge. Upon the closing of the acquisition, each of Xeris Pharma and Strongbridge became our wholly-owned subsidiaries. Our principal offices are located at 180 N. LaSalle Street, Suite 1600, Chicago, Illinois 60601, and our telephone number is (844) 445-5704. Our website address is www.xerispharma.com. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus. You should not rely on any such information in making your decision whether to purchase our common stock. Our common stock trades on The Nasdaq Global Select Market under the symbol "XERS".

Implications of being an emerging growth company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- Only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- Reduced disclosure about our executive compensation arrangements;
- No advisory votes on executive compensation or golden parachute arrangements; and
- Exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.07 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus supplement. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock.

We are also a “smaller reporting company” as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that the value of our voting and non-voting common stock held by non-affiliates is more than \$250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than \$100 million during the most recently completed fiscal year and the value of our voting and non-voting common stock held by non-affiliates is more than \$700 million measured on the last business day of our second fiscal quarter.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include research and development costs, including the conduct of one or more clinical trials and process development and manufacturing of our product candidates, sales and marketing expenses to support commercialization of Gvoke, Keveyis and Recorlev, potential strategic acquisitions of complementary businesses, services or technologies, expansion of our technology infrastructure and capabilities, working capital, capital expenditures and other general corporate purposes. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including investment grade, interest bearing instruments and U.S. government securities, until they are used for their stated purpose. 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.

SECURITIES WE MAY OFFER

This prospectus contains summary descriptions of the securities we may offer from time to time. These summary descriptions are not meant to be complete descriptions of each security. The particular terms of any security will be described in the applicable prospectus supplement. This prospectus provides you with a general description of the securities we may offer. Each time we sell securities described herein, we will provide prospective investors with a supplement to this prospectus that will contain specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered.

We may sell the securities to or through underwriters, dealers or agents, directly to purchasers or through a combination of any of these methods of sale or as otherwise set forth below under "Plan of Distribution." We, as well as any agents acting on our behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. Any prospectus supplement will set forth the names of any underwriters, dealers, agents or other entities involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them.

DESCRIPTION OF CAPITAL STOCK

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 amended and restated certificate of incorporation, or our charter, and amended and restated by-laws, or our by-laws, 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.

Authorized Capital Stock

Our authorized capital stock consists of 350,000,000 shares of common stock, par value \$0.0001 per share, and 25,000,000 shares of preferred stock, par value \$0.0001 per share, all of which shares of preferred stock are undesignated.

As of January 25, 2022, 135,112,224 shares of our common stock were outstanding and held by 256 stockholders of record.

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 the stockholders. Holders of our common stock are entitled to receive dividends as may be declared from time to time by our board of directors out of funds legally available therefor. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock have no preemptive, subscription, redemption or conversion rights, and no sinking fund provisions are applicable to our common stock.

In the event of our dissolution, liquidation or winding up, holders of our common stock are entitled to share pro rata 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. 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.

All outstanding shares are fully paid and non-assessable. When we issue shares of common stock under this prospectus, the shares will fully be paid and non-assessable and will not have, or be subject to, any preemptive or similar rights.

Preferred Stock

Our board of directors is authorized, without further action by the stockholders, to designate and issue up to an aggregate of 25,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. 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 and the likelihood that such holders will receive dividend payments and payments upon our liquidation.

The purpose of authorizing our board of directors to issue preferred stock in one or more series and determine the number of shares in the series and its rights, preferences, privileges and restrictions is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing

[Table of Contents](#)

flexibility in connection with possible future financings and acquisitions and other corporate purposes, could, under certain circumstances, have the effect of delaying, deferring or preventing a change in control of our company, as further discussed below under “—Anti-Takeover Effects of Delaware Law and Provisions of our Charter and our By-laws—Provisions of our Charter and our By-laws—Undesignated Preferred Stock.”

When we issue shares of preferred stock under this prospectus, the shares will be fully paid and non-assessable and will not be subject to any preemptive or similar rights.

Registration Rights

Pursuant to the terms of Xeris Pharma’s investors’ rights agreement, dated as of December 31, 2015, certain of our stockholders are entitled to rights with respect to the registration of their shares under the Securities Act until the earliest of the fifth (5th) anniversary of our initial public offering, or such holder’s registrable securities could be sold without any restriction on volume or manner of sale on any 90-day period under Rule 144 or any successor rule, as described below. We refer to these shares collectively as registrable securities.

