

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549**

**FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

PIERIS PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Nevada
(State or other jurisdiction of
incorporation or organization)

30-0784346
(I.R.S. Employer
Identification No.)

255 State Street, 9th Floor
Boston, MA 02109
(857) 246-8998

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

Ahmed S. Mousa, Esq.
General Counsel
Pieris Pharmaceuticals, Inc.
255 State Street, 9th Floor
Boston, MA 02109
(857) 246-8998

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

Copy to:

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Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
One Financial Center
Boston, MA 02111
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Approximate date of commencement of proposed sale to the public: From time to time or at one time after the effective date of this Registration Statement.

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 being offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, 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, a 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

Accelerated filer

Non-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 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 (1)	Proposed maximum offering price per share	Proposed maximum aggregate offering price	Amount of registration fee
Common Stock, par value \$0.001 per share	3,584,230(2)	\$1.80(3)	\$6,451,614	\$703.87
Total:	3,584,230			

(1) This Registration Statement also relates to an indeterminate number of shares of common stock, par value \$0.001 per share ("Common Stock"), of Pieris Pharmaceuticals, Inc. (the "Registrant") that may be offered or issued to prevent dilution resulting from stock splits, stock dividends or similar transactions in accordance with Rule 416 under the Securities Act of 1933, as amended (the "Securities Act").

(2) Represents the number of shares of Common Stock issued to the selling shareholder in a private placement.

(3) In accordance with Rule 457(c) under the Securities Act, the aggregate offering price of the common stock is estimated solely for the calculation of the registration fees due for this filing. This estimate was based on the average of the high and low sales price of our stock reported by The Nasdaq Capital Market on May 11, 2021.

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, 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 without notice. The selling shareholder may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and the selling shareholder named in this prospectus is not soliciting offers to buy these securities in any state where the offer or sale of these securities is not permitted.

Subject to completion, dated May 17, 2021

PRELIMINARY PROSPECTUS



PIERIS PHARMACEUTICALS, INC.

3,584,230 Shares of Common Stock

This prospectus relates to the offer and sale by the selling shareholder identified in this prospectus, and any of its pledgees, donees, transferees, or other successors in interest, of up to 3,584,230 shares of common stock of Pieris Pharmaceuticals, Inc. (the "Common Stock"), as further described in this prospectus.

We are filing the registration statement of which this prospectus is a part at this time to fulfill contractual obligations to do so pursuant to a subscription agreement, as further described in this prospectus. We will not receive any of the proceeds from the sale of the Common Stock by the selling shareholder.

The selling shareholder and its pledgees, donees, transferees, or other successors in interest may offer the shares of Common Stock in one or more transactions at fixed prices, at prevailing market prices at the time of sale, at varying prices determined at the time of sale, at negotiated prices, or in trading markets for our Common Stock. Additional information on the selling shareholder, and the times and manner in which it may offer and sell shares of our Common Stock under this prospectus, is provided under "Selling Shareholder" and "Plan of Distribution" in this prospectus.

Our Common Stock is quoted on The Nasdaq Capital Market under the symbol "PIRS." On May 13, 2021, the last reported sale price of our Common Stock was \$1.87 per share.

Investing in our Common Stock involves certain risks. See "[Risk Factors](#)" beginning on page 3 of this prospectus for the risks that you should consider. You should read this entire prospectus carefully before you make your investment decision.

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 May 17, 2021

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ABOUT THIS PROSPECTUS

Except where the context requires otherwise, in this prospectus the terms “Company,” “our company,” “Pieris,” “we,” “us,” and “our” refer to Pieris Pharmaceuticals, Inc., a Nevada corporation, and, where appropriate, its direct and indirect subsidiaries.

You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. For further information, please see the section of this prospectus entitled “Where You Can Find More Information.” The selling shareholder is not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted.

You should not assume that the information appearing in this prospectus is accurate as of any date other than the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or any sale of a security. Our business, financial condition, results of operations, and prospects may have changed since those dates.

