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): October 21, 2016

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 October 21, 2016, Pieris Pharmaceuticals, Inc. presented a poster titled “Costimulatory T-cell engagement by PRS-343, a CD137 (4-1BB)/HER2 bispecific, leads to tumor growth inhibition and CD8(+) T-cell expansion in humanized mouse model” at an American Association for Cancer Research conference in Boston, Massachusetts. 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 presentations at research and development conferences.

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 October 2016.
99.2 Press Release dated October 20, 2016.

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: October 24, 2016

PIERIS PHARMACEUTICALS, INC.

By: /s/ Darlene Deptula-Hicks
Name: Darlene Deptula-Hicks
Title: Chief Financial Officer

EXHIBIT INDEX

Exhibit No.	Description
99.1	Industry Conference Presentation of Pieris Pharmaceuticals, Inc., dated October 2016.
99.2	Press Release dated October 20, 2016.

Costimulatory T-cell engagement by PRS-343, a CD137 (4-1BB)/HER2 bispecific, leads to tumor growth inhibition and CD8(+) T cell expansion in humanized mouse model

Marlon J. Hinner[1], Rachida-Siham Bel Aiba[1], Corinna Schlosser[1], Thomas Jaquin[1], Andrea Allersdorfer[1], Sven Berger[1], Alexander Wiedenmann[1], Gabriele Matschiner[1], Julia Schüler[2], Ulrich Moebius[1], Christine Rothe[1], Shane A. Olwill[1]

[1]Pieris Pharmaceuticals, Inc., 255 State Street, Boston, Massachusetts; [2]Oncotest GmbH, Am Flughafen 12, Freiburg, Germany.

Abstract

Background. 4-1BB (CD137) is a potent costimulatory immunoreceptor and a highly promising target for immunostimulatory cancer therapy. Conventional 4-1BB-targeting antibodies, however, suffer from a lack of tumor-selective activity, which may lead to peripheral toxicity and reduce the available therapeutic window. To develop a therapeutic that facilitates a 4-1BB-based activation of T cells that is both tumor-target driven and tumor localized, we have generated PRS-343, a 4-1BB/HER2 bispecific. PRS-343 was made by genetic fusion of a 4-1BB-binding Anticalin® to modified trastuzumab. We have shown previously that PRS-343 targets 4-1BB and HER2 in a bispecific manner and efficiently activates T cells ex vivo in the presence of HER2-positive cells. Here, we present in vivo proof of concept data and tumor infiltrating lymphocyte (TIL) phenotyping.

Results. We tested PRS-343 efficacy in a humanized mouse model in immunocompromised mice using the SK-OV-3 cell line as a HER2-positive xenograft. The data indicate that PRS-343 displays dual activity based on monospecific HER2-targeting and bispecific, tumor-localized costimulation of 4-1BB. Tumor response was accompanied by a significantly higher frequency of hCD45(+) TIL's as determined by immunohistochemistry (IHC). TIL phenotyping indicated that the rise in TIL frequency was due to an expansion of CD3(+)CD8(+) T cells. Interestingly, we observed neither tumor growth inhibition nor an increase in human TIL's with the anti-4-1BB benchmark. In contrast to PRS-343, the anti-4-1BB benchmark displayed an increased toxicity due to accelerated graft-versus-host-disease (GvHD). The accelerated GvHD correlated with CD8+ T cell expansion in the peripheral blood. The data therefore support the concept that tumor-localized costimulatory T cell activation by a bispecific such as PRS-343 may lead to higher efficacy and reduced systemic toxicity compared to conventional anti-4-1BB mAbs.

Conclusion. The positive functional ex vivo and in vivo data of PRS-343 as well as the excellent developability profile support investigation of its anti-cancer activity in clinical trials. A first-in-patient study is planned to commence in the first half of 2017.

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

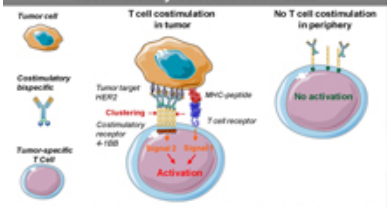


Figure 1. Concept of costimulatory T cell engagement by PRS-343: Within a patient's tumor, tumor-specific T cells are bridged with tumor cells by the costimulatory bispecific PRS-343 which simultaneously binds the tumor target HER2 and the immune receptor 4-1BB. The resulting clustering of 4-1BB provides 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.

