

**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): September 16, 2018

PIERIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in its Charter)

Nevada
(State of
Incorporation)

001-37471
(Commission
File Number)

EIN 30-0784346
(IRS Employer
Identification No.)

255 State Street, 9th Floor
Boston, MA 02109
United States
(Address of principal executive offices, including zip code)

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

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))

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.

On September 16, 2018, Pieris Pharmaceuticals, Inc. presented preclinical data regarding PRS-060. The poster is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

The information set forth under this “Item 7.01. Regulation FD Disclosure,” including the exhibits attached hereto, shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits

(d) *Exhibits.*

99.1 [Conference Poster, Dated September 2018.](#)

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: September 17, 2018

/s/ Allan Reine

Allan Reine

Chief Financial Officer

The Discovery and Development of AZD1402/PRS-060 a Potent and Selective Blocker of the IL-4 Receptor alpha

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Introduction

In 5-10% of asthma patients control of disease is not achieved with standard of care therapies (inhaled corticosteroids in combination with long-acting beta-2 agonists). This inability to achieve asthma control significantly impacts patients' quality of life and healthcare costs. Type 2 (T2) cytokines, specifically interleukin (IL)-4, IL-5, and IL-13, play crucial roles in asthma pathogenesis¹⁻³. Dupilumab, a fully human anti-IL-4 receptor alpha (IL-4R α) monoclonal antibody given by subcutaneous injection, inhibits IL-4 and IL-13 signalling, key drivers of T2-mediated inflammation, and has been shown to reduce exacerbations and improve lung function in moderate to severe asthma subjects⁴. Pitrakinra, an inhaled IL-4 mAb that antagonises IL-4R α , has also been shown to have beneficial effects in a subset of asthma patients⁵. PRS-060/AZD1402, is a human tear lipocalin derived Anticalin antagonist that has a high potency and selectivity for the human IL-4 receptor alpha. Selectivity has been established by testing against a range of cytokine receptors. PRS-060/AZD1402 is being developed as an inhaled treatment for moderate to severe asthma.

Methods

TF1 cells, known to express IL-4R α , were used in a FACS assay measuring the signal transducer and activator of transcription 6 (STAT6) phosphorylation following IL-4 or IL-13 stimulation in the presence and absence of PRS-060/AZD1402. To demonstrate functional activity of PRS-060/AZD1402, a proliferation assay using hGM-CSF starved TF1 cells stimulated with a low dose of IL-4 (0.1 nM) or IL-13 (30 nM) was set up, using as readout the release of ATP by living cells.

In a human airway epithelium culture system (3D MucilAirTM), incubation with IL-13 (10 ng/ml), every 2 days for a total of 14 days induced a goblet cell metaplasia as assessed by in situ Alcian blue staining.

As PRS-060/AZD1402 does not cross react with IL-4R α from species commonly used for *in vivo* efficacy studies, a syntenic (humanised) mouse was generated by Dr. Beverly Koller at UNC-Chapel Hill and the mouse studies were performed in her laboratory. In this mouse the genes for IL-4R α and IL-4/13 were replaced with the respective human orthologues. This mouse both responds to human IL-4 and IL-13 but also generates human IL-4 and IL-13 when the T2 cytokine pathway is activated.

A pharmacodynamic murine model for the evolution of the potency and duration of action of PRS-060/AZD1402 was developed in this mouse. Human IL-13 (1 μ g) was given via the intra-tracheal (i.t.) route and the expression of C111 (eotaxin-1) was quantified in lung tissue by qPCR 24-hour post challenge.

An ovalbumin (OVA) model of asthma was also developed in these mice. Mice were sensitised to OVA (20 μ g OVA in Alum i.p.) on day 0 and day 7 and were challenged with an aerosol of OVA on day 14. Animals were sacrificed 24 and 48h later and the inflammatory response was assessed in the bronchoalveolar lavage fluid by performing total and differential cell counts. In separate animals, lungs were perfused with PBS/heparin followed by 4% PFA in PBS. Lungs were then inflated with 4% PFA/PBS at a constant head pressure of 20 cm H₂O, and then maintained in the inflation solution until fixation. Three serial sagittal lung sections were then prepared from formalin fixed, paraffin blocked lung tissue and stained for haematoxylin and eosin, Periodic-acid Schiff and trichrome demonstrations, respectively.

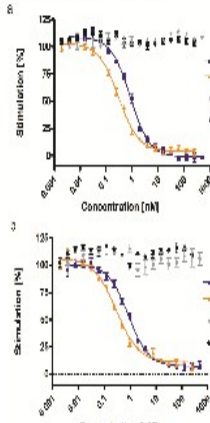
Results 1

Table 1. Dual inhibition of hIL-4 and hIL-13 induced STAT6 phosphorylation in TF1 cells by PRS-060/AZD1402

Test substance	IL-13 [10nM] induced TF-1 pSTAT6 K ₅₀ (mean \pm SD)	IL-4 [0.1nM] induced TF-1 pSTAT6 K ₅₀ (mean \pm SD)
PRS-060	0.097 nM \pm 0.007	0.14 nM \pm 0.04
IL-4 mAb (Pitrakinra)	9.1 nM \pm 1.088	7.12 nM \pm 0.06

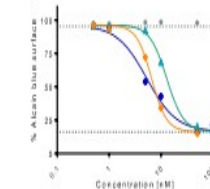
* In an *in vitro* assay using TF-1 cells, PRS-060/AZD1402 showed dual inhibition of IL-4R and IL-13R signalling by inhibiting both the IL-4 and IL-13 induced STAT6 phosphorylation with 50 - 90 fold greater potency compared to pitrakinra (table 1), respectively.

