

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

XERIS BIOPHARMA HOLDINGS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

87-1082097
(I.R.S. Employer
Identification Number)

**180 N. LaSalle Street, Suite 1600
Chicago, Illinois 60601
(844) 445-5704**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Paul R. Edick
Chairman and Chief Executive Officer
Xeris Biopharma Holdings, Inc.
180 N. LaSalle Street, Suite 1600
Chicago, IL 60601
(844) 445-5704**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

**With copies to:
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Stephanie A. Richards, Esq.
Goodwin Procter LLP
100 Northern Avenue
Boston, Massachusetts 02210
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Approximate date of commencement of proposed sale to the public: From time to time after this Registration Statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

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

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

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered	Proposed Maximum Offering Price Per Share ⁽²⁾	Proposed Maximum Aggregate Offering Price ⁽²⁾	Amount of Registration Fee ⁽⁴⁾
Common Stock, par value \$0.0001 per share ⁽¹⁾	10,238,908	\$2.09	\$21,399,318	\$1,983.72
Common Stock underlying Warrants ⁽³⁾	5,119,454	\$2.09	\$10,699,659	\$991.86
Total	15,358,362		\$32,098,977	\$2,975.58

- (1) Consists of an aggregate of 10,238,908 shares of the registrant's common stock, par value \$0.0001 per share ("Common Stock"), all of which were acquired by the selling stockholder in a private placement. Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), this registration statement also registers an indeterminate number of shares of the registrant's Common Stock which may become issuable by reason of any stock dividend, stock split or other similar transaction effected without the receipt of consideration that results in an increase in the number of the outstanding shares of the registrant's Common Stock.
- (2) Estimated solely for the purpose of calculating the registration fee in accordance with Rule 457(c) under the Securities Act. The price per share and aggregate offering price are based on the average of the high and low sales price of the registrant's Common Stock reported by the Nasdaq Global Select Market on January 25, 2022.
- (3) Represents the maximum number of shares of Common Stock issuable upon exercise of the warrants as described herein.
- (4) The registration fee has been calculated in accordance with Rule 457(o) under the Securities Act.

THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(a) OF THE SECURITIES ACT OF 1933, AS AMENDED, OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE SECURITIES AND EXCHANGE COMMISSION ACTING PURSUANT TO SAID SECTION 8(a) MAY DETERMINE.

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

SUBJECT TO COMPLETION, DATED JANUARY 28, 2022

PROSPECTUS

15,358,362 Shares



Common Stock

This prospectus relates to the possible resale, from time to time, by the selling stockholder identified in this prospectus of up to (i) 10,238,908 shares of our common stock, par value \$0.0001 per share (the "Common Stock"), initially issued in a private placement (the "Private Placement"), pursuant to a securities purchase agreement, dated as of January 2, 2022, by and between us and the selling stockholder (the "Securities Purchase Agreement") and (ii) 5,119,454 shares of Common Stock underlying warrants issued in the Private Placement.

The selling stockholders may offer the shares from time to time as the selling stockholder may determine through public or private transactions or through other means described in the section entitled "Plan of Distribution" or a supplement to this prospectus. The selling stockholder may also sell shares under Rule 144 under the Securities Act of 1933, as amended, if available, rather than under this prospectus.

The registration of these shares does not necessarily mean that any holders will sell any of their shares or exercise their warrants. We are not offering for sale any shares of our Common Stock pursuant to this prospectus. We will not receive any proceeds from the sale of these shares. We will, however, receive cash proceeds equal to the total exercise price of warrants that are exercised for cash.

We are paying the cost of registering the shares of Common Stock covered by this prospectus as well as various related expenses. The selling stockholder is responsible for all selling commissions, transfer taxes and other costs related to the offer and sale of their shares.

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.

We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. You should read the entire prospectus and any amendments or supplements carefully before you make your investment decision.