This prospectus contains trademarks, tradenames, service marks, and service names of the Company.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference herein include “forward-looking statements” within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements, other than statements of historical facts, included in this prospectus and the information incorporated by reference herein regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth are forward-looking statements. The words “anticipate,” “believe,” “contemplate,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements may include, among other things, statements about:

- the accuracy of our estimates regarding expenses, future revenues, uses of cash, capital requirements and the need for additional financing;
- the initiation, cost, timing, progress and results of our development activities, preclinical studies and clinical trials;
- the timing of and our ability to obtain and maintain regulatory approval of our existing product candidates, any product candidates that we may develop, and any related restrictions, and/or limitations;
- our plans to research, develop and commercialize our current and future product candidates and Anticalin platform;
- our collaborators’ election to pursue or continue research, development and commercialization activities;
- our ability to obtain future reimbursement and/or milestone payments from our collaborators;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- our ability to successfully commercialize our product candidates;

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- the size and growth of the markets for our product candidates and our ability to serve those markets;
- the rate and degree of market acceptance of any future products;
- the success of competing drugs that are or may become available;
- regulatory developments in the United States and other countries;
- the performance of our third-party suppliers and manufacturers and our ability to obtain alternative sources of raw materials;
- our ability to obtain additional financing;
- our use of the proceeds from our securities offerings;
- any restrictions on our ability to use our net operating loss carryforwards; and
- our ability to attract and retain key personnel.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus and the information incorporated by reference herein, particularly in the “Risk Factors” sections of this prospectus and of our Annual Report on Form 10-K for the year ended December 31, 2020, which is incorporated by reference herein, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.

You should read this prospectus and the information incorporated by reference herein completely and with the understanding that our actual future results may be materially different from what we expect. Any forward-looking statement speaks only as of the date of this prospectus. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PROSPECTUS SUMMARY

This prospectus summary highlights important features of this offering and the information included or incorporated by reference in this prospectus. Because it is a summary, it may not contain all of the information that may be important to you. You should carefully read this entire prospectus, including the section entitled “Risk Factors.”

Overview of Pieris

We are a clinical-stage biotechnology company that discovers and develops Anticalin-based drugs to target validated disease pathways in unique and transformative ways. Our clinical pipeline includes an inhaled IL-4R α antagonist Anticalin protein to treat moderate-to-severe asthma and an immuno-oncology, or IO, bispecific targeting 4-1BB and HER2. Proprietary to us, Anticalin proteins are a novel class of therapeutics validated in the clinic and through partnerships with leading pharmaceutical companies.

Anticalin proteins are a class of low molecular-weight therapeutic proteins derived from lipocalins, which are naturally occurring proteins typically found in human blood plasma and other bodily fluids. Anticalin proteins function similarly to monoclonal antibodies by binding tightly and specifically to a diverse range of targets. An antibody is a large protein used by the immune system to recognize a target molecule, called an antigen. We believe Anticalin proteins possess numerous advantages over antibodies in certain applications. For example, Anticalin proteins are relatively small in size and comprised of a single polypeptide chain whereas antibodies are much bigger and comprised of four polypeptide chains. The potentially greater stability and smaller size of Anticalin proteins as compared to antibodies potentially enable unique routes of Anticalin protein drug administration such as inhaled delivery. Higher-molecular-weight entities, such as antibodies, are often too large to be delivered effectively through these methods. Our Anticalin technology is modular, which allows us to design multimeric Anticalin-based bi- and multi-specific proteins to bind with specificity to two or more targets at the same time. This multispecificity offers advantages in biological settings where binding to multiple targets can enhance the ability of a drug to achieve its desired effects, such as facilitating the killing of cancer cells. Moreover, unlike antibodies, the pharmacokinetic, or PK, profile of Anticalin proteins can be adjusted to potentially enable program-specific optimal drug exposure. Such differentiating characteristics suggest that Anticalin proteins have the potential, in certain cases, to become best-in-class drugs.

We have intellectual property rights directed to various aspects of our Anticalin technology platform, allowing for further development and advancement of both our platform and drug candidates. We believe that our ownership or exclusive license of intellectual property related to the Anticalin platform provides us with a strong intellectual property position, particularly in cases where we are seeking to address targets and diseases in a novel way and for which there is existing antibody intellectual property. We also believe that the drug-like properties of the Anticalin drug class have been demonstrated in various clinical trials with different Anticalin-based drug candidates, including PRS-060/AZD1402, cinrebafusp alfa and others.