Building block: Anticalin targeting 4-1BB

Discovery
- Phage display of lipocalin library against 4-1BB, followed by affinity maturation

Binding to 4-1BB
- K_D = 2.3nM (SPR)
- EC50(FACS) = 5.9nM
- Non-competitive binding vs 4-1BBL

Biophysical properties
- 100% monomeric expression
- T_M =74°C (DSC)
- Fully stable after 1 week at 37°C in PBS pH7.4, human plasma or mouse plasma

Functional activity
- Ex vivo activation of T cells when coated; no activation when in solution

PRS-343 was selected from four 4-1BB/HER2 bispecifics based on functionality

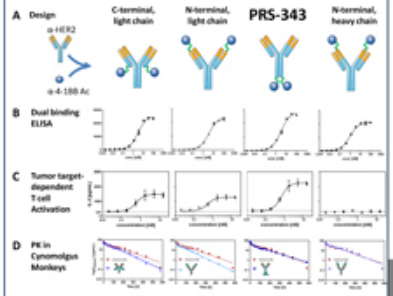
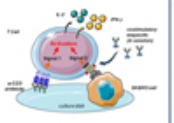
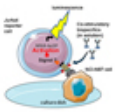


Figure 2. Design and selected functional data of four 4-1BB/HER2 bispecifics. (A) Design: genetic fusions of backbone-engineered trastuzumab to the anti-4-1BB Anticalin were generated to any of the four termini of the antibody. The IgG1 backbone of trastuzumab was exchanged for an engineered IgG4 backbone. (B) Dual binding: 4-1BB/HER2 bispecifics are capable of binding both targets at the same time according to Sandwich ELISA. (C) Ex vivo T cell activation: 4-1BB/HER2 bispecifics display different capabilities of eliciting IL-2 production by costimulatory engagement (see method description below). (D) Pharmacokinetics of PRS-343 compared to trastuzumab: male cynomolgus monkeys received test articles as an intravenous infusion at a dose of 3mg/kg. Drug levels were detected using Sandwich-ELISA.

Brief methods ex vivo T cell activation.
SKBR3 tumor cells were grown overnight on 96-well plates that had been precoated with anti-CD3 antibody. The next day, T cells purified from healthy donor PBMC were added to the wells together with the titrated 4-1BB/HER2 bispecific molecules (constructs A-D). After three days in culture, IL-2 and IFNg levels in the culture supernatants were measured by an electrochemoluminescence immunoassay.



PRS-343 activates 4-1BB pathway only in presence of HER2-expressing cells



Brief methods.
HER2^{high} expressing NCI-N87 tumor cells were grown overnight on 96-well plates. Jurkat NF-κB reporter cells, over-expressing 4-1BB and carrying a NF-κB-Luciferase reporter gene, were then added to the plates together with the titrated 4-1BB/HER2 bispecific construct PRS-343 (A) or anti-4-1BB benchmark mAb (B). After incubation, the T cell reporter signal was measured by luminescence. The impact of 4-1BB-targeting on 4-1BB downstream signaling was also investigated in the absence of tumor cells at a single concentration of 4-1BB agonists (10nM).

- 4-1BB downstream signaling activation by the 4-1BB/HER2 bispecific drug candidate PRS-343 was investigated by an NF-κB-luciferase reporter assay
- PRS-343 strongly activated the 4-1BB pathway in the presence of HER2^{high} NCI-N87 target cells; no activation occurred in the absence of NCI-N87 tumor cells
- An anti-4-1BB benchmark mAb activated the 4-1BB pathway both in the absence and presence of tumor cells

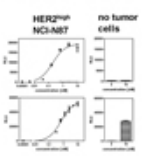


Figure 3. Activation of the 4-1BB signaling pathway in Jurkat T cells was measured by an NF-κB-Luciferase reporter assay. The luminescence signal was used as a relative measure of 4-1BB pathway activation. (A) PRS-343 drug candidate (solid line), negative control trastuzumab (light grey dashed line). (B) Anti-4-1BB benchmark mAb.