We are an "emerging growth company" as defined under the federal securities laws and, as such, are eligible for reduced public company reporting requirements. See "Prospectus Summary—Emerging Growth Company".

Investing in our Common Stock 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 January 28, 2022.

TABLE OF CONTENTS

	<u>Page</u>
About this Prospectus	ii
Risk Factors	1
Cautionary Statement Regarding Forward-Looking Statements	2
Prospectus Summary	4
Use of Proceeds	9
Determination of Offering Price	10
Description of Capital Stock	11
Selling Stockholder	16
Plan of Distribution	17
Legal Matters	19
Experts	19
Where You Can Find More Information	19
Incorporation by Reference	20

ABOUT THIS PROSPECTUS

We have not, and the selling stockholder has not, authorized anyone to give you any information other than the information contained in this prospectus, the information incorporated by reference herein, any applicable prospectus supplement or any free writing prospectus filed with the Securities and Exchange Commission (the “SEC”). We and the selling stockholder take no responsibility for, and can provide no assurances as to the reliability of, any other information that others may give you. Neither we nor the selling stockholder have authorized anyone to provide you with additional information or information different from that contained in this prospectus filed with the SEC. The selling stockholder is offering to sell, and seeking offers to buy, shares of our Common Stock only in jurisdictions where offers and sales are permitted. You should assume that the information appearing in this prospectus, the applicable prospectus supplement and any related free writing prospectus is accurate only as of the respective dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

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.

For Non-U.S. investors

Neither we nor the selling stockholder have done anything that would permit this offering or possession or distribution of this prospectus, any prospectus supplement or free writing prospectus filed with the SEC, in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus, any prospectus supplement or free writing prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of Common Stock and the distribution of this prospectus, any prospectus supplement or free writing prospectus outside the United States.

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;
- 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 certain information about us, this offering and selected information contained elsewhere in this prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in the securities covered by this prospectus. For a more complete understanding of the Company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus, any related prospectus supplement and any related free writing prospectus, including the information set forth in the section titled "Risk Factors" in this prospectus, any related prospectus supplement and any related free writing prospectus in their entirety before making an investment decision.

About the Company

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.

Private Placement

On January 2, 2022, we entered into the Securities Purchase Agreement with the selling stockholder named in this prospectus, pursuant to which we sold and issued (i) 10,238,908 shares of our Common Stock at a purchase price of \$2.93 per share and (ii) warrants to purchase 5,119,454 shares of Common Stock at an exercise price of \$3.223 per share. The total purchase price paid by the selling stockholder at closing was approximately \$30.0 million and the sale of the warrants would result in aggregate gross proceeds of approximately \$16.5 million if fully exercised.

Under the terms of the Securities Purchase Agreement, we agreed to prepare and file, within 30 days after the closing of the Private Placement, one or more registration statements with the SEC to register for resale the shares of our Common Stock and warrants issued under the Securities Purchase Agreement, and generally to cause the applicable registration statement(s) to become effective as soon as practicable and in any event within 150 days from the filing of the applicable registration statement with the SEC.

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;
- 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.

THE OFFERING

Common stock offered by selling stockholder	15,358,362 shares
Common stock outstanding as of December, 31, 2021	124,852,815 shares
Use of proceeds	We will not receive any proceeds from the sale of the shares of Common Stock offered by the selling stockholder.
Offering price	The selling stockholder will offer the shares of Common Stock offered by this prospectus at the prevailing market prices or privately negotiated price.
Risk factors	You should read the "Risk Factors" section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our Common Stock.