Our principal executive offices are located at 255 State Street, 9th Floor, Boston, Massachusetts 02109 and our telephone number is (857) 246-8998. Our website address is www.pieris.com. The information on our website is not intended to be a part of this prospectus, and you should not rely on any of the information provided there in making your decision to invest in our securities. Our website address referenced above is intended to be an inactive textual reference only and not an active hyperlink to our website.

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The Offering

Common Stock offered	Up to 3,584,230 shares
Common Stock outstanding before this offering	63,303,219 shares as of May 12, 2021
Common Stock outstanding after this offering	66,887,449 shares
Use of proceeds	We will not receive any proceeds from the sale of shares of Common Stock in this offering. See the section entitled "Use of Proceeds."
Nasdaq Capital Market symbol	PIRS
Risk factors	You should consider carefully the information set forth in the section entitled "Risk Factors," beginning on page 3 of this prospectus, in deciding whether or not to invest in our Common Stock.
Plan of distribution	The selling shareholder and its pledgees, donees, transferees, or other successors in interest may offer the shares of Common Stock in one or more transactions at fixed prices, at prevailing market prices at the time of sale, at varying prices determined at the time of sale, at negotiated prices, or in trading markets for our Common Stock. See the section entitled "Plan of Distribution" beginning on page 7 of this prospectus for a complete description of the manner in which the shares registered hereby may be distributed.

RISK FACTORS

An investment in our securities involves a high degree of risk. Before making an investment decision you should carefully read and consider the risks and uncertainties and all of the other information, documents or reports included or incorporated by reference in this prospectus, including, without limitation, the risk factors in the section entitled “Risk Factors” in our most recent Annual Report on Form 10-K, which is on file with the SEC, as updated by our subsequent filings with the SEC under the Exchange Act. If any of the risks set forth in our most recent Annual Report on Form 10-K or subsequent Exchange Act reports actually occur, our business, financial condition, and/or results of operations could suffer. In that case, the market price of our Common Stock offered by this prospectus could decline, and you may lose all or part of your investment. You should read the section entitled “Special Note Regarding Forward-Looking Statements” above for a discussion of what types of statements are forward-looking statements, as well as the significance of such statements in the context of this prospectus. Additional risks and uncertainties that we do not presently know or that we currently deem immaterial may also have a material adverse effect on our business.

DESCRIPTION OF THE TRANSACTION

Subscription Agreement

On March 29, 2021, we and AstraZeneca AB (“AstraZeneca” or the “selling shareholder”) entered into (1) Amendment No. 1 to the Non-exclusive Anticalin® Platform License Agreement dated May 2, 2017 and (2) Amendment No. 2 to the License and Collaboration Agreement dated May 2, 2017, as previously amended by Amendment No. 1 dated September 14, 2020 (collectively, the Amended Collaboration Agreement). Under the Amended Collaboration Agreement, the parties agreed to restructure certain commercial economics for the AZD1402/PRS-060 program by increasing potential sales milestones and reducing potential sales royalties, while fundamentally maintaining the overall value split between AstraZeneca and us.

In connection with the Amended Collaboration Agreement, we and AstraZeneca entered into a Subscription Agreement pursuant to which we agreed to issue to AstraZeneca, and AstraZeneca agreed to acquire from us, 3,584,230 shares of our common stock for a total purchase price of \$10.0 million, or \$2.79 per share, in a private placement transaction pursuant to Section 4(a)(2) of the Securities Act. The shares were issued on April 1, 2021.

The Subscription Agreement contains customary representations, warranties and covenants. Pursuant to the Subscription Agreement, we are required to file an initial registration statement on Form S-3 with the SEC within 60 days after the Closing, registering for resale the shares of Common Stock that were issued to AstraZeneca. We are required to use our commercially reasonable efforts to cause the registration statement to be declared effective within 90 days after the Closing, or 120 days in the event the registration statement is reviewed by the SEC and comments are provided. In addition, we are required to prepare and file any amendments and supplements to the registration statements as well as Rule 424 prospectuses to the extent necessary to keep the registration statement effective as to the shares issued to AstraZeneca.