Demand Registration Rights

The holders of 1,387,985 shares of our common stock are entitled to demand registration rights. Under the terms of the investors’ rights agreement, we will be required, upon the written request of holders of at least 20% of the securities eligible for registration then outstanding or such lesser percentage that would result in an aggregate offering price of at least \$10.0 million, to file a registration statement and use commercially reasonable efforts to effect the registration of all or a portion of these shares for public resale. We are required to effect only two registrations pursuant to this provision of the investors’ rights agreement.

Short-Form Registration Rights

Pursuant to the investors’ rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of majority in interest of these holders to sell registrable securities at an aggregate price of at least \$1.0 million, we will be required to use commercially reasonable efforts to effect a registration of such shares. We are not required to effect more than two registrations that have been declared or ordered effective by the SEC pursuant to this provision of the investors’ rights agreement. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Piggyback Registration Rights

Pursuant to the investors’ rights agreement, if we register any of our securities either for our own account or for the account of other security holders, the holders of 1,387,985 shares of our common stock are entitled to include their shares in the registration. Subject to certain exceptions contained in the investors’ rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our investors’ rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The demand registration rights and short form registration rights granted under the investors’ rights agreement will terminate on the fifth anniversary of the completion of Xeris Pharma’s initial public offering or at

such time after such offering when the holders' shares may be sold without restriction pursuant to Rule 144 within a 90-day period.

Anti-Takeover Effects of Delaware Law and Provisions of our Certificate of Incorporation and our By-laws

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge 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; and
- 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.

Choice of Forum

Our bylaws provide that unless we consent in writing to the selection of an alternative forum, 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 the company, (ii) any action asserting a claim of, or a claim based on, a breach of a fiduciary duty owed by any company director, officer or other employee to the company or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the DGCL, or (iv) any action asserting a claim governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein (the “Delaware Forum Provision”). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Securities Exchange Act of 1934. In addition, our bylaws further provide that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the “Federal Forum Provision”).

Our bylaws also provide that any person or entity purchasing or otherwise acquiring any interest in shares of our Common Stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision.

We recognize that the Delaware Forum Provision and the Federal Forum Provision in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware. Additionally, the Delaware Forum Provision and/or the Federal Forum Provision may limit a stockholder’s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. The Court of Chancery of the State of Delaware or the federal district courts of the United States, as applicable, may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders.

Provisions of our Charter and our Bylaws

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies. Our certificate of incorporation provides for the division of our board of directors 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. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

Meetings of Stockholders. Our certificate of incorporation and bylaws provide that special meetings of stockholders may be called at any time by the board of directors, or by a majority of the members of the board of directors, or by a committee of the board of directors which has been duly designated by the board of directors and whose powers and authority, as provided in a resolution of the board of directors or in these bylaws, include the power to call such meetings, but such special meetings may not be called by any other person or persons.

Advance Notice Requirements Our bylaws provide that stockholders must give timely written notice to bring business before an annual meeting of stockholders or to nominate candidates for election as directors at an annual

[Table of Contents](#)

meeting of stockholders. Generally, to be timely, a stockholder's notice will be required to be delivered to our principal executive offices not later than the 90th day nor earlier than the 120th day prior to the one (1)-year anniversary of the preceding year's annual meeting; provided, however, that if the date of the annual meeting is more than thirty (30) days before or more than sixty (60) days after such anniversary date, notice by the stockholder to be timely must be so delivered, or mailed and received, not later than the 90th day prior to such annual meeting or, if later, the tenth day following the day on which public disclosure of the date of such annual meeting was first made. Our bylaws also specify the form and content of a stockholder's notice.

Amendment to Bylaws. Our board of directors is authorized to amend, alter, change, adopt and repeal our bylaws by a majority vote. Our stockholders also have the power to amend, alter, change, adopt and repeal our bylaws by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote on such an amendment or repeal, voting as a single class; provided, however, that if our board of directors recommends that stockholders approve such amendment or repeal at such meeting of stockholders, such amendment or repeal shall only require the affirmative vote of the majority of outstanding shares entitled to vote on such amendment or repeal, voting together as a single class.