All information in this prospectus related to the number of shares of our Common Stock to be outstanding immediately after this offering is based on 126,857,856 shares of our Common Stock outstanding as of December 31, 2021, which includes 2,005,041 shares of unvested restricted stock and excludes as of that date, unless otherwise indicated:

- 1,795,607 shares 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 \$4.10 per share;
- 2,939,335 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 \$6.28 per share;
- 187,848 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 \$6.30 per share;
- 4,581,563 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 \$5.07 per share;
- 998,069 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 \$5.66 per share;
- 648,649 shares of Common Stock issuable upon exercise of options issued under Strongbridge Biopharma plc's Non-Employee Director Equity Compensation Plan at a weighted-average exercise price of \$9.65 per share;
- 211,265 shares of Common Stock issuable upon exercise of options issued under Strongbridge Biopharma plc's Written Stock Option Agreements (outside of the 2015 Plan and the Non-Employee Director Plan) at a weighted-average exercise price of \$21.06 per share;
- 6,373,452 shares of Common Stock issuable upon the exercise of warrants to purchase Common Stock at a weighted-average exercise price of \$4.90 per share;
- 1,569,336 shares of Common Stock reserved for issuance under Xeris Pharmaceuticals, Inc.'s 2018 Stock Option and Incentive Plan;
- 477,727 shares of Common Stock reserved for future issuance under Xeris Pharmaceuticals, Inc.'s 2018 Employee Stock Purchase Plan;
- 197,621 shares of Common Stock reserved for future issuance under Xeris Pharmaceuticals, Inc.'s Inducement Equity Plan;

- 1,830,653 shares of Common Stock reserved for future issuance under Strongbridge Biopharma plc's 2015 Equity Compensation Plan; and
- 1,068,378 shares of Common Stock reserved for future issuance under Strongbridge Biopharma plc's 2017 Inducement Plan.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale of the shares offered by this prospectus. The selling stockholder will receive all of the proceeds from this offering.

DETERMINATION OF OFFERING PRICE

The selling stockholder will offer the shares of Common Stock offered by this prospectus at the prevailing market prices or privately negotiated price. The offering price of our Common Stock does not necessarily bear any relationship to our book value, assets, past operating results, financial condition or any other established criteria of value. Our Common Stock might not trade at market prices in excess of the offering price as prices for Common Stock in any public market will be determined in the marketplace and may be influenced by many factors, including the depth and liquidity. See "Plan of Distribution" above for more information.

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 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 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.

SELLING STOCKHOLDER

The table below sets forth information concerning the resale of our shares by the selling stockholder. Armistice Capital Master Fund Ltd. (“Armistice”) acquired its securities being registered hereunder in the Private Placement. The total number of shares of Common Stock sold under this prospectus may be adjusted to reflect adjustments due to stock dividends, stock distributions, splits, combinations or recapitalizations with regard to the Common Stock and warrants. Unless otherwise stated below in the footnotes, to our knowledge, neither the selling stockholder, nor any affiliate of such stockholder: (i) has held any position or office with us during the three years prior to the date of this prospectus; or (ii) is a broker-dealer, or an affiliate of a broker-dealer.

Armistice may exercise its warrants at any time in its sole discretion. Set forth below is the name of the selling stockholder and the amount and percentage of Common Stock owned by such selling stockholder (including shares which such stockholder has the right to acquire within 60 days, including upon exercise of warrants) prior to the offering, the shares to be sold in the offering, and the percentage of Common Stock to be owned by the selling stockholder (including shares which such stockholder has the right to acquire within 60 days, including upon exercise of warrants) after the offering assuming all shares are sold. The footnotes provide information about persons who have voting and dispositive power with respect to shares held by the selling stockholder.

We have registered up to 15,358,362 shares of our Common Stock, including 5,119,454 shares of Common Stock underlying warrants to purchase Common Stock issued to Armistice in connection with the Private Placement. See “Prospectus Summary” above.

The following table is based on information provided to us by the selling stockholder and is as of January 25, 2022. The selling stockholder may sell all or some of the shares of Common Stock it is offering, and may sell, unless indicated otherwise in the footnotes below, shares of our Common Stock otherwise than pursuant to this prospectus. The tables below assume that the selling stockholder sells all of the shares offered by it in offerings pursuant to this prospectus, and does not acquire any additional shares. We are unable to determine the exact number of shares that will actually be sold or when or if these sales will occur.