USE OF PROCEEDS

We will not receive any proceeds from the sale of the shares of Common Stock by the selling shareholder.

The selling shareholder will pay all underwriting discounts, selling commissions and expenses incurred by it for brokerage, accounting, tax or legal services or the services of any other advisor to the selling shareholder incurred by the selling shareholder in connection with the sale of the shares, if any. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, Nasdaq listing fees and fees and expenses of our counsel and our accountants.

SELLING SHAREHOLDER

The shares of Common Stock being offered for resale by the selling shareholder pursuant to the Form S-3 of which this prospectus forms a part are the shares of Common Stock issued to the selling shareholder pursuant to the Subscription Agreement. For additional information regarding the issuance of those shares and our relationship with the selling shareholder, see “Description of the Transaction” above. We are registering the shares of Common Stock in order to permit the selling shareholder to offer the shares for resale from time to time.

The table below lists the selling shareholder and other information regarding the beneficial ownership of shares of Common Stock by the selling shareholder. The second column lists the number of shares of Common Stock beneficially owned by the selling shareholder. The third column lists the shares of Common Stock being offered by this prospectus by the selling shareholder. The fourth column lists the shares of Common Stock held by the selling shareholder after completion of this offering. The fifth column lists the percentage ownership held by the selling shareholder after completion of this offering to the extent such percentage exceeds 1% of the total number of shares of Common Stock outstanding at that time. The information presented regarding the selling shareholder is based, in part, on information the selling shareholder provided to us in writing specifically for use in this prospectus.

The information below assumes the offer and sale of all of the shares of Common Stock registered hereby and assumes no further acquisitions or dispositions of Common Stock by the selling shareholder. The selling shareholder may sell all, some or none of its shares in this offering. See “Plan of Distribution.”

In addition to the assumptions described above, beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power over securities. To our knowledge, unless otherwise indicated, the entity named in the table below has sole voting and investment power with respect to its shares of Common Stock. Percentage of beneficial ownership is based on 63,303,219 shares of our Common Stock outstanding as of May 12, 2021.

Name of Selling Shareholder	Number of Shares of Common Stock Owned Prior to Offering	Maximum Number of Shares of Common Stock to be Sold Pursuant to this Prospectus	Number of Shares of Common Stock Owned After Offering	Percentage of Shares of Common Stock Owned After Offering (to the extent greater than 1%)
AstraZeneca AB	3,584,230	3,584,230	0	—

* Denotes less than 1%.

PLAN OF DISTRIBUTION

We are registering the shares of Common Stock issued pursuant to the Subscription Agreement to permit the resale of these shares of Common Stock by the selling shareholder from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling shareholder of the shares of Common Stock.

The selling shareholder, 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 shareholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of its 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 varying prices determined at the time of sale, at negotiated prices, or in trading markets for the Common Stock.

The selling shareholder 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 effected after the date the registration statement of which this prospectus is a part is declared effective by the Securities and Exchange Commission;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- in “at the market” offerings, as defined in Rule 415 under the Securities Act, at negotiated prices, at prices prevailing at the time of sale or prices related to such prevailing market prices, including sales made directly on a national securities exchange or sales made through a market maker other than on an exchange or other similar offerings through sales agents;
- broker-dealers may agree with the selling shareholder to sell a specified number of such shares at a stipulated price per share;
- one or more underwritten offerings on a firm commitment or best effort basis;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The selling shareholder may, from time to time, pledge or grant a security interest in some or all of the shares of the Common Stock owned by it, from time to time, under this prospectus. The selling shareholder 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 Common Stock or interests therein, the selling shareholder 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 it assumes. The selling shareholder may also sell shares of Common Stock short and deliver these securities to close out its short positions, or loan or pledge the Common

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Stock to broker-dealers that in turn may sell these securities. The selling shareholder may also enter into option 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).