Undesignated Preferred Stock. Our certificate of incorporation provides for 25,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors 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 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 control of us.

Nasdaq Global Select Market Listing

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

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 250 Royall Street, Canton, Massachusetts 02021, and its telephone number is (800) 962-4284.

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior or subordinated. We refer to senior debt securities and subordinated debt securities collectively as debt securities. Each series of debt securities may have different terms. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The senior indenture and form of subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. Together, the senior indenture and the subordinated indenture are referred to as the indentures and, together, the senior trustee and the subordinated trustee are referred to as the trustees. This prospectus briefly outlines some of the provisions of the indentures. The following summary of the material provisions of the indentures is qualified in its entirety by the provisions of the indentures, including definitions of certain terms used in the indentures. Wherever we refer to particular sections or defined terms of the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information. As used in this prospectus, the term “debt securities” includes the debt securities being offered by this prospectus and all other debt securities issued by us under the indentures.

General

The indentures:

- do not limit the amount of debt securities that we may issue;
- allow us to issue debt securities in one or more series;
- do not require us to issue all of the debt securities of a series at the same time; and
- allow us to reopen a series to issue additional debt securities without the consent of the holders of the debt securities of such series.

Unless otherwise provided in the applicable prospectus supplement, the senior debt securities will be unsubordinated obligations and will rank equally with all of our other unsecured and unsubordinated indebtedness. Payments on the subordinated debt securities will be subordinated to the prior payment in full of all of our senior indebtedness, as described under “—Subordination” and in the applicable prospectus supplement.

Each indenture provides that we may, but need not, designate more than one trustee under an indenture. Any trustee under an indenture may resign or be removed and a successor trustee may be appointed to act with respect to the series of debt securities administered by the resigning or removed trustee. If two or more persons are acting as trustee with respect to different series of debt securities, each trustee shall be a trustee of a trust under the applicable indenture separate and apart from the trust administered by any other trustee. Except as otherwise indicated in this prospectus, any action described in this prospectus to be taken by each trustee may be taken by each trustee with respect to, and only with respect to, the one or more series of debt securities for which it is trustee under the applicable indenture.

The prospectus supplement for each offering will provide the following terms, where applicable:

- the title of the debt securities and whether they are senior or subordinated;

Table of Contents

- the aggregate principal amount of the debt securities being offered, the aggregate principal amount of the debt securities outstanding as of the most recent practicable date and any limit on their aggregate principal amount, including the aggregate principal amount of debt securities authorized;
- the price at which the debt securities will be issued, expressed as a percentage of the principal and, if other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof or, if applicable, the portion of the principal amount of such debt securities that is convertible into common stock or other securities of ours or the method by which any such portion shall be determined;
- if convertible, the terms on which such debt securities are convertible, including the initial conversion price or rate and the conversion period and any applicable limitations on the ownership or transferability of common stock or other securities of ours received on conversion;
- the date or dates, or the method for determining the date or dates, on which the principal of the debt securities will be payable;
- the fixed or variable interest rate or rates of the debt securities, or the method by which the interest rate or rates is determined;
- the date or dates, or the method for determining the date or dates, from which interest will accrue;
- the dates on which interest will be payable;
- the record dates for interest payment dates, or the method by which such dates will be determined;
- the persons to whom interest will be payable;
- the place or places where the principal of, and any premium or make-whole amount, and interest on, the debt securities will be payable;
- where the debt securities may be surrendered for registration of transfer or conversion or exchange;
- the times, prices and other terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem, repay or repurchase the debt securities pursuant to any sinking fund or analogous provision or at the option of holders of the debt securities, and the times and prices at which we must redeem, repay or repurchase the debt securities as a result of such obligation;
- the currency or currencies in which the debt securities are denominated and payable if other than United States dollars, which may be a foreign currency or units of two or more foreign currencies or a composite currency or currencies and the terms and conditions relating thereto, and the manner of determining the equivalent of such foreign currency in United States dollars;
- whether the principal of, and any premium or make-whole amount, or interest on, the debt securities of the series are to be payable, at our election or at the election of a holder, in a currency or currencies other than that in which the debt securities are denominated or stated to be payable, and other related terms and conditions;
- whether the debt securities will be in registered form, bearer form, or both, and (i) if in registered form, the person to whom any interest shall be payable, if other than the person in whose name the security is registered at the close of business on the regular record date for such interest, or (ii) if in bearer form, the manner in which, or the person to whom, any interest on the security shall be payable if otherwise than upon presentation and surrender upon maturity;
- any restrictions applicable to the offer, sale or delivery of securities in bearer form and the terms upon which securities in bearer form of the series may be exchanged for securities in registered form of the series and vice versa, if permitted by applicable laws and regulations;
- whether any debt securities of the series are to be issuable initially in temporary global form and whether any debt securities of the series are to be issuable in permanent global form with or without