Name of Selling Stockholder	Shares Owned Pre-Offering	Common Stock Being Offered in this Offering ⁽¹⁾⁽³⁾	Shares Owned Post-Offering(%) ⁽¹⁾⁽²⁾	
			Amount	Percentage
Armistice Capital Master Fund Ltd. ⁽³⁾	15,358,362	15,358,362	—	—

(1) Applicable percentage ownership is based on 135,112,224 shares of our Common Stock outstanding as of January 25, 2022.

(2) Assumes the sale of all shares offered in this prospectus without regard to the beneficial ownership limitation applicable to the warrants, as described in footnote 3.

(3) Consists of 10,238,908 shares of Common Stock and 5,119,454 shares of Common Stock underlying warrants issued in the Private Placement, which securities are directly held by Armistice Capital Master Fund Ltd., a Cayman Islands exempted company (the “Master Fund”), and may be deemed to be indirectly beneficially owned by: (i) Armistice Capital, LLC (“Armistice Capital”), as the investment manager of the Master Fund, and (ii) Steven Boyd, as the Managing Member of Armistice Capital. Armistice Capital and Steven Boyd disclaim beneficial ownership of the securities except to the extent of their respective pecuniary interests therein. The 5,119,454 shares of Common Stock underlying the warrants are subject to a beneficial ownership limitation that prevents the Master Fund from exercising any portion of the warrants if such exercise would result in the Master Fund owning greater than 4.99% of our outstanding Common Stock following such exercise. The address of the Master Fund is c/o Armistice Capital, LLC, 510 Madison Avenue, 7th Floor, New York, New York 10022.

PLAN OF DISTRIBUTION

The selling stockholder, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling shares of Common Stock or interests in shares of Common Stock received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of Common Stock or interests in shares of Common Stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling stockholder may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholder to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The selling stockholder may, from time to time, pledge or grant a security interest in some or all of the shares of Common Stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of Common Stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholder also may transfer the shares of Common Stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our Common Stock or interests therein, the selling stockholder may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the Common Stock in the course of hedging the positions they assume. The selling stockholder may also sell shares of our Common Stock short and deliver these securities to close out their short positions, or loan or pledge the Common Stock to broker-dealers that in turn may sell these securities. The selling stockholder may also enter into options or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling stockholder from the sale of the Common Stock offered by them will be the purchase price of the Common Stock less discounts or commissions, if any. The selling stockholder reserves the

right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of Common Stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling stockholder and any underwriters, broker-dealers or agents that are involved in selling the Common Stock or interests therein may be deemed to be “underwriters” within the meaning of Section 2(a)(11) of the Securities Act. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. The selling stockholder in the Private Placement has informed us that it does not have any agreement or understanding, directly or indirectly, with any person to distribute the Common Stock. If the selling stockholder is deemed to be an “underwriter” within the meaning of the Securities Act, it will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the shares of our Common Stock to be sold, the name of the selling stockholder, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to this registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the Common Stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the Common Stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholder that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholder and their affiliates. In addition, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholder for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholder may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling stockholder against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling stockholder to keep this registration statement of which this prospectus constitutes a part effective for five years from the date it is declared effective by the SEC or until the date on which all of the shares required to be registered by us have been transferred other than to certain enumerated permitted assignees under the Registration Rights Agreement.

LEGAL MATTERS

The validity of the shares of our Common Stock being offered by this prospectus will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts.

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.

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.

15,358,362 Shares



Common Stock

PROSPECTUS

, 2022

We have not authorized any dealer, salesperson or other person to give any information or represent anything not contained in this prospectus. You must not rely on any unauthorized information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not offer to sell any securities in any jurisdiction where it is unlawful. Neither the delivery of this prospectus, nor any sale made hereunder, shall create any implication that the information in this prospectus is correct after the date hereof.