Broker-dealers engaged by the selling shareholder may arrange for other broker-dealers to participate in sales. If the selling shareholder effects certain transactions by selling shares of Common Stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from such selling shareholder or commissions from purchasers of the Common Stock for whom they may act as agent or to whom they may sell as principal. Such commissions will be in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with applicable rules of the Financial Industry Regulatory Authority, or FINRA; and in the case of a principal transaction, a markup or markdown in compliance with applicable FINRA rules.

The aggregate proceeds to the selling shareholder from the sale of the Common Stock offered by its will be the purchase price of the Common Stock less discounts or commissions, if any. The selling shareholder reserves the right to accept and, together with its agent 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 shareholder also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, if available, or pursuant to other available exemptions from the registration requirements under the Securities Act, rather than this prospectus, provided that it meets the criteria and conform to the requirements of that rule. Registration of the shares of Common Stock covered by this prospectus does not mean that any shares of the Common Stock will be offered or sold.

The selling shareholder may engage in at-the-market offerings and offer the Common Stock into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act on the terms described in the prospectus supplement relating thereto. Underwriters, dealers and agents who participate in any at-the-market-offerings will be described in the prospectus supplement relating thereto.

The selling shareholder and any underwriters, broker-dealers or agents that participate in the sale of the Common Stock or interests therein may be “underwriters” within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit it earns on any resale of the shares may be underwriting discounts and commissions under the Securities Act. If the selling shareholder is an “underwriter” within the meaning of Section 2(11) 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 shareholder, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, and 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 the 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.

If at the time of any offering made under this prospectus, a member of FINRA participating in the offering has a “conflict of interest” as defined in FINRA Rule 5121 (“Rule 5121”), that offering will be conducted in accordance with the relevant provisions of Rule 5121.

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We have advised the selling shareholder that the anti-manipulation rules of Regulation M promulgated under the Exchange Act may apply to sales of shares in the market and to the activities of the selling shareholder and its affiliates. In addition, to the extent applicable we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling shareholder for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling shareholder 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 shareholder 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 shareholder to use our commercially reasonable efforts to keep the registration statement of which this prospectus constitutes a part effective until the date on which all of the shares included in the registration statement have actually been sold.

We will pay all expenses of the registration of the shares of Common Stock pursuant to the Subscription Agreement, including, without limitation, Securities and Exchange Commission filing fees and expenses of compliance with state securities or "blue sky" laws; provided, however, that a selling shareholder will pay all underwriting discounts and selling commissions, if any.

LEGAL MATTERS

The validity of the Common Stock registered hereunder has been passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, MA.

EXPERTS

The consolidated financial statements of Pieris Pharmaceuticals, Inc. appearing in Pieris Pharmaceuticals, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2020, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

As permitted by SEC rules, this prospectus, which constitutes a part of a registration statement on Form S-3 that we have filed with the SEC, omits certain of the information set forth in the registration statement. Accordingly, you should refer to the registration statement and its exhibits for further information with respect to us and our Common Stock. Copies of the registration statement and its exhibits are on file at the offices of the SEC. This prospectus contains statements concerning documents filed as exhibits. For the complete text of any of these documents, we refer you to the copy of the document filed as an exhibit to the registration statement.

We file annual, quarterly and current reports, proxy and information statements and other information with the SEC. The SEC also maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is www.sec.gov.

We also maintain a website at <http://www.pieris.com> with information about our company and through which you may access these materials and other filings with the SEC free of charge as soon as reasonably practicable after they are filed electronically with, or furnished to, the SEC. Except for the documents incorporated by reference as described below under "Incorporation of Certain Documents by Reference", information contained on our website or any other website is not incorporated into this prospectus and does not constitute a part of this prospectus. Our website address referenced above is intended to be an inactive textual reference only and not an active hyperlink to our website.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” into this prospectus the information we file with the SEC, which means that we can disclose important information to you by referring you to other documents filed separately with the SEC. The information incorporated by reference is considered part of this prospectus, and any information that we file with the SEC subsequent to this prospectus and prior to the termination of the offering referred to in this prospectus will automatically be deemed to update and supersede this information. We incorporate by reference into this prospectus the documents listed below (excluding any portions of such documents that have been “furnished” but not “filed” for purposes of the Exchange Act unless specifically incorporated by reference herein or therein):

