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): April 4, 2017

PIERIS PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in its Charter)

Nevada	**001-37471**	**EIN 30-0784346**
(State of Incorporation)	**(Commission File Number)**	**(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))

Item 7.01 Regulation FD Disclosure.

On April 4, 2017, Pieris Pharmaceuticals, Inc. presented IND-enabling data for PRS-343, a first-in-class 4-1BB/HER2 bispecific, in a poster session at the American Association for Cancer Research conference ("AACR") in Washington, D.C. The poster is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

Attached hereto as Exhibit 99.2 and incorporated by reference herein is press release regarding the presentation at AACR.

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 Industry Conference Presentation of Pieris Pharmaceuticals, Inc., dated April 2017.

99.2 Press Release dated April 4, 2017.

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.

Dated: April 4, 2017

PIERIS PHARMACEUTICALS, INC.

By: /s/ Lance Thibault
Name: Lance Thibault
Title: Acting Chief Financial Officer

EXHIBIT INDEX

Exhibit No.	Description
99.1	Industry Conference Presentation of Pieris Pharmaceuticals, Inc., dated April 2017.
99.2	Press Release dated April 4, 2017.

Preclinical toxicology and pharmacology for the 4-1BB/HER2 bispecific PRS-343: A first-in-class costimulatory T cell engager

Marlon J. Hinner, Rachida-Siham Bel Aiba, Thomas Jaquin, Sven Berger, Manuela Dürr, Corinna Schlosser, Andrea Allersdorfer, Christine Rothe, Louis A. Matis, Shane A. Olwill

Pieris Pharmaceuticals, Inc., 255 State Street, Boston, Massachusetts

AACR Annual Meeting 2017
Abstract 3673

Background

4-1BB (CD137) is a key costimulatory immunoreceptor and a highly promising therapeutic target in cancer. To overcome toxicity and efficacy limitations of current 4-1BB-targeting antibodies, we have developed PRS-343, a 4-1BB/HER2 bispecific based on Anticalin® technology. We have previously reported on the generation and characterization of PRS-343 with regard to preclinical proof-of-concept and basic drug-like properties (1). Here, we describe the preclinical dataset supporting initiation of a first-in-patient trial.

The pharmacology of PRS-343 is investigated by ex vivo assays based on mixed culture of human PBMC and tumor cell lines. The assays are used to determine the cytokine profile of T cells costimulated by PRS-343-induced 4-1BB clustering. Using a set of immortal cancer cell lines and primary cells spanning a range of HER2 surface copy numbers, we identify the threshold required to elicit a costimulatory response, and a lower threshold below which costimulation can be reliably excluded. The risk of PRS-343-mediated, systemic 4-1BB activation and concomitant toxicity is investigated in a cytokine release assay and in a mouse toxicology model of human PBMC-induced xenograft-vs-host disease (xGvHD). HER2-mediated toxicity is studied in a GLP-compliant, repeat-dose toxicology study in cynomolgus monkeys.

The combined dataset provides an overview on the pharmacology, mode of action and safety profile of PRS-343.

Concept: tumor-specific and tumor-localized costimulatory activation of T cells

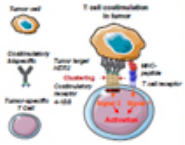

Figure 1. Concept of costimulatory T cell engagement by PRS-343. Within a patient's tumour, tumor-specific T cells are bridged with tumor cells by the costimulatory bispecific PRS-343 which simultaneously binds the tumor target HER2 and the immune receptor 4-1BB. The resulting clustering of 4-1BB provides a local co-activatory signal to the T cell, further enhancing its T cell receptor (TCR)-mediated activity and leading to tumor destruction. Toxic side effects are expected to be manageable, as PRS-343 does not induce clustering and activation of 4-1BB in the absence of target-positive cells, and healthy tissue is spared by tumor-costimulated T cells due to the absence of a primary, TCR-mediated signal.