PART II—INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The expenses payable by Xeris Biopharma Holdings, Inc. (the “Registrant” or the “Company”) in connection with the issuance and distribution of the securities being registered (other than underwriting discounts and commissions, if any) are set forth below. Each item listed is estimated, except for the Securities and Exchange Commission (the “SEC”) registration fee.

SEC registration fee	\$	2,975.58	*
FINRA filing fee			*
Legal fees and expenses			*
Accounting fees and expenses			*
Printing fees and expenses			*
Transfer agent and trustee fees			*
Miscellaneous			*
Total	\$		*

* Estimated expenses not presently known

Item 15. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law (the “DGCL”) authorizes a corporation to indemnify its directors and officers against liabilities arising out of actions, suits and proceedings to which they are made or threatened to be made a party by reason of the fact that they have served or are currently serving as a director or officer to a corporation. The indemnity may cover expenses (including attorneys’ fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the director or officer in connection with any such action, suit or proceeding. Section 145 permits corporations to pay expenses (including attorneys’ fees) incurred by directors and officers in advance of the final disposition of such action, suit or proceeding. In addition, Section 145 provides that a corporation has the power to purchase and maintain insurance on behalf of its directors and officers against any liability asserted against them and incurred by them in their capacity as a director or officer, or arising out of their status as such, whether or not the corporation would have the power to indemnify the director or officer against such liability under Section 145.

We have adopted provisions in our amended and restated certificate of incorporation and amended and restated by-laws that limit or eliminate the personal liability of our directors to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director’s duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any unlawful payments related to dividends or unlawful stock purchases, redemptions or other distributions; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not alter director liability under the federal securities laws and do not affect the availability of equitable remedies such as an injunction or rescission.

In addition, our amended and restated by-laws provide that:

- we will indemnify our directors, officers and, in the discretion of our board of directors, certain employees to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended; and

- we will advance reasonable expenses, including attorneys' fees, to our directors and, in the discretion of our board of directors, to our officers and certain employees, in connection with legal proceedings relating to their service for or on behalf of us, subject to limited exceptions.

We have entered into indemnification agreements with each of our directors and with certain of our executive officers. These agreements provide that we will indemnify each of our directors, certain of our executive officers and, at times, their affiliates to the fullest extent permitted by Delaware law. We will advance expenses, including attorneys' fees (but excluding judgments, fines and settlement amounts), to each indemnified director, executive officer or affiliate in connection with any proceeding in which indemnification is available and we will indemnify our directors and officers for any action or proceeding arising out of that person's services as a director or officer brought on behalf of us and/or in furtherance of our rights. Additionally, each of our directors may have certain rights to indemnification, advancement of expenses and/or insurance provided by their affiliates, which indemnification relates to and might apply to the same proceedings arising out of such director's services as a director referenced herein. Nonetheless, we have agreed in the indemnification agreements that our obligations to those same directors are primary and any obligation of the affiliates of those directors to advance expenses or to provide indemnification for the expenses or liabilities incurred by those directors are secondary.

We also maintain general liability insurance which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the Securities Act of 1933, as amended.

Item 16. Exhibits

A list of all exhibits filed with this registration statement on Form S-3 is set forth on the Exhibit Index and is incorporated herein by reference.

Item 17. Undertakings

The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
 - (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement; provided, however, that paragraphs (1)(i), (1)(ii) and (1)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement;

- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof;
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering;
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
 - (i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof; provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date;
- (5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
 - (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
 - (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
 - (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
 - (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser;
- (6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof;

- (7) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue;
- (8) That, for purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective;
- (9) That, for the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof; and
- (10) To file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act of 1939 in accordance with the rules and regulations prescribed by the Securities and Exchange Commission under Section 305(b)(2) of the Trust Indenture Act of 1939.

