

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): August 24, 2021

PIERIS PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Nevada
(State or other jurisdiction of
Incorporation)

001-37471
(Commission
File Number)

30-0784346
(IRS Employer
Identification No.)

255 State Street, 9th Floor
Boston, MA
(Address of principal executive offices)

02109
(Zip Code)

Registrant's telephone number, including area code: 857-246-8998
N/A

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.001 par value per share	PIRS	The Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

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 13(a) of the Exchange Act.

Item 7.01: Regulation FD Disclosure.

Attached hereto as Exhibit 99.1 and incorporated by reference herein is the August 2021 PRS-220 European Respiratory Society (ERS) International Congress Poster.

The information set forth under this "Item 7.01. Regulation FD Disclosure," including Exhibit 99.1 attached hereto, shall not be deemed "filed" for any purpose, and shall not be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, regardless of any general incorporation language in any such filing except as shall be expressly set forth by specific reference in such filing.

Item 8.01: Other Events.

On August 24, 2021, Pieris Pharmaceuticals, Inc. (the "Company") issued a press release announcing the presentation of preclinical data for PRS-220, a connective tissue growth factor inhibitor the Company is developing for the treatment of idiopathic fibrosis via oral inhaled administration, at the ERS International Congress 2021.

A copy of this press release is attached hereto as Exhibit 99.2 and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits
(d) Exhibits.

99.1 [PRS-220 ERS Poster, Dated August 2021.](#)

99.2 [Press Release, Dated August 24, 2021.](#)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

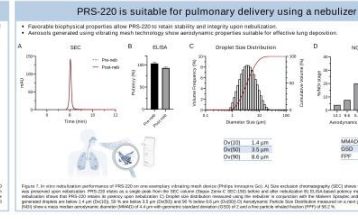
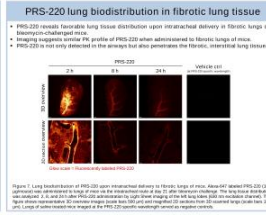
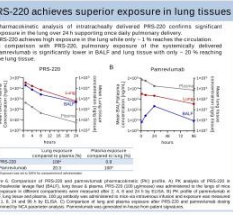
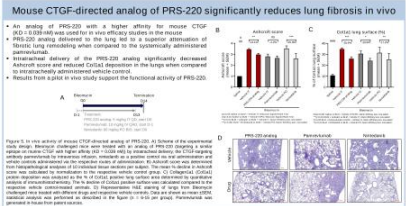
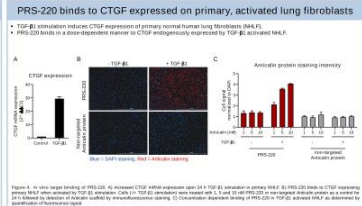
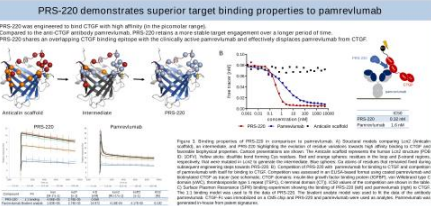
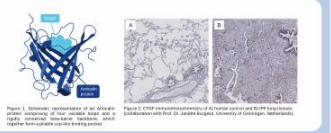
PIERIS PHARMACEUTICALS, INC.

Dated: August 24, 2021

/s/ Tom Bures
Tom Bures
Vice President, Finance

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, and ultimately fatal lung disease of unknown cause characterized by progressive scarring of the interstitial lung tissue. Median survival is two to five years from the time of diagnosis, with standard of care conferring only modest benefit for patients. In addition, adverse events often lead to the withdrawal of standard of care treatments. To overcome the limitations of current IPF therapies, we developed PRS-220, a 20 kDa protein suitable for inhalation, based on the Anticalin technology targeting connective tissue growth factor (CTGF/CCN2). Pieris Pharmaceuticals' proprietary Anticalin platform comprises a novel class of biotherapeutics derived from lipocalins, low molecular weight proteins that are abundantly expressed in human tissues and body fluids including the lung. Like antibodies, Anticalin proteins are engineered to bind a variety of therapeutically relevant targets but, in contrast to antibodies, are smaller in size and composed of a single polypeptide chain. Most importantly, the biophysical properties of Anticalin proteins allow for inhaled delivery, making them ideal for local interventions in the lung and driving more targeted biology in lung diseases. CTGF, a protein localized in the extracellular matrix, is a driver of fibrotic tissue remodeling. Over-expression of this target is observed in lung tissues of patients suffering from IPF (Shi et al., Eur Resp J 2001) and Figure 2) and Phase 2 clinical data with a systemically-delivered antibody indicate that inhibition of CTGF reduces the decline in lung function among these patients (Richards et al., Lancet Respir Med 2019).