PRS-343 induces T cell activation when tumor HER2 levels are high, but not at physiological levels

- T cell activation assays were performed using the HER2^{high} SKBR3 and BT474 cell lines and cancer cell lines with HER2 expression levels that are similar to healthy tissue, HepG2 and MCF7
- IL-2 production was determined as a measure of T cell activation
- PRS-343 selectively leads to activation of T cells with SKBR3 and BT474 cells
- Anti-4-1BB benchmark mAb leads to T cell activation with all cell lines

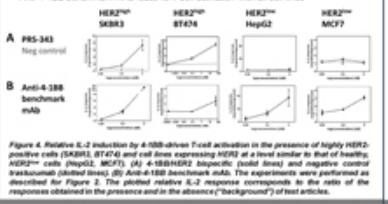


Figure 4. Relative IL-2 induction by 4-1BB-driven T cell activation in the presence of highly HER2-positive cells (SKBR3, BT474) and cell lines expressing HER2 at a level similar to that of healthy. HER2low cells (HepG2, MCF7). (A) 4-1BB/HER2 bispecific (solid lines) and negative control trastuzumab (dotted lines). (B) Anti-4-1BB benchmark mAb. The experiments were performed as described for Figure 2. The plotted relative IL-2 response corresponds to the ratio of the responses obtained in the presence and in the absence ("background") of test articles.

Activity in humanized mouse model: PRS-343 leads to TGI and increased hCD45-positive cells in tumor

- 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 different doses
- Control molecules were IgG4 isotype, an anti-4-1BB benchmark antibody and trastuzumab with an IgG4 backbone (Tras-IgG4)
- Tumor IHC staining for the human lymphocyte marker CD45 shows a dose-dependent increase in the frequency of human TIL for PRS-343, but not for controls, suggesting successful tumor-localized T cell activation by PRS-343
- PRS-343 showed dose-dependent tumor growth inhibition (TGI) comparable to Tras-IgG4, indicating that TGI is dominated by HER2 antagonism in this model

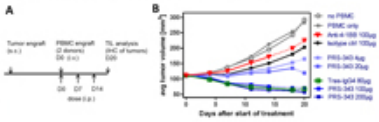


Figure 5. PRS-343 activity in NOG mice engrafted with HER-2 positive SK-OV-3 cell line and human PBMC. NOG mice were subcutaneously (s.c.) injected with SK-OV-3 cells and tumors were allowed to grow to an average of 120mm³ prior to randomization into treatment groups (n=10). Mice were engrafted with fresh human PBMC intravenously (i.v.) into a tail vein and treatment commenced 1 hour later. Mice received 3 weekly intraperitoneal (i.p.) doses of treatment (4µg, 20µg, 100µg or 200µg) or controls. Tumor growth was recorded twice weekly. Tumors from up to six mice were harvested on day 20 post treatment (anti-4-1BB benchmark mAb: day 17) and assessed for infiltration of human T cells by immunohistochemistry. (A) Graphical overview. (B) Median of tumor growth. Data points that no longer represent the full group size of 10 mice are connected by dotted lines.

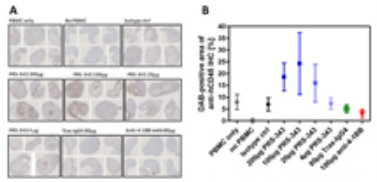


Figure 6. Immunohistochemistry of tumors after study end. (A) Sections of formalin-fixed and paraffin-embedded tumors (5 or 6 per group) were stained for human CD45. (B) The frequency of CD45+ cells was quantified by dedicated software. The data shows that PRS-343 induces a dose-dependent increase in the frequency of human CD45+ cells in the tumor compared to negative controls, while monospecific antibodies targeting HER2 (Tras-IgG4) or 4-1BB lack this activity.

PRS-343 leads to an expansion of CD8$^+$ T_{eff} cells in the tumor unlike 4-1BB mAb

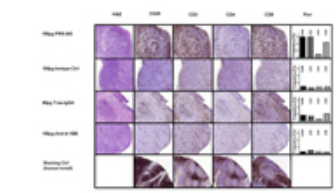


Figure 7. Phenotyping of tumors after study end by immunohistochemistry. Sections of formalin-fixed and paraffin-embedded tumors were stained for human CD45, CD3, CD4 and CD8. The frequency of marker positive cells was quantified by dedicated software. The data shows that PRS-343 induces an increase in the frequency of human CD8+ cells in the tumor compared to controls. H&E staining was also performed.