EXHIBIT INDEX

Exhibit No.	Description
2.1	Form of Securities Purchase Agreement between the Registrant and Armistice Capital Master Fund Ltd. dated as of January 2, 2022 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-40880) filed with the Securities and Exchange Commission on January 3, 2022)
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K12B (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
3.2	Amended and Restated By-laws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K12B (File No. 001-40880) filed with the Securities and Exchange Commission on October 5, 2021)
4.1*	Form of Specimen Common Stock Certificate
4.2	Second Amended and Restated Investors' Rights Agreement by and among Xeris Pharmaceuticals, Inc. and certain of its stockholders, dated December 31, 2015 (incorporated by reference to Exhibit 4.1 to the Xeris Pharmaceuticals, Inc. Registration Statement on Form S-1 (File No. 333-225191) filed with the Securities and Exchange Commission on May 24, 2018)
4.3	Form of Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-40880) filed with the Securities and Exchange Commission on January 3, 2022)
4.4	Form of Registration Rights Agreement between the Registrant and Armistice Capital Master Fund Ltd. dated as of January 2, 2022 (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-40880) filed with the Securities and Exchange Commission on January 3, 2022)
5.1*	Opinion of Goodwin Procter LLP
23.1*	Consent of KPMG LLP, independent registered public accounting firm for Xeris Pharmaceuticals, Inc.
23.2*	Consent of Ernst & Young LLP, independent registered public accounting firm for Strongbridge Biopharma plc
23.3*	Consent of Goodwin Procter LLP (included in Exhibit 5.1)
24.1*	Power of Attorney (included on the signature page to this registration statement)

* Filed herewith

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Chicago, State of Illinois, on this 28th day of January, 2022.

XERIS BIOPHARMA HOLDINGS, INC.

By: /s/ Paul R. Edick
Paul R. Edick
Chief Executive Officer and Chairman

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below hereby severally constitutes and appoints each of Paul Edick and Steven Pieper, and each of them singly, as such person's true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for such person and in such person's name, place and stead, in any and all capacities, to sign any or all amendments (including, without limitation, post-effective amendments) to this registration statement (or any registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933), and to file the same, with all exhibits thereto, and all documents in connection therewith, with the Securities and Exchange Commission, granting unto each said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that any said attorney-in-fact and agent, or any substitute or substitutes of any of them, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Paul R. Edick</u> Paul R. Edick	Chief Executive Officer and Chairman (Principal Executive Officer)	January 28, 2022
<u>/s/ Steven M. Pieper</u> Steven M. Pieper	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	January 28, 2022
<u>/s/ BJ Bormann</u> BJ Bormann	Director	January 28, 2022
<u>/s/ Dawn Halkuff</u> Dawn Halkuff	Director	January 28, 2022
<u>/s/ John H. Johnson</u> John H. Johnson	Director	January 28, 2022
<u>/s/ Garheng Kong</u> Garheng Kong	Director	January 28, 2022
<u>/s/ Marla Persky</u> Marla Persky	Director	January 28, 2022
<u>/s/ John Schmid</u> John Schmid	Director	January 28, 2022
<u>/s/ Jeffrey Sherman</u> Jeffrey Sherman	Director	January 28, 2022

ZQ|CERT#|COY|CLS|RGSTRY|ACCT#|TRANSTYPE|RUN#|TRANS#

COMMON STOCK
PAR VALUE \$0.0001

COMMON STOCK



Certificate Number
ZQ00000000

Shares
*****000000*****
*****000000*****
*****000000*****
*****000000*****
*****000000*****