PRS-220 was selected from Pieris' proprietary Anticalin libraries using phage display technology to bind CTGF and was engineered to optimize high affinity and specificity. In addition, PRS-220 was designed with favorable biophysical properties giving this biologic the robustness and stability for large-scale manufacturing and reduced inhaled administration. The local administration of PRS-220 directly into the lung offers the benefit of enhanced drug exposure and local target engagement while avoiding the systemic side effects of CTGF and leading potentially to a more efficient CTGF inhibition than systemically administered antibodies. Compared with parental delivery, which is the most common route of administration for biologics, pulmonary delivery offers a non-invasive alternative which is of greater convenience for patients. Here we provide preclinical data set demonstrating the best-in-class potential of PRS-220. PRS-220 binds to the functionally active epitope of CTGF and shows more stable target engagement than the clinically validated anti-CTGF antibody pamrevumab. PRS-220 has a favorable pharmacokinetic profile and lung biodistribution pattern upon lung delivery in mice. Nebulization of PRS-220 using a vibrating mesh nebulizer shows aerosol characteristics and molecular integrity suitable for effective lung deposition.



Conclusions

- PRS-220 is an Anticalin-based biotherapeutic for the treatment of IPF designed for inhaled delivery via the nebulized route of administration.
- PRS-220 binds the functionally active epitope of CTGF with high affinity and shows more stable target engagement than the clinically active antibody pamrevumab.
- An analog of PRS-220 targeting a similar epitope on the mouse CTGF is functional in a preclinical model of lung fibrosis.
- PRS-220 lung biodistribution behavior in mice supports once-daily inhaled dosing.
- PRS-220 is suitable for inhaled administration using a vibrating mesh nebulizer.

PRS-220 preclinical data supports proceeding to clinical development with a planned start of Phase 1 studies in 2022. In addition to IPF, PRS-220 will be explored for the treatment of post-COVID-19 (PASC) and idiopathic pulmonary fibrosis (IPF).

ACKNOWLEDGEMENTS: We would like to especially thank the scientists and research assistants who performed these experiments or provided important pre-work to the presented experiments: Alexander Mann, Martina Mauer, Christine Gassner, Kristine Hefner, Nicolas Quidé, Sarah Schönbach, Theresa Mosbach, David Gorenz, Patrick Ziegel and Adam Citty.

FUNDING: This work is partially funded by a grant from the Bavarian Ministry of Economic Affairs, Regional Development and Energy within the framework of the Bavarian Thermo Stability to combat the COVID-19 pandemic (ThermoStability).

PRESS RELEASE

PIERIS PHARMACEUTICALS ANNOUNCES PRS-220 PRESENTATION AT ERS HIGHLIGHTING PRECLINICAL DATA FOR CTGF INHIBITOR

BOSTON, MA, August 24, 2021 - *Pieris Pharmaceuticals, Inc. (NASDAQ: PIRS)*, a clinical-stage biotechnology company advancing novel biotherapeutics through its proprietary Anticalin® technology platform for respiratory diseases, cancer, and other indications, announced today the presentation of preclinical data for PRS-220, a connective tissue growth factor (CTGF) inhibitor the Company is developing for the treatment of idiopathic pulmonary fibrosis (IPF) via oral inhaled administration, at the European Respiratory Society (ERS) International Congress 2021. The poster is now available for viewing by registered participants, and a copy of the poster is available [here](#). A presentation accompanying the poster will take place during a session scheduled on Sunday, September 5, 2021, 1:15PM – 2:15PM CET.