Table of Contents

coupons and, if so, whether beneficial owners of interests in any such permanent global security may, or shall be required to, exchange their interests for other debt securities of the series, and the manner in which interest shall be paid;

- the applicability, if any, of the defeasance and covenant defeasance provisions described in this prospectus or in the applicable indenture;
- whether and under what circumstances we will pay any additional amounts on the debt securities in respect of any tax, assessment or governmental charge;
- whether and under what circumstances the debt securities being offered are convertible into common stock or other securities of ours, as the case may be, including the conversion price or rate and the manner or calculation thereof;
- the identity of the depositary for securities in registered form, if such series are to be issuable as a global security;
- the name of the applicable trustee and the nature of any material relationship with us or any of our affiliates, and the percentage of debt securities of the class necessary to require the trustee to take action; and
- any other terms of such debt securities not inconsistent with the provisions of the applicable indenture.

We may issue debt securities that provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity of the debt securities. We refer to any such debt securities throughout this prospectus as “original issue discount securities.” The applicable prospectus supplement will describe the United States federal income tax consequences and other relevant considerations applicable to original issue discount securities.

Except as described under “—Merger, Consolidation or Sale of Assets” or as may be set forth in any prospectus supplement, the debt securities will not contain any provisions that (i) would limit our ability to incur indebtedness or (ii) would afford holders of debt securities protection in the event of (a) a highly leveraged or similar transaction involving us, or (b) a change of control or reorganization, restructuring, merger or similar transaction involving us that may adversely affect the holders of the debt securities. In the future, we may enter into transactions, such as the sale of all or substantially all of our assets or a merger or consolidation, that may have an adverse effect on our ability to service our indebtedness, including the debt securities, by, among other things, substantially reducing or eliminating our assets.

Our governing instruments do not define the term “substantially all” as it relates to the sale of assets. Additionally, Delaware cases interpreting the term “substantially all” rely upon the facts and circumstances of each particular case. Consequently, to determine whether a sale of “substantially all” of our assets has occurred, a holder of debt securities must review the financial and other information that we have disclosed to the public.

We will provide you with more information in the applicable prospectus supplement regarding any deletions, modifications, or additions to the events of default or covenants that are described below, including any addition of a covenant or other provision providing event risk or similar protection.

Payment

Unless otherwise provided in the applicable prospectus supplement, the principal of, and any premium or make-whole amount, and interest on, any series of the debt securities will be payable by mailing a check to the address of the person entitled to it as it appears in the applicable register for the debt securities or by wire transfer of funds to that person at an account maintained within the United States.

All monies that we pay to a paying agent or a trustee for the payment of the principal of, and any premium or make-whole amount, or interest on, any debt security will be repaid to us if unclaimed at the end of two years

[Table of Contents](#)

after the obligation underlying payment becomes due and payable. After funds have been returned to us, the holder of the debt security may look only to us for payment, without payment of interest for the period which we hold the funds.

Denomination, Interest, Registration and Transfer

Unless otherwise provided in the applicable prospectus supplement, the debt securities of any series will be issuable in denominations of \$1,000 and integral multiples of \$1,000.

Interest on the debt securities shall be computed on the basis of a 360-day year composed of twelve 30-day months.

Subject to the limitations imposed upon debt securities that are evidenced by a computerized entry in the records of a depository company rather than by physical delivery of a note, a holder of debt securities of any series may:

- exchange them for any authorized denomination of other debt securities of the same series and of a like aggregate principal amount and kind upon surrender of such debt securities at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose; and
- surrender them for registration of transfer or exchange at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose.