XERIS BIOPHARMA HOLDINGS, INC.
INCORPORATED UNDER THE LAWS OF THE STATE OF DELAWARE

THIS CERTIFIES THAT

MR. SAMPLE & MRS. SAMPLE & MR. SAMPLE & MRS. SAMPLE

SEE REVERSE FOR CERTAIN DEFINITIONS
CUSIP **98422E 10 3**

is the owner of

*****ZERO HUNDRED THOUSAND ZERO HUNDRED AND ZERO*****

THIS CERTIFICATE IS TRANSFERABLE IN CITIES DESIGNATED BY THE TRANSFER AGENT, AVAILABLE ONLINE AT www.computershare.com

FULLY-PAID AND NON-ASSESSABLE SHARES OF COMMON STOCK OF

Xeris Biopharma Holdings, Inc. (hereinafter called the "Company"), transferable on the books of the Company in person or by duly authorized attorney, upon surrender of this Certificate properly endorsed. This Certificate and the shares represented hereby, are issued and shall be held subject to all of the provisions of the Certificate of Incorporation, as amended, and the By-Laws, as amended, of the Company (copies of which are on file with the Company and with the Transfer Agent), to all of which each holder, by acceptance hereof, assents. This Certificate is not valid unless countersigned and registered by the Transfer Agent and Registrar.

Witness the facsimile seal of the Company and the facsimile signatures of its duly authorized officers.

John S. [Signature]
President and COO



[Signature]
Chief Legal Office and Corporate Secretary

DATED **DD-MMM-YYYY**

COUNTERSIGNED AND REGISTERED:
COMPUTERSHARE TRUST COMPANY, N.A.
TRANSFER AGENT AND REGISTRAR.

By _____ AUTHORIZED SIGNATURE



MR. A. SAMPLE
DESIGNATION (if any)
ADD 1
ADD 2
ADD 3
ADD 4

CUSIP/IDENTIFIER	Holder ID	Insurance Value	Number of Shares	DTC	Certificate Numbers	Num/No.	Denom.	Total
XXXXXXXXXX	XXXXXXXXXX	1,000,000.00		123456	12345678	1	1	1
			2			2	2	2
			3			3	3	3
			4			4	4	4
			5			5	5	5
			6			6	6	6
			7			7	7	7
								Total Transaction

1234567

SECURITY INSTRUCTIONS ON REVERSE

XERIS BIOPHARMA HOLDINGS, INC.

THE COMPANY WILL FURNISH WITHOUT CHARGE TO EACH SHAREHOLDER WHO SO REQUESTS, A SUMMARY OF THE POWERS, DESIGNATIONS, PREFERENCES AND RELATIVE, PARTICIPATING, OPTIONAL OR OTHER SPECIAL RIGHTS OF EACH CLASS OF STOCK OF THE COMPANY AND THE QUALIFICATIONS, LIMITATIONS OR RESTRICTIONS OF SUCH PREFERENCES AND RIGHTS, AND THE VARIATIONS IN RIGHTS, PREFERENCES AND LIMITATIONS DETERMINED FOR EACH SERIES, WHICH ARE FIXED BY THE CERTIFICATE OF INCORPORATION OF THE COMPANY, AS AMENDED, AND THE RESOLUTIONS OF THE BOARD OF DIRECTORS OF THE COMPANY, AND THE AUTHORITY OF THE BOARD OF DIRECTORS TO DETERMINE VARIATIONS FOR FUTURE SERIES. SUCH REQUEST MAY BE MADE TO THE OFFICE OF THE SECRETARY OF THE COMPANY OR TO THE TRANSFER AGENT. THE BOARD OF DIRECTORS MAY REQUIRE THE OWNER OF A LOST OR DESTROYED STOCK CERTIFICATE, OR HIS LEGAL REPRESENTATIVES, TO GIVE THE COMPANY A BOND TO INDEMNIFY IT AND ITS TRANSFER AGENTS AND REGISTRARS AGAINST ANY CLAIM THAT MAY BE MADE AGAINST THEM ON ACCOUNT OF THE ALLEGED LOSS OR DESTRUCTION OF ANY SUCH CERTIFICATE.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM - as tenants in common	UNIF GIFT MIN ACT Custodian.....
	(Cust)	(Minor)
TEN ENT - as tenants by the entireties		under Uniform Gifts to Minors Act.....
		(State)
JT TEN - as joint tenants with right of survivorship and not as tenants in common	UNIF TRF MIN ACT Custodian (until age.....)
	(Cust)	(State)
	 under Uniform Transfers to Minors Act.....
	(Minor)	(State)

Additional abbreviations may also be used though not in the above list.