PRS-343 design, target binding and activity in reporter and T cell costimulation assay

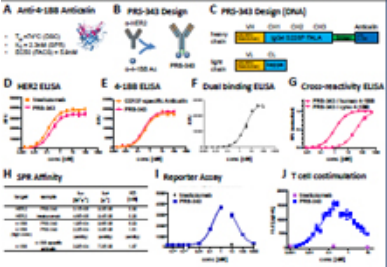

Figure 2. PRS-343 Design, target binding and cell-based activity. (A) 4-1BB binding Anticalin. (B,C) Design. (D) HER2 ELISA shows similar potency of PRS-343 compared to trastuzumab. (E) 4-1BB ELISA shows similar potency of PRS-343 compared to 4-1BB-specific Anticalin. (F) Dual binding: 4-1BB/HER2 bispecifics are capable of binding both targets at the same time according to Sandwich ELISA. (G) Cross-reactivity: PRS-343 displays reduced cross-reactivity to 4-1BB from cynomolgus monkey. (H) On-rate, off-rate and KD of binding to targets HER2 and 4-1BB for PRS-343 and reference molecules trastuzumab and 4-1BB specific Anticalin. 4-1BB binding affinity was determined using different target coating concentrations minimizing or favoring avidity effects, respectively. (I) PRS-343 induces 4-1BB clustering and downstream signaling in a Jurkat NFAB reporter cell line in the presence of HER2-positive NCI-N87 cells with a potency of 80pM. (J) PRS-343 induces IL-2 production in a costimulatory T cell activation assay in the presence of HER2-positive SKBR-3 cells, with a potency of 20pM. In both types of cell-based assays, the response is bell-shaped as expected for ternary complex formation between PRS-343 and target cells (2).

PRS-343-costimulated T cells express IL-2, GM-CSF, IFNγ and TNFα

- T cells were co-incubated with HER2^{high} NCI-N87 cells and PRS-343.
- Supernatant concentrations were determined for a panel of cytokines
- Cytokines prominently induced by PRS-343-mediated costimulation were GM-CSF, IL-2, IFNγ and TNFα
- These cytokines may serve as pharmacodynamic biomarkers in clinical studies

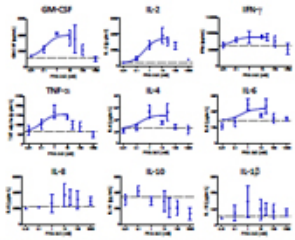

Figure 3. Cytokines induced by human T cells co-stimulated by PRS-343 in the presence of HER2-positive NCI-N87 cells in a T cell co-stimulation assay. Cytokine levels in the culture supernatants were measured by an electrochemiluminescence (ECL) immunoassay.

PRS-343-induced cytokine release in the absence of T cell receptor stimulation is negligible

- A cytokine release assay (3) was performed in the absence of T cell receptor (TCR) stimulation and presenting PRS-343 to PBMC in solution, well-coated and air-dried
- PRS-343 shows negligible cytokine induction activity compared to the positive anti-CD3 control OKT3 independent of presentation strategy
- The data confirms that 4-1BB is a costimulatory receptor that requires a primary TCR signal; the risk of systemic cytokine release syndrome in clinical studies appears low

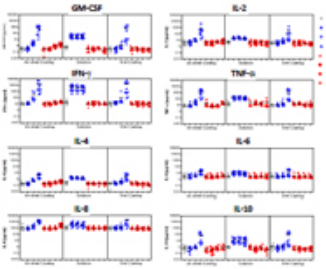

Figure 4. Cytokine release assay with PRS-343. PBMC were isolated from the blood of twelve healthy donors and incubated for 72 hours with PRS-343 either air dried, in soluble form, or well coated. Four concentrations of PRS-343 in a volume of 90µl were tested in each setting as indicated in the figure. The anti-CD3 monoclonal antibody OKT3 at three different concentrations served as the positive control, and an IgG4 isotype antibody was the negative control. Supernatant levels of ten cytokines (IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12p70, GM-CSF, IFN-γ and TNFα) were analyzed. The figure shows the average response for the ten donors that displayed a significant response to OKT3, and for a selection of the most relevant cytokines.