Every debt security surrendered for registration of transfer or exchange must be accompanied by a written instrument of transfer satisfactory to the applicable trustee or transfer agent. Payment of a service charge will not be required for any registration of transfer or exchange of any debt securities, but we or the trustee may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection therewith. We may at any time designate additional transfer agents for any series of debt securities.

Neither we, nor any trustee, will be required to:

- issue, register the transfer of or exchange debt securities of any series during a period beginning at the opening of business 15 days before the day that the notice of redemption of any debt securities selected for redemption is mailed and ending at the close of business on the day of such mailing;
- register the transfer of or exchange any debt security, or portion thereof, so selected for redemption, in whole or in part, except the unredeemed portion of any debt security being redeemed in part; and
- issue, register the transfer of or exchange any debt security that has been surrendered for repayment at the option of the holder, except the portion, if any, of such debt security not to be so repaid.

Merger, Consolidation or Sale of Assets

The indentures provide that we may, without the consent of the holders of any outstanding debt securities, (i) consolidate with, (ii) sell, lease or convey all or substantially all of our assets to, or (iii) merge with or into, any other entity provided that:

- either we are the continuing entity, or the successor entity, if other than us, assumes the obligations (a) to pay the principal of, and any premium or make-whole amount, and interest on, all of the debt securities and (b) to duly perform and observe all of the covenants and conditions contained in the applicable indenture;
- after giving effect to the transaction, there is no event of default under the applicable indentures and no event which, after notice or the lapse of time, or both, would become such an event of default, occurs and continues; and
- an officers' certificate and legal opinion covering such conditions are delivered to each applicable trustee.

Events of Default, Notice and Waiver

Unless the applicable prospectus supplement states otherwise, when we refer to “events of default” as defined in the indentures with respect to any series of debt securities, we mean:

- default in the payment of any installment of interest on any debt security of such series continuing for 90 days unless such date has been extended or deferred;
- default in the payment of principal of, or any premium or make-whole amount on, any debt security of such series when due and payable unless such date has been extended or deferred;
- default in the performance or breach of any covenant or warranty in the debt securities or in the indenture by us continuing for 90 days after written notice described below;
- bankruptcy, insolvency or reorganization, or court appointment of a receiver, liquidator or trustee of us; and
- any other event of default provided with respect to a particular series of debt securities.

If an event of default occurs and is continuing with respect to debt securities of any series outstanding, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the principal amount of all the debt securities of that series to be due and payable. If the debt securities of that series are original issue discount securities or indexed securities, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the portion of the principal amount as may be specified in the terms thereof to be due and payable. However, at any time after such a declaration of acceleration has been made, but before a judgment or decree for payment of the money due has been obtained by the applicable trustee, the holders of at least a majority in principal amount of outstanding debt securities of such series or of all debt securities then outstanding under the applicable indenture may rescind and annul such declaration and its consequences if:

- we have deposited with the applicable trustee all required payments of the principal, any premium or make-whole amount, interest and, to the extent permitted by law, interest on overdue installment of interest, plus applicable fees, expenses, disbursements and advances of the applicable trustee; and
- all events of default, other than the non-payment of accelerated principal, or a specified portion thereof, and any premium or make-whole amount, have been cured or waived.

The indentures require each trustee to give notice to the holders of debt securities within the later of 90 days after an event of default and 30 days after the event of default is actually known to a responsible officer of such trustee, unless such default has been cured or waived. However, the trustee may withhold notice if specified persons of such trustee consider such withholding to be in the interest of the holders of debt securities.

The indentures provide that holders of debt securities of any series may not institute any proceedings, judicial or otherwise, with respect to such indenture or for any remedy under the indenture, unless the trustee fails to act for a period of 90 days after the trustee has received a written request to institute proceedings in respect of an event of default from the holders of 25% or more in principal amount of the outstanding debt securities of such series, as well as an offer of indemnity reasonably satisfactory to the trustee. However, this provision will not prevent any holder of debt securities from instituting suit for the enforcement of payment of the principal of, and any premium or make-whole amount, and interest on, such debt securities at the respective due dates thereof.