- Our Annual Report on [Form 10-K](#) for the year ended December 31, 2020, filed with the SEC on March 31, 2021;
- Our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2021, filed with the SEC on May 17, 2021;
- The portions of our Definitive Proxy Statement on [Schedule 14A](#) filed with the SEC on April 29, 2021 that are deemed “filed” with the SEC under the Exchange Act;
- Our Current Reports on Form 8-K filed [March 25, 2021](#), [March 30, 2021](#) and [April 26, 2021](#); and
- The description of our common stock contained in our registration statement on [Form 8-A12B](#) filed June 24, 2015, including any other amendments or reports filed for the purpose of updating such description (other than any portion of such filings that are furnished under applicable SEC rules rather than filed).

We also incorporate by reference all documents we subsequently file with the SEC (other than information furnished pursuant to Item 2.02 or Item 7.01 of Form 8-K or as otherwise permitted by SEC rules) pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the initial filing of the registration statement of which this prospectus is a part (including prior to the effectiveness of the registration statement) and prior to the termination of the offering.

This prospectus is part of a registration statement on Form S-3 that we have filed with the SEC relating to the securities. As permitted by SEC rules, this prospectus does not contain all of the information included in the registration statement and the accompanying exhibits and schedules we file with the SEC. We have filed certain legal documents that control the terms of the Common Stock offered by this prospectus as exhibits to the registration statement. We may file certain other legal documents that control the terms of the Common Stock offered by this prospectus as exhibits to reports we file with the SEC. You may refer to the registration statement and the exhibits and schedules for more information about us and our securities. The registration statement and exhibits and schedules are also available through the SEC’s website at www.sec.gov.

We will provide, without charge and upon oral or written request, to each person, including any beneficial owner, to whom a copy of this prospectus has been delivered, a copy of any of the documents referred to above as being incorporated by reference into this prospectus but not delivered with it. You may obtain a copy of these filings, at no cost, by writing or calling us at Pieris Pharmaceuticals, Inc., 255 State Street, 9th Floor, Boston, MA 02109, (857) 246-8998. Exhibits to the filings will not be provided, however, unless those exhibits have been specifically incorporated by reference in this prospectus.

PART II. INFORMATION NOT REQUIRED IN PROSPECTUS**Item 14. Other Expenses of Issuance and Distribution**

The following expenses incurred in connection with the sale of the securities being registered will be borne by the registrant. Other than the SEC registration fee, the amounts stated are estimates.

SEC Registration Fee	\$ 703.87
Legal Fees and Expenses	\$ 30,000
Accounting Fees and Expenses	\$ 15,000
Miscellaneous	\$ 0
Total	\$ 45,703.87

Item 15. Indemnification of Directors and Officers

The Nevada Revised Statutes (NRS) empower us to indemnify our directors and officers against expenses relating to certain actions, suits or proceedings as provided for therein. In order for such indemnification under the statutes to be available, the applicable director or officer must not have acted in a manner that constituted a breach of his or her fiduciary duties and involved intentional misconduct, fraud or a knowing violation of law and was material to the action, or must have acted in good faith and reasonably believed that his or her conduct was in, or not opposed to, our best interests. In the event of a criminal action, the applicable director or officer must not have had reasonable cause to believe his or her conduct was unlawful. However, the indemnification pursuant to the NRS and advancement of expenses authorized in or ordered by a court pursuant to the statutes does not exclude any other rights to which a person seeking indemnification or advancement of expenses may be entitled under our amended and restated articles of incorporation or any bylaw, agreement, vote of stockholders or disinterested directors or otherwise, for either an action in the person's official capacity or an action in another capacity while holding office, except that indemnification, unless ordered by a court pursuant to NRS 78.7502 or for the advancement of expenses made pursuant to NRS 78.751(2), may not be made to or on behalf of any director or officer if a final adjudication establishes that the director's or officer's acts or omissions involved intentional misconduct, fraud or a knowing violation of the law and was material to the cause of action.