PRS-343-mediated T cell costimulation requires supraphysiological HER2 levels

- The costimulatory T cell activation assay was performed for a series of tumor cell lines and primary cells covering a wide range of HER2 positivity
- An anti-4-1BB benchmark mAb was used as a positive control
- Response specificity was controlled by competition with an excess of trastuzumab
- The series of experiments shows
  - (i) reliable costimulation above HER2 levels corresponding to 14% of SKBR-3 (HER2 2+)
  - (ii) no costimulation in the physiological HER2 expression range (<2% of SKBR-3)
  - (iii) variable donor-dependent results in the intermediate range (2%-11%)
- Costimulatory activity was observed in SUM225 and JIMT-1 cell lines described as resistant to conventional HER2-targeted therapy (4-6)

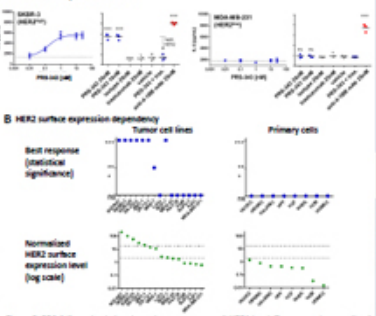

Figure 5. PRS-343 costimulation dependence on target cell HER2 level. Tumor or primary cells of different HER2 positivity were subjected to a T cell costimulatory activation assay using IL-2 supernatant levels as the readout. Experiments for each cell line were performed with at least two different donors. (A) Exemplar results. PRS-343 at various concentrations, target cells and healthy donor T cells were co-incubated in the presence of coated anti-CD3 antibody. Negative controls used were IgG4 isotype, trastuzumab or vehicle. Anti-4-1BB benchmark mAb was the positive control. The experiment was performed also in the presence of an excess of trastuzumab to inhibit the binding of PRS-343 to the SKBR3 cells. (B) Top: The best statistical significance obtained for any donor vs. control levels is reported for tumor cell lines and primary cells (p<0.001 (***), p<0.01 (**) or p<0.05 (*). Values of p>0.05 were considered not statistically significant (ns)). Bottom: relative cell surface HER2 levels (normalized against SKBR3 expression levels) are plotted for each tumor cell line and primary cell type on a logarithmic scale.

PRS-343 leads to TGI and tumor-localized increase in hCD45(+) cells in tumor in humanized mice

- Immuno-compromised mice engrafted with HER2-positive tumor cells (SK-OV-3) were injected with human PBMC and treated over 3 weeks with PRS-343 at four dose levels
- Control molecules were IgG4 isotype, an anti-4-1BB benchmark antibody and trastuzumab with an IgG4 backbone (Tras-IgG4)
- Tumor IHC staining for human CD45 shows a dose-dependent increase in the frequency of human TIL for PRS-343 vs controls, suggesting tumor-localized T cell activation
- PRS-343 showed dose-dependent tumor growth inhibition (TGI) comparable to Tras-IgG4, indicating that TGI is dominated by HER2 antagonism in this model

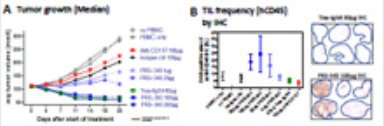

Figure 6. PRS-343 activity in NOG mice engrafted with HER2-positive SK-OV-3 cell line and human PBMC. (A) Median of tumor growth. (B) Frequency of CD45$^+$ cells determined by immunohistochemistry of tumors after study end. Examples for sections of formalin-fixed and paraffin-embedded tumors stained for human CD45 are provided on the right. See reference (1) for further experimental details.