The indentures provide that, subject to provisions in each indenture relating to its duties in the case of a default, a trustee has no obligation to exercise any of its rights or powers at the request or direction of any holders of any series of debt securities then outstanding under the indenture, unless the holders have offered to the trustee reasonable security or indemnity. The holders of at least a majority in principal amount of the outstanding debt securities of any series or of all debt securities then outstanding under an indenture shall have the right to direct

Table of Contents

the time, method and place of conducting any proceeding for any remedy available to the applicable trustee, or of exercising any trust or power conferred upon such trustee. However, a trustee may refuse to follow any direction which:

- is in conflict with any law or the applicable indenture;
- may involve the trustee in personal liability; or
- may be unduly prejudicial to the holders of debt securities of the series not joining the proceeding.

Within 120 days after the close of each fiscal year, we will be required to deliver to each trustee a certificate, signed by one of our several specified officers, stating whether or not that officer has knowledge of any default under the applicable indenture. If the officer has knowledge of any default, the notice must specify the nature and status of the default.

Modification of the Indentures

The indentures provide that modifications and amendments may be made only with the consent of the affected holders of a majority in principal amount of all outstanding debt securities issued under that indenture:

We and our respective trustee may make modifications and amendments of an indenture without the consent of any holder of debt securities for any of the following purposes:

- to evidence the succession of another person to us as obligor under such indenture;
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants for the benefit of the holders of all or any series of debt securities or to surrender any right or power conferred upon us in such indenture;
- to add events of default for the benefit of the holders of all or any series of debt securities;
- 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;
- to make any change that does not adversely affect the rights of any securityholder in any material respect;
- to establish the form or terms of debt securities of any series;
- to provide for the acceptance of appointment by a successor trustee or facilitate the administration of the trusts under an indenture by more than one trustee; or
- to cure any ambiguity, defect or inconsistency in an indenture, provided that such action shall not adversely affect the interests of holders of debt securities of any series issued under such indenture.

Voting

The indentures provide that in determining whether the holders of the requisite principal amount of outstanding debt securities of a series have given any request, demand, authorization, direction, notice, consent or waiver under the indentures or whether a quorum is present at a meeting of holders of debt securities, the principal amount of an original issue discount security that shall be deemed to be outstanding shall be the amount of the principal thereof that would be due and payable as of the date of such determination upon declaration of acceleration of the maturity thereof.

Subordination

Unless otherwise provided in the applicable prospectus supplement, subordinated debt securities will be subject to the following subordination provisions.

Table of Contents

Upon any distribution to our creditors in a liquidation, dissolution or reorganization, the payment of the principal of and interest on any subordinated debt securities will be subordinated to the extent provided in the applicable indenture in right of payment to the prior payment in full of all senior debt. However, our obligation to make payments of the principal of and interest on such subordinated debt securities otherwise will not be affected. No payment of principal or interest will be permitted to be made on subordinated debt securities at any time if a default on senior debt exists that permits the holders of such senior debt to accelerate its maturity and the default is the subject of judicial proceedings or we receive notice of the default. After all senior debt is paid in full and until the subordinated debt securities are paid in full, holders of subordinated debt securities will be subrogated to the rights of holders of senior debt to the extent that distributions otherwise payable to holders of subordinated debt securities have been applied to the payment of senior debt. The subordinated indenture will not restrict the amount of senior debt or other indebtedness of ours. As a result of these subordination provisions, in the event of a distribution of assets upon insolvency, holders of subordinated debt securities may recover less, ratably, than our general creditors.

No restrictions will be included in any indenture relating to subordinated debt securities upon the creation of additional senior debt.

If this prospectus is being delivered in connection with the offering of a series of subordinated debt securities, the accompanying prospectus supplement or the information incorporated in this prospectus by reference will set forth the approximate amount of senior debt outstanding as of the end of our most recent fiscal quarter.

Discharge, Defeasance and Covenant Defeasance

Unless otherwise provided in the applicable prospectus supplement, the indentures allow us to discharge our obligations to holders of any series of debt securities issued under any indenture when:

- either (i) all securities of such series have already been delivered to the applicable trustee for cancellation; or (ii) all securities of such series have not already been delivered to the applicable trustee for cancellation but (a) have become due and payable, (b) will become due and payable within one year, or (c) if redeemable at our option, are to be redeemed within one year, and we have irrevocably deposited with the applicable trustee, in trust, funds in such currency or currencies, currency unit or units or composite currency or currencies in which such debt securities are payable, an amount sufficient to pay the entire indebtedness on such debt securities in respect of principal and any premium or make-whole amount, and interest to the date of such deposit if such debt securities have become due and payable or, if they have not, to the stated maturity or redemption date;
- we have paid or caused to be paid all other sums payable; and
- an officers' certificate and an opinion of counsel stating the conditions to discharging the debt securities have been satisfied have been delivered to the trustee.