The poster presentation provides the rationale and supportive data for the advantages of a local intervention against CTGF with PRS-220. Based on head-to-head preclinical studies, the data show that PRS-220 demonstrates a more potent and durable target engagement profile compared to a clinical-stage, systemically delivered anti-CTGF antibody benchmark. Additionally, the targeting of CTGF locally in the lung shows increased attenuation of fibrotic lung remodeling *in vivo* compared to the systemically delivered antibody. This outcome correlates with superior lung tissue exposure of PRS-220 compared to that of the systemically administered antibody in head-to-head studies, where intratracheally administered PRS-220 efficiently penetrates the fibrotic, interstitial lung tissue of mice. Finally, the drug-like properties data demonstrate the suitability of PRS-220 for delivery to the lung via nebulization.

"PRS-220 exemplifies our respiratory strategy of advancing programs addressing clinically-validated targets where a local approach may provide significant benefit to patients," said Shane Olwill, Ph.D., Chief Development Officer of Pieris. "We look forward to beginning phase 1 studies for this novel inhaled approach to CTGF-mediated disease next year."

About PRS-220:

PRS-220 is an oral inhaled Anticalin protein targeting connective tissue growth factor (CTGF), also known as CCN2, for the treatment of idiopathic pulmonary fibrosis (IPF). IPF affects over three million patients worldwide and roughly 130,000 patients in the United States. Mean survival is two to five years from the time of diagnosis, with standard of care conferring only modest benefit. CTGF, a protein localized in the extracellular matrix, is a driver of fibrotic tissue remodeling as a consequence of an aberrant wound healing process. Over-expression of this target in lung tissue is observed in patients suffering from IPF, and clinical data indicate inhibition of CTGF reduces the decline in lung function among these patients. In addition to IPF, Pieris will evaluate PRS-220 for the treatment of COVID-19-related pulmonary fibrosis, supported by a grant from the Bavarian government.

About Pieris Pharmaceuticals:

Pieris is a clinical-stage biotechnology company that combines leading protein engineering capabilities and deep understanding into molecular drivers of disease to develop medicines that drive local biology to produce superior clinical outcomes for patients. Our pipeline includes inhalable Anticalin proteins to treat respiratory diseases and locally-activated bispecifics for immuno-oncology. Proprietary to Pieris, Anticalin proteins are a novel class of therapeutics validated in the clinic and by respiratory and immuno-oncology focused partnerships with leading pharmaceutical companies. For more information, visit www.pieris.com.

Forward Looking Statements:

This press release contains forward-looking statements as that term is defined in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Statements in this press release that are not purely historical are forward-looking statements. Such

forward-looking statements include, among other things, the timing for initiation of clinical trials of PRS-220, whether PRS-220 will provide a clinical benefit in the treatment of IPF and PASC-related fibrosis; the expected timing and potential outcomes of the reporting by the Company of key clinical data from its programs, references to novel technologies and methods and our business and product development plans, including the Company's cash resources, the advancement of our proprietary and co-development programs into and through the clinic and the expected timing for reporting data, making IND filings or achieving other milestones related to our programs, including PRS-060/AZD1402, cinrebafusp alfa, PRS-344, and PRS-352 and the expected timing of the initiation of the next stage of cinrebafusp alfa's development in gastric cancer. Actual results could differ from those projected in any forward-looking statements due to numerous factors. Such factors include, among others, our ability to raise the additional funding we will need to continue to pursue our business and product development plans; the inherent uncertainties associated with developing new products or technologies and operating as a development stage company; our ability to develop, complete clinical trials for, obtain approvals for and commercialize any of our product candidates, including our ability to recruit and enroll patients in our studies; our ability to address the requests of the U.S. Food and Drug Administration; competition in the industry in which we operate; delays or disruptions due to COVID-19; and market conditions. These forward-looking statements are made as of the date of this press release, and we assume no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law. Investors should consult all of the information set forth herein and should also refer to the risk factor disclosure set forth in the reports and other documents we file with the Securities and Exchange Commission available at www.sec.gov, including without limitation the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020 and the Company's Quarterly Reports on Form 10-Q.

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