Humanized Mouse Toxicology: PRS-343 avoids systemic 4-1BB activation in contrast to benchmark

- Immuno-compromised, tumor-free mice were injected with human PBMC and treated over 3 weeks with PRS-343 or controls (Ig04 isotype or anti-4-1BB benchmark mAb)
- PRS-343 showed unchanged dynamics of xenograft-versus-host disease compared to isotype control, while anti-4-1BB benchmark significantly accelerated mortality
- The results support a potentially improved safety profile of PRS-343 over benchmark by lack of systemic activation and concomitant toxicity

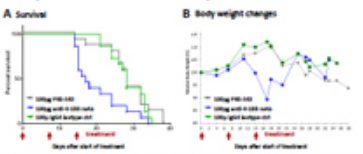

Figure 7. Immuno-compromised female NOG mice were engrafted with 7 × 10^6 fresh human PBMC, followed by weekly (q. treatment with PRS-343, a 4-1BB benchmark agonist or isotype control at 100 µg/dose (i.p.) for 3 weeks. Mice (n=15 per group) remained on the study until spontaneous death or if ethical sacrifice was required. (A) Survival plot. (B) Relative median body weight of surviving animals.

PRS-343 is Well Tolerated in Repeat-Dose Cynomolgus Monkey Toxicology Study

- The safety of PRS-343 was investigated in a GLP-compliant cynomolgus monkey study
- PRS-343 was given in weekly doses of 0, 10 and 120mg/kg over 4 weeks as an intravenous infusion of 120 min duration (see Table 1 for study design)
- Delayed onset or reversibility of toxicity was studied in recovery groups (0 and 120 mg/kg
- PRS-343 was well tolerated at both doses tested, with no significant findings
- TK analysis demonstrated full, dose-proportional exposure at both dose levels, with a terminal half-life of 5-6 days

Table 1. Study Design.

Group	Group Description	Dose Level (mg/kg/week)	Number of Animals			
			Toxicity		Recovery	
			Male	Female	Male	Female
1	Control	0	3	3	2	2
2	Low	10	3	3	-	-
3	High	120	3	3	2	2

Conclusion

- PRS-343 is a 4-1BB/HER2 bispecific based on the genetic fusion of a high-affinity 4-1BB-binding Anticalin and modified trastuzumab
- The presented preclinical pharmacology and toxicology studies confirm previous results (1) and support that PRS-343 elicits its costimulatory effects strictly on T cells also receiving a primary TCR signal and strictly localized to HER2-positive tumors:
  - PRS-343-mediated 4-1BB activation requires supraphysiological HER2 levels
  - PRS-343 costimulation leads to increased production of multiple pro-inflammatory cytokines associated with anti-tumor immune response
  - The risk of systemic 4-1BB activation is low based on negligible cytokine release in the absence of primary T cell receptor stimulation
  - This is supported by a humanized mouse toxicology study, where PRS-343 avoids the systemic peripheral activation of CD8$^+$ T cells observed with a benchmark 4-1BB antibody
  - A GLP-compliant cynomolgus monkey toxicology study demonstrates that the benign toxicity profile of trastuzumab is retained in PRS-343 with regard to HER2 targeting
- The reported data support evaluation of PRS-343 in a Phase 1 study in patients with HER2-positive advanced or metastatic solid tumors.

References: (1) Cancer Immunol Res 2016;4(1 Suppl):Abstract nr B016; (2) J Am Chem Soc 2013; 135, 9592-9595; (3) J Immunol 2007; 179, 3326-3331; (4) Mol Cancer Ther 2010; 9, 1459-1552; (5) Oncogene 2007; 26, 7160-7169; (6) Mol Cancer Ther 2004; 3, 1505-1563.

