September 20, 2020

Pieris Pharmaceuticals Presents Updated Data from Phase 1 Monotherapy and Atezolizumab Combination Studies of 4-1BB/HER2 Bispecific PRS-343 at the European Society for Medical Oncology (ESMO) Virtual Congress 2020

- ***Clinical benefit in both trials, including one confirmed complete response and three partial responses in the monotherapy trial and four confirmed partial responses in the atezolizumab combination trial***
- ***Robust durability of response in both trials, including more than 18 months in the combination trial***
- ***Biomarker data, including substantial CD8+ T cell expansion and soluble 4-1BB increase, suggest 4-1BB-driven activity***

BOSTON, MA / ACCESSWIRE / September 20, 2020 /*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, today presented a clinical data update from the phase 1 monotherapy and atezolizumab combination studies of PRS-343, a 4-1BB/HER2 bispecific for the treatment of HER2-positive solid tumors, in an oral presentation at the European Society for Medical Oncology (ESMO) Virtual Congress 2020. PRS-343 continues to demonstrate durable clinical benefit in the active dose cohorts, including a confirmed complete response, in heavily pre-treated patients across multiple HER2-positive tumor types. Additionally, a significant expansion of CD8+ T cells in the tumor microenvironment of responders and a substantial increase of soluble 4-1BB were observed in the active dose cohorts, suggesting 4-1BB-mediated target engagement driving clinical benefit. PRS-343 also shows an acceptable safety profile at all doses and schedules tested in each clinical study. The Company reaffirms its commitment to moving PRS-343 into a phase 2 trial in second-line gastric cancer in combination with paclitaxel and ramucirumab.

"PRS-343 has shown remarkable clinical benefit in the treatment of patients who have cancers that are refractory to standard treatments. I am particularly impressed with the single-agent activity in these heavily pre-treated patients as well with as the durability of response," said Geoffrey Y. Ku, MD, Assistant Attending and Head, Esophagogastric Section, Gastrointestinal Oncology Service at Memorial Sloan Kettering and a principal

investigator for the PRS-343 monotherapy trial. "I look forward to assessing the benefit of PRS-343 in combination with standard of care therapy, ramucirumab and paclitaxel, in second line HER2-positive gastric cancer."

The phase 1 first-in-human, open-label multicenter monotherapy trial has enrolled 74 patients, including 21 additional patients enrolled in higher dose cohorts (≥2.5 mg/kg) since the data presented at the Society for Immunotherapy of Cancer (SITC) 2019 Annual Meeting. Thirteen dose levels have been evaluated, 11 of which have been evaluated at a Q3W dosing schedule. The 11th dose level (8 mg/kg) has also been evaluated at a Q2W dosing schedule, including a Q2W dosing schedule in combination with obinutuzumab, and at a Q1W dosing schedule. The 12th (12 mg/kg) and 13th (18 mg/kg) dose levels have been evaluated exclusively at a Q2W dosing schedule.

The phase 1 first-in-human, open-label multicenter atezolizumab combination trial has enrolled 41 patients. Seven dose cohorts have been evaluated at a Q3W dosing schedule ranging from 0.05 mg/kg to 8 mg/kg in combination with a fixed 1200 mg dose of atezolizumab.

Primary objectives of both trials include characterizing the safety profile of PRS-343 in monotherapy or in combination with atezolizumab and identifying the maximum tolerated dose (MTD) and/or the recommended phase 2 dose (RP2D) of PRS-343 alone and in combination with atezolizumab. Secondary objectives include assessing potential immunogenicity and pharmacodynamic effects, characterizing the pharmacokinetic profile, investigating a dosing schedule, and investigating efficacy.

As of the cut-off date of July 27, 2020, 33 patients in the monotherapy trial and 29 patients in the atezolizumab combination trial were evaluable for a response at active dose levels in the trials, which began at cohort 9 (2.5 mg/kg) in the monotherapy trial and cohort 4 (1 mg/kg) in the atezolizumab combination trial.

- In the monotherapy study, one patient with stage 4 rectal adenocarcinoma achieved a confirmed complete response at the 18 mg/kg Q2W dose level and three patients achieved a partial response at the 8 mg/kg Q2W dose level.
- In the atezolizumab combination trial, four patients achieved a confirmed partial response at active dose levels.
- Across the active dose levels and schedules, 13 patients in the monotherapy trial and 8 patients in the atezolizumab combination trial experienced stable disease.
- As of the cutoff date, treatment duration across active dose levels is over 66 weeks in the monotherapy trial and over 78 weeks in the atezolizumab combination trial for at least one patient.
- Post-treatment increases in CD8+ Tumor Infiltrating Lymphocytes and blood-based s4-1BB suggest clinical benefit is linked to 4-1BB activity
- Treatment-related adverse events (TRAEs) in both trials were primarily grade 1 and 2. The most common TRAEs in the monotherapy trial were infusion-related reactions. Less than 6% of TRAEs in the monotherapy trial were grade 3, and one TRAE in that trial was grade 4 (infusion-related reaction). The most common TRAEs in the atezolizumab combination trial were infusion-related reactions and vomiting. Less than 6% of TRAEs in the atezolizumab combination trial were grade 3, and there were two grade 3 or above events (grade 4 AST increase and grade 3 transaminitis that became

grade 5 hepatic failure).

"The newly presented data reinforce our conviction in the significant potential of PRS-343, the only HER2-targeted adaptive immune system engager in clinical development, to improve the lives of patients with few treatment options," said Stephen S. Yoder, President and Chief Executive Officer of Pieris. "In addition to showing single-agent clinical benefit, including complete response, PRS-343 continues to show impressive durability of response. Furthermore, the biomarker data are consistent with a 4-1BB mechanism of action, validating our 4-1BB bispecific approach. We look forward to completing the in-use studies necessary for resolution of the partial hold and beginning the phase 2 trial of PRS-343 in combination with ramucirumab and paclitaxel alongside our clinical trial collaborator Eli Lilly and Company."

A copy of the presentation is available at thislink.

***About PRS-343**:*

PRS-343 is a 4-1BB/HER2 fusion protein comprising a 4-1BB-targeting Anticalin protein and a HER2-targeting antibody. The drug candidate is currently in development for the treatment of HER2-positive solid tumors. Ongoing phase 1 studies of PRS-343 include a monotherapy study and a combination study with atezolizumab. Based on encouraging initial results from both studies, which demonstrated clinical benefit and biomarker data indicative of a 4-1BB-driven mechanism of action, the Company is actively working towards completing the required in-use studies, resolving the partial hold and initiating a phase 2 study of PRS-343 in combination with ramucirumab and paclitaxel for the treatment of HER2-positive gastric cancer in a second line setting.

***About Pieris Pharmaceuticals**:*

Pieris 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 inhalable Anticalin proteins to treat respiratory diseases and immuno-oncology multi-specifics tailored for the tumor microenvironment. Proprietary to Pieris, Anticalin proteins are a novel class of 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.

Forward Looking Statement:

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, the timing for, and outcome of, the additional in-use and compatibility study for PRS-343 as requested by the FDA; whether data from patients enrolled to date will be sufficient to inform the recommended phase 2 dose for the Company's planned proof of concept study of PRS-343 in gastric cancer; 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 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, PRS-343, PRS-344, and PRS-352 and the expected timing of the initiation of the next stage of PRS-343'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 FDA, including with respect to the additional in-use and compatibility study for PRS-343, and the resolution of the partial clinical hold relating to that drug candidate; 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 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, 2019 and the Company's Quarterly Reports on Form 10-Q.

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