Unless otherwise provided in the applicable prospectus supplement, the indentures provide that, upon our irrevocable deposit with the applicable trustee, in trust, of an amount, in such currency or currencies, currency unit or units or composite currency or currencies in which such debt securities are payable at stated maturity, or government obligations, or both, applicable to such debt securities, which through the scheduled payment of principal and interest in accordance with their terms will provide money in an amount sufficient to pay the principal of, and any premium or make-whole amount, and interest on, such debt securities, and any mandatory sinking fund or analogous payments thereon, on the scheduled due dates therefor, the issuing company shall be released from its obligations with respect to such debt securities under the applicable indenture or, if provided in the applicable prospectus supplement, its obligations with respect to any other covenant, and any omission to comply with such obligations shall not constitute an event of default with respect to such debt securities.

Notwithstanding the above, we may not elect to defease and be discharged from the obligation to pay any additional amounts upon the occurrence of particular events of tax, assessment or governmental charge with

[Table of Contents](#)

respect to payments on such debt securities and the obligations to register the transfer or exchange of such debt securities, to replace temporary or mutilated, destroyed, lost or stolen debt securities, to maintain an office or agency in respect of such debt securities, or to hold monies for payment in trust.

The applicable prospectus supplement may further describe the provisions, if any, permitting such defeasance or covenant defeasance, including any modifications to the provisions described above, with respect to the debt securities of or within a particular series.

Conversion Rights

The terms and conditions, if any, upon which the debt securities are convertible into common stock or other securities of ours will be set forth in the applicable prospectus supplement. The terms will include whether the debt securities are convertible into shares of common stock or other securities of ours, the conversion price, or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at the issuing company's option or the option of the holders, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption of the debt securities and any restrictions on conversion.

No Recourse

No recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the debt securities, waives and releases all such liability.

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.

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 will 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;
- federal income tax consequences 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 United States 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 applicable prospectus supplements.

Issuance in Series

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.

Table of Contents

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, including modifying 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

Table of Contents

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.

Governing Law

The unit agreements and the units will be governed by Delaware law.

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 offered through this prospectus and any accompanying prospectus supplement, if required, in any of the following ways: (i) to or through underwriters or dealers, (ii) directly to purchasers, including our affiliates, (iii) through agents, or (iv) through a combination of any of these methods. The securities may be distributed at a fixed price or prices, which may be changed, market prices prevailing at the time of sale, prices related to the prevailing market prices, or negotiated prices, either:

- on or through the facilities of The Nasdaq Global Select Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or
- to or through a market maker otherwise than on The Nasdaq Global Select Market or such other securities exchanges or quotation or trading services.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. In the prospectus supplement relating to such offering, we will name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay to any such agent. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are used in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement, sales agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

In connection with the offering of securities, we may grant to the underwriters an option to purchase additional securities with an additional underwriting commission, as may be set forth in the accompanying prospectus supplement. If we grant any such option, the terms of such option will be set forth in the prospectus supplement for such securities.

If a dealer is used in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer, who may be deemed to be an “underwriter” as that term is defined in the Securities Act, may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

Table of Contents

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Offered securities may also be offered and sold, if so indicated in the prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreement, if any, with us and its compensation will be described in the applicable prospectus supplement. Remarketing firms may be deemed to be underwriters in connection with their remarketing of offered securities.

Certain agents, underwriters and dealers, and their associates and affiliates, may be customers of, have borrowing relationships with, engage in other transactions with, or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may over allot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities 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

[Table of Contents](#)

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.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading market for any of the 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.

The anticipated date of delivery of offered securities will be set forth in the applicable prospectus supplement relating to each offer.

LEGAL MATTERS

Certain legal matters in connection with this offering will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Any underwriters will also be advised about the validity of the securities and other legal matters by their own counsel, which will be named in the prospectus supplement.