Figure 1. Inhibition of a) IL-4 and b) IL-13 induced TF1 cell proliferation by PRS-060/AZD1402



* In a functional cell-based assay, PRS-060/AZD1402 inhibited IL-4 and IL-13 induced proliferation of TF-1 cells with similar potency to dupilumab (figure 1).

Figure 2. Inhibition of IL-13-induced goblet cell metaplasia by PRS-060/AZD1402



Results 2

* In a human airway epithelium culture system (3D MucilAirTM), PRS-060/AZD1402 effectively inhibits IL-13 induced goblet cell metaplasia with a similar potency to AMG317, an anti-IL-4 receptor alpha (IL-4R α) monoclonal antibody, and a greater potency than pitrakinra (figure 2).

Figure 3. Effect of PRS-060/AZD1402 on IL-13-induced increases in eotaxin gene expression in murine PD model

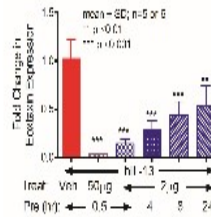
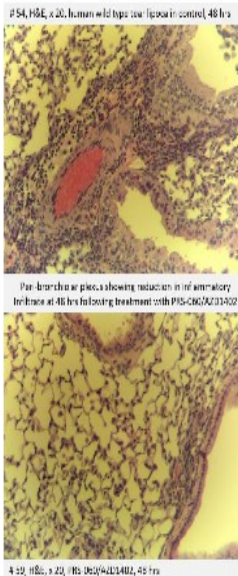


Figure 4. Effect of PRS-060/AZD1402 on OVA induced histopathological outcomes 48 hours post challenge in a murine asthma model

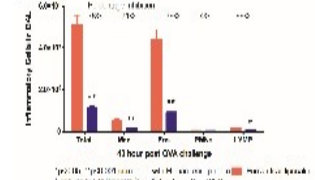


Par-bronchioles showing reduction in inflammatory infiltrate at 48 hrs following treatment with PRS-060/AZD1402

4 x 20, H&E, x20, PRS-060/AZD1402, 48 hrs

Results 3

Figure 5. Effect of PRS-060/AZD1402 on OVA induced inflammation 48 hours post challenge in a murine asthma model



* In an *in vivo* pharmacodynamic model developed in humanised mice, pre-treatment with PRS-060/AZD1402 given via the i.t. route, inhibited IL-13-induced eotaxin gene expression. A dose of 2 μ g/mouse inhibited this response over a 24-hour period (figure 3).

* In a murine asthma model developed in the humanised mouse, PRS-060/AZD1402 given i.t. (30 μ g/mouse) twice, 0.5 hours prior to and 24 hours post OVA challenge, inhibited antigen-induced pulmonary inflammation in the BAL 48 hours post challenge (figure 5). In this model, treatment with PRS-060/AZD1402 was associated with histologically significant reductions in bronchiolar and alveolar inflammation, eosinophil, neutrophil, macrophage infiltration, bronchiolar epithelial hyperplasia and fibroplasia (figure 4).

Summary

- PRS-060/AZD1402 is a potent and selective antagonist of the IL-4R α that has a comparable profile to the monoclonal antibody to this receptor, dupilumab, and 50-90 fold greater potency than the inhaled IL-4 mAb, pitrakinra.
- PRS-060/AZD1402 effectively inhibits IL-13 induced goblet cell metaplasia *in vitro* supporting the concept that treatment will reduce mucus hypersecretion in moderate to severe asthma patients.
- In a murine PD model a single intra-tracheal dose of PRS-060/AZD1402 potently inhibited an IL-13 induced response and had a 24-hour duration of action.
- In a murine asthma model, intra-tracheal PRS-060/AZD1402 reduced pulmonary inflammation as assessed by an inhibition of BAL cell recruitment and via a reduction in antigen-induced histopathological changes.

Conclusions

The overall profile of PRS-060/AZD1402 supports its development as an inhaled therapy for moderate to severe asthma. Non-clinical safety studies suggest that this inhaled Anticalin therapeutic is safe and well tolerated and it is currently being evaluated clinically for safety, tolerability and efficacy in two Phase 1 studies (NCT03384290 and NCT03574805).

References

1. Wankings et al. *J Exp Med*. 2006;203:1459-68.
2. Leachon et al. 2010. 349777-86.
3. Wenzel et al. *Lancet*. 2016; 388:33-44.
4. Lichten et al. *J Clin Invest* 2015; 125: 122-32.
5. Koller et al. *Mol Ther* 2015; 130: 514-22.
6. <http://www.aafp.com/onlineonly/reader>

Disclosure of Commercial Support and Relevant Financial Interests: Dr. Matschiner is an employee of Pieris Pharmaceuticals, Dr. Fitzgerald is a consultant for Pieris Pharmaceuticals, and Dr. Keeling is an employee of AstraZeneca. Professor Koller has provided scientific support and advice on the development of mouse models and the testing of novel Anticalin proteins.