Under applicable provisions of the NRS, our amended and restated articles of incorporation, amended and restated bylaws or any separate agreement may provide for our payment of expenses incurred by any such director or officer in advance of the final disposition of the applicable action, suit or proceeding, upon delivery by such director or officer of an undertaking to repay all amounts so advanced if it is ultimately determined that the director or officer is not entitled to be indemnified by us.

Our amended and restated articles of incorporation provide for indemnification of our directors and officers substantially identical in scope to that permitted under applicable Nevada law. Our amended and restated articles of incorporation also provide that the expenses of our directors and officers incurred in defending any applicable action, suit or proceeding must be paid by us as they are incurred and in advance of the final disposition of the action, suit or proceeding, provided that the required undertaking by the director or officer is delivered to us.

We have also entered into separate indemnification agreements with each of our current directors and executive officers consistent with Nevada law and in the form approved by our Board of Directors and our stockholders, and we contemplate entering into such indemnification agreements with directors and certain executive officers that may be elected or appointed in the future. Those indemnification agreements require that under the circumstances and to the extent provided for therein, we indemnify such persons to the fullest extent permitted by applicable law against certain expenses incurred by any such person as a result of such person being made a party to certain actions, suits and proceedings by reason of the fact that such person is or was a director, officer, employee or agent of our company, any entity that was a predecessor corporation of our company or any of our affiliates. The rights of each person who is a party to such an indemnification agreement are in addition to any

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other rights such person may have under applicable Nevada law, our amended and restated articles of incorporation, our amended and restated bylaws, any other agreement, a vote of our stockholders, a resolution adopted by our Board of Directors or otherwise. The foregoing is only a brief description of the form of indemnification agreement, does not purport to be a complete description of the rights and obligations of the parties thereunder and is qualified in its entirety by reference to the form of indemnification agreement filed as an exhibit to the registration statement of which this prospectus forms a part and incorporated herein by reference.

We also maintain a customary insurance policy that indemnifies our directors and officers against various liabilities, including liabilities arising under the Securities Act that may be incurred by any director or officer in his or her capacity as such.

At present, there is no pending litigation or proceeding involving any of our directors or officers for which indemnification is sought, nor are we aware of any threatened litigation that is likely to result in claims for indemnification.

Any underwriting agreements that we may enter into will likely provide for the indemnification of us, our controlling persons, our directors and certain of our officers by the underwriters against certain liabilities, including liabilities under the Securities Act of 1933, as amended.

Item 16. Exhibits

The exhibits to this registration statement are listed in the Exhibit Index immediately prior the signature page hereto, which Exhibit Index is hereby incorporated by reference into this Item 16 by reference.

Item 17. Undertakings

(a) 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 Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% 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 (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) 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 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.

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- (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
 - (i) 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.

(b) The undersigned registrant hereby undertakes 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.

(b) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant, 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 Act 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 Act and will be governed by the final adjudication of such issue.

EXHIBIT INDEX

<u>Exhibit Number</u>	<u>Item</u>
4.1	Amended and Restated Articles of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 333-190728) filed on December 18, 2014).
4.2	Certificate of Designation of Series A Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37471) filed with the Commission on August 11, 2016).
4.3	Certificate of Designation of Series B Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37471) filed with the Commission on February 4, 2019).
4.4	Certificate of Designation of Series C Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37471) filed with the Commission on November 4, 2019).
4.5	Certificate of Designation of Series D Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37471) filed with the Commission on April 6, 2020).
4.6	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-37471) filed on September 3, 2019).
4.7	Form of Common Stock certificate (incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K (File No. 001-37471) filed with the Commission on March 23, 2016).
5.1*	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
10.1	Subscription Agreement, dated March 29, 2021, by and between the Registrant and AstraZeneca AB (incorporated by reference to Exhibit 10.6 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37471) filed with the Commission on May 17, 2021).
23.1*	Consent of Ernst & Young LLP.
23.2*	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (contained in Exhibit 5.1 hereto).
24.1*	Powers of Attorney (included in the signature page of 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 Boston, Commonwealth of Massachusetts, on May 17, 2021.

PIERIS PHARMACEUTICALS, INC.