Safety in humanized mouse model: PRS-343 avoids CD8$^+$ T_{eff} expansion in periphery unlike 4-1BB mAb

- Anti-4-1BB mAb treatment led to accelerated graft-versus-host disease with significantly increased mortality compared to control and PRS-343 groups on day 20
- PBMC phenotyping results indicate that increased mortality induced by benchmark anti-4-1BB mAb is caused by strongly increased expansion of CD8$^+$ human effector T cells in anti-4-1BB group compared to control or PRS-343 groups

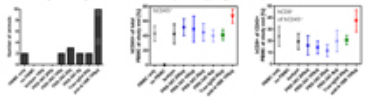


Figure 8. Mortality and PBMC phenotyping in humanized NOG mouse SK-OV-3 tumor model. (A) Mortality. Plotted values correspond to number of mice per group of ten that died spontaneously or needed to be sacrificed based on defined general condition criteria. (B) PBMC phenotyping. PBMC were isolated from mouse blood samples taken on day 20 after PBMC engraftment and analysed by multicolor FACS for human surface markers CD45, CD3 and CD8. PBMC from surviving animals of the group treated with anti-4-1BB benchmark mAb were phenotyped on day 17.

Summary

- **PRS-343 is a 4-1BB/HER2 bispecific based on the genetic fusion of a high-affinity 4-1BB-binding Anticalin and modified trastuzumab**
- **PRS-343 displays a differentiated profile when compared to a benchmark 4-1BB-targeting antibody**
  - **Reporter assay: PRS-343 leads to 4-1BB activation in presence of HER2-positive tumor cells, but not in their absence**
  - **Ex vivo: PRS-343 induces strong T cell activation via tumor target-dependent costimulatory T cell engagement**
  - **In vivo: PRS-343 displays dual activity based on monospecific HER2-targeting and bispecific, tumor-localized costimulation of 4-1BB, leading to increased density of CD8+ cells in the tumor**
  - **In vivo: PRS-343 avoids the systemic peripheral activation of CD8$^+$ T cells observed with benchmark 4-1BB antibody, which supports a better safety profile**
- **PRS-343 path to clinic: IND-enabling activities are ongoing with an anticipated first-in-patient study planned for the first half of 2017**

Parts of images on this poster based on material from Servier Medical Art under a Creative Commons Attribution 3.0 unported license.

Exhibit 99.2

PRESS RELEASE

PIERIS ANNOUNCES PRESENTATIONS AT UPCOMING R&D CONFERENCES

BOSTON, MA, October 20, 2016 – Pieris Pharmaceuticals, Inc. (NASDAQ:PIRS), a clinical-stage biotechnology company advancing novel biotherapeutics through its proprietary Anticalin® technology platform for cancer and other diseases, announced today presentations at two upcoming R&D conferences focused on immuno-oncology.

The details for each presentation are as follows:

American Association of Cancer Research (AACR) Special Conference on Tumor Immunology and Immunotherapy, Boston Marriott Copley Plaza, Boston, MA, October 20 – 23, 2016

Presentation Time: Friday, October 21, 2016, 5:15 pm-7:45 pm, Back Bay room

Presentation: A poster presentation entitled, "Costimulatory T-cell engagement by PRS-343, a CD137 (4-1BB)/HER2 bispecific, leads to tumor growth inhibition and CD8(+) T cell expansion in a humanized mouse model".

Society of Immunotherapy of Cancer (SITC), Gaylord National Hotel & Convention Center, National Harbor, Maryland, November 9 – 13, 2016

Oral Presentation: An oral presentation entitled "PRS-343, a CD137 (4-1BB)/HER2 Bispecific" will be given on Wednesday, November 9, 2016, 11:50 am

Poster Presentation: New Cancer Immunotherapy - A poster presentation will be presented on Saturday, November 12, 2016, 11:45 am – 1:00 pm and 6:45 pm – 8:00 pm

About Pieris

Pieris Pharmaceuticals is a clinical-stage biotechnology company that discovers and develops Anticalin® protein-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 protein to treat uncontrolled asthma and a half-life-optimized Anticalin protein to treat anemia. Proprietary to Pieris, Anticalin proteins 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. For more information visit www.pieris.com.

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