EXPERTS

The consolidated financial statements of Xeris Pharmaceuticals, Inc. as of December 31, 2020 and 2019, and for each of the years in the two-year period ended December 31, 2020, 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.

The consolidated financial statements of Strongbridge Biopharma plc at December 31, 2020 and 2019, and for each of the three years in the period ended December 31, 2020, incorporated by reference in this Prospectus and Registration Statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon incorporated elsewhere herein, and are incorporated herein in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. These documents may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (www.sec.gov). Copies of certain information filed by us with the SEC are also available on our website at <http://www.xerispharma.com>. The information contained on our website is not incorporated by reference into this prospectus and, therefore, is not part of this prospectus or any accompanying prospectus supplement.

This prospectus is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with SEC rules and regulations. For more detail about us and any securities that may be offered by this prospectus, you may examine the registration statement on Form S-3 and the exhibits filed with it at the locations listed in the previous paragraph. Please be aware that statements in this prospectus referring to a contract or other document are summaries and you should refer to the exhibits that are part of the registration statement for a copy of the contract or document.

INCORPORATION 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 considered to be a part of this prospectus, and the information that we file later with the SEC will automatically update and, where applicable, supersede the information already incorporated by reference. We incorporate by reference the documents listed below that we filed with the SEC:

- our Quarterly Report on [Form 10-Q](#) for the quarter ended September 30, 2021 filed with the SEC on November 10, 2021;
- our Current Reports on Form 8-K filed with the SEC [October 5, 2021](#), [October 5, 2021](#), [October 8, 2021](#), [January 3, 2022](#) and [January 28, 2022](#);
- the description of our common stock, par value \$0.0001 per share, contained in our Current Report on [Form 8-K](#) filed with the SEC on October 5, 2021;
- Xeris Pharmaceuticals, Inc.'s Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2020 filed with the SEC on March 9, 2021;
- the information specifically incorporated by reference into Xeris Pharmaceuticals, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2020 from Xeris Pharmaceuticals, Inc.'s definitive proxy statement on [Schedule 14A](#) (other than information furnished rather than filed) filed with the SEC on April 29, 2021;
- Xeris Pharmaceuticals, Inc.'s Quarterly Reports on Form 10-Q for the quarter ended March 31, 2021 filed with the SEC on [May 13, 2021](#), and for the quarter ended June 30, 2021 filed with the SEC on [August 5, 2021](#);
- Xeris Pharmaceuticals, Inc.'s Current Reports on Form 8-K filed with the SEC on [March 11, 2021](#) (only with respect to Item 5.02), [May 6, 2021](#), [May 24, 2021](#), [June 8, 2021](#), [July 19, 2021](#), [July 29, 2021](#) (only with respect to Item 5.02), [July 30, 2021](#), [September 14, 2021](#), [October 5, 2021](#) and [October 5, 2021](#);
- Strongbridge's Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2020 filed with the SEC on March 3, 2021;
- Strongbridge's Quarterly Reports on Form 10-Q for the quarter ended March 31, 2021 filed with the SEC on [May 12, 2021](#), and for the quarter ended June 30, 2021 filed with the SEC on [August 5, 2021](#);
- Strongbridge's Current Reports on Form 8-K filed with the SEC on [February 16, 2021](#), [March 2, 2021](#), [March 26, 2021](#), [May 13, 2021](#), [May 14, 2021](#), [May 24, 2021](#), [July 7, 2021](#), [July 26, 2021](#), [August 30, 2021](#), [September 8, 2021](#) and [October 5, 2021](#); and
- all future documents filed by us with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, including all filings made after the date of the filing of this registration statement and prior to the effectiveness of this registration statement, prior to the termination of the offering of the underlying securities; provided, however, that we are not incorporating by reference any additional documents or information furnished and not filed with the SEC.

Upon request, either orally or in writing, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, a copy of the documents incorporated by reference into this prospectus but not delivered with the prospectus. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing us at the following address: Xeris Biopharma Holdings, Inc., 180 N. LaSalle Street, Suite 1600, Chicago, IL 60601.

[Table of Contents](#)

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.



Up to \$75,000,000

Common Stock

Prospectus Supplement

Jefferies

May 11, 2022