By: /s/ Stephen S. Yoder

Stephen S. Yoder
President and Chief Executive Officer

POWER OF ATTORNEY

We, the undersigned officers and directors of Pieris Pharmaceuticals, Inc., hereby severally constitute and appoint Stephen S. Yoder and Thomas Bures and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him or her and in his or her name, place and stead, and in any and all capacities, to sign any and all amendments (including, without limitation, post-effective amendments) to this registration statement (or any other 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 other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes 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/ Stephen S. Yoder</u> Stephen S. Yoder	President and Chief Executive Officer (Principal Executive Officer) and Director	May 17, 2021
<u>/s/ Thomas Bures</u> Thomas Bures	Vice President, Finance and Treasurer (Principal Financial and Accounting Officer)	May 17, 2021
<u>/s/ James Geraghty</u> James Geraghty	Director	May 17, 2021
<u>/s/ Michael Richman</u> Michael Richman	Director	May 17, 2021
<u>/s/ Ann Barbier, M.D., Ph.D.</u> Ann Barbier, M.D., Ph.D.	Director	May 17, 2021
<u>/s/ Christopher Kiritsy</u> Christopher Kiritsy	Director	May 17, 2021
<u>/s/ Peter Kiener, D.Phil.</u> Peter Kiener, D.Phil.	Director	May 17, 2021

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<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Matthew L. Sherman, M.D.</u> Matthew L. Sherman, M.D.	Director	May 17, 2021
<u>/s/ Maya R. Said, Sc.D.</u> Maya R. Said, Sc.D.	Director	May 17, 2021



May 17, 2021

Pieris Pharmaceuticals, Inc.
255 State Street, 9th Floor
Boston, MA 02109

Ladies and Gentlemen:

We have acted as counsel to Pieris Pharmaceuticals, Inc. (the “Company”) in connection with the filing by the Company of a Registration Statement on Form S-3 (as amended, the “Registration Statement”) with the Securities and Exchange Commission (the “Commission”) relating to the registration under the Securities Act of 1933, as amended (the “Securities Act”), the offering from time to time by the selling stockholders, as described in the Registration Statement, of up to 3,584,230 shares of the Company’s common stock, par value \$0.001 per share (the “**Common Shares**”). The Common Shares were issued to AstraZeneca AB pursuant to a Subscription Agreement dated March 29, 2021.

In connection with this opinion, we have examined the Company’s Amended and Restated Articles of Incorporation and Amended and Restated Bylaws, each as currently in effect; such other records of the corporate proceedings of the Company and certificates of the Company’s officers as we have deemed relevant; and the Registration Statement and the exhibits thereto.

In our examination, we have assumed the genuineness of all signatures, the legal capacity of natural persons, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as certified or photostatic copies and the authenticity of the originals of such copies, and the truth and correctness of any representations and warranties contained therein. As to questions of fact material to this opinion, we have relied upon certificates or comparable documents of public officials and of officers and representatives of the Company.

Our opinion is limited to the general corporate laws of the State of Nevada and we express no opinion with respect to the laws of any other jurisdiction. No opinion is expressed herein with respect to the qualification of the Common Shares under the securities or blue sky laws of any state or any foreign jurisdiction.

Based upon and subject to the foregoing, it is our opinion that the Common Shares are validly issued, fully paid and non-assessable.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters. This opinion is based upon currently existing statutes, rules, regulations and judicial decisions, and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein.

BOSTON LONDON LOS ANGELES NEW YORK SAN DIEGO SAN FRANCISCO WASHINGTON

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C.

We understand that you wish to file this opinion with the Commission as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K promulgated under the Securities Act and to reference the firm's name under the caption "Legal Matters" in the prospectus which forms part of the Registration Statement, and we hereby consent thereto. In giving this consent, we do not admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission promulgated thereunder.

Very truly yours,

/s/ Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

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 Pieris Pharmaceuticals, Inc. for the registration of 3,584,230 shares of its common stock and to the incorporation by reference therein of our report dated March 31, 2021, with respect to the consolidated financial statements of Pieris Pharmaceuticals, Inc. 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

Boston, Massachusetts
May 17, 2021