For value received, _____ hereby sell, assign and transfer unto PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS, INCLUDING POSTAL ZIP CODE, OF ASSIGNEE)

_____ Shares
of the common stock represented by the within Certificate, and do hereby irrevocably constitute and appoint

_____ Attorney
to transfer the said stock on the books of the within-named Company with full power of substitution in the premises.

Dated: _____ 20____

Signature: _____

Signature: _____

Notice: The signature to this assignment must correspond with the name as written upon the face of the certificate, in every particular, without alteration or enlargement, or any change whatever.

Signature(s) Guaranteed: Medallion Guarantee Stamp
THE SIGNATURE(S) SHOULD BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION (Banks, Stockbrokers, Savings and Loan Associations and Credit Unions) WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM, PURSUANT TO S.E.C. RULE 17Ad-15.

SECURITY INSTRUCTIONS
 THIS IS WATERMARKED PAPER. DO NOT ACCEPT WITHOUT NOTING WATERMARK. HOLD TO LIGHT TO VERIFY WATERMARK.



The IRS requires that the named transfer agent ("we") report the cost basis of certain shares or units acquired after January 1, 2011. If your shares or units are covered by the legislation, and you requested to sell or transfer the shares or units using a specific cost basis calculation method, then we have processed as you requested. If you did not specify a cost basis calculation method, then we have defaulted to the first in, first out (FIFO) method. Please consult your tax advisor if you need additional information about cost basis.
 If you do not keep in contact with the issuer or do not have any activity in your account for the time period specified by state law, your property may become subject to state unclaimed property laws and transferred to the appropriate state.

1534291

January 28, 2022

Xeris Biopharma Holdings, Inc.
180 N. LaSalle Street, Suite 1600
Chicago, IL 60601

Re: Securities Registered under Registration Statement on Form S-3

We have acted as counsel to you in connection with your filing of a Registration Statement on Form S-3 (as amended or supplemented, the "Registration Statement") filed on January 28, 2022 with the Securities and Exchange Commission (the "Commission") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), relating to the registration of 15,358,362 shares (the "Shares") of common stock, par value \$0.0001 per share (the "Common Stock"), of Xeris Biopharma Holdings, Inc., a Delaware corporation (the "Company"), to be sold from time to time by the selling stockholder listed in the Registration Statement under "Selling Stockholder."

We have reviewed such documents and made such examination of law as we have deemed appropriate to give the opinions set forth below. We have relied, without independent verification, on certificates of public officials and, as to matters of fact material to the opinions set forth below, on certificates of officers of the Company.

The opinion set forth below is limited to the Delaware General Corporation Law.

Based on the foregoing, we are of the opinion that the Shares have been duly authorized and validly issued and are fully paid and nonassessable.

We hereby consent to the inclusion of this opinion as Exhibit 5.1 to the Registration Statement and to the references to our firm under the caption "Legal Matters" in the Registration Statement. In giving our consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations thereunder.

Very truly yours,

/s/ Goodwin Procter LLP

GOODWIN PROCTER LLP

Consent of Independent Registered Public Accounting Firm

We consent to the use of our report dated March 9, 2021, with respect to the consolidated financial statements of Xeris Pharmaceuticals, Inc., incorporated herein by reference and to the reference to our firm under the heading “Experts” in the prospectus.

/s/ KPMG LLP

Chicago, Illinois

January 27, 2022

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" in the Registration Statement (Form S-3) and related Prospectus of Xeris Biopharma Holdings, Inc. and to the incorporation by reference therein of our report dated March 3, 2021, with respect to the consolidated financial statements of Strongbridge Biopharma plc, included in its Annual Report (Form 10-K) for the year ended December 31, 2020, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania
January 28, 2022