Exhibit 99.2

PRESS RELEASE

Pieris Pharmaceuticals Presents IND-enabling Data for Bispecific Immuno-Oncology Drug Candidate, PRS-343, in Poster Session at the 2017 Meeting of the American Association for Cancer Research (AACR)

BOSTON, MA — (Marketwired) — 04/04/17 — Pieris Pharmaceuticals, Inc. (NASDAQ: PIRS), a clinical-stage biotechnology company advancing novel biotherapeutics through its proprietary Anticalin® technology platform, announced today the presentation of data informing the design of a first-in-patient clinical trial for PRS-343, a first-in-class 4-1BB/HER2 bispecific in a poster session at the 2017 Annual Meeting of the American Association for Cancer Research (AACR).

Complementing previously disclosed preclinical data demonstrating that PRS-343 elicits robust T cell expansion in the tumor microenvironment while avoiding unwanted peripheral T cell activation in HER2-positive cancer models, the data presented today demonstrate:

- PRS-343 elicited robust T cell activation when engaging HER2 on cell lines derived from tumors resistant to trastuzumab therapy, as well as tumor cell lines with elevated HER2 expression in the IHC 2+ range
- 4-1BB-mediated T cell activation by PRS-343 resulted in the expression of a broad spectrum of inflammatory cytokines associated with anti-tumor immune responses
- PRS-343 was well tolerated and led to no significant findings in IND-enabling preclinical safety and non-human primate toxicology studies

Today's presented data suggest the clinical potential of PRS-343 in a broad population of patients with HER2-expressing cancers," commented Louis Matis, MD, Chief Development Officer of Pieris. "Moreover, the preclinical pharmacokinetic and safety profile of PRS-343 supports the initiation of clinical development, which we anticipate during the first half of this year." A copy of the poster can be viewed here.

About PRS 343:

PRS-343 is a bispecific monoclonal antibody/Anticalin fusion protein comprised of a HER2 tumor-targeting mAb genetically linked to a potent Anticalin specific for the immune costimulatory TNF family receptor 4-1BB (CD137). PRS-343 is being developed as the first 4-1BB based therapeutic to mediate the activation of tumor-specific T lymphocytes selectively within the tumor microenvironment (TME). 4-1BB is a potent costimulatory immunoreceptor and an established marker for tumor-specific infiltrating T lymphocytes (TILs), and is, therefore, an attractive target for cancer immunotherapy. In *in vivo* preclinical tumor models, PRS-343 has demonstrated potent T lymphocyte activation localized to the TME of established HER2-positive tumors, indicating the potential for both enhanced safety and efficacy.

About Pieris Pharmaceuticals:

Pieris is a clinical stage biotechnology company that discovers and develops Anticalin-based drugs to target validated disease pathways in a unique and transformative way. Our pipeline includes immuno-oncology multi-specifics tailored for the tumor micro-environment, an inhaled Anticalin to treat uncontrolled asthma and a half-life-optimized Anticalin to treat anemia. Proprietary to Pieris, Anticalins are a novel class of protein therapeutics validated in the clinic and by partnerships with leading pharmaceutical companies. Anticalin®, is a registered trademark of Pieris. Pieris has partnerships with Servier, ASKA, Roche, Sanofi, Daiichi Sankyo and Zydus. 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 and Section 21E of the Securities Exchange Act of 1934. Statements in this press release that are not purely historical are forward-looking statements. Such forward-looking statements include, among other things, references to novel technologies and methods; our business and product development plans and timelines; the timing and progress of our studies, development of therapeutic programs; ability to receive research funding; our liquidity and ability to fund our future operations; our ability to achieve certain milestones and receive future milestone or royalty payments; current or future partnerships; or market information. 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; competition in the industry in which we operate 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 SEC available at www.sec.gov, including without limitation the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and the Company's Quarterly Reports on Form 10-Q.

Contacts at Pieris:

Company Contact:
Pieris Pharmaceuticals, Inc.
Lance Thibault
Acting Chief Financial Officer
+1-857-246-8998
thibault@pieris.com

Investor Relations Contact:
The Trout Group
Thomas Hoffmann
+1-646-378-2931
thoffmann@troutgroup.com

Media Inquiries:
Mario Brkulj
+49 175 5010575
mbrkulj@macbiocom.com

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