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 10, 2021

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

Nevada	**001-37471**	**30-0784346**
(State or other jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

225 State Street, 9th Floor	**02109**
Boston, MA	
(Address of principal executive offices)	**(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 and incorporated by reference herein are: The Cinrebafusp Alfa American Association for Cancer Research (AACR) Presentation, Dated April 2021 (Exhibit 99.1), the PRS-344 AACR Presentation, Dated April 2021 (Exhibit 99.2), a Press Release of Pieris Pharmaceuticals, Inc., Dated April 10, 2021 (Exhibit 99.3), and the April 2021 Investor Presentation of Pieris Pharmaceuticals, Inc. (Exhibit 99.4).

The information set forth under this "Item 7.01. Regulation FD Disclosure," including Exhibits 99.1, 99.2, 99.3, and 99.4 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 9.01 Financial Statements and Exhibits
(d) Exhibits.

99.1 Cinrebafusp Alfa AACR Presentation, Dated April 2021.

99.2 PRS-344 AACR Poster, Dated April 2021.

99.3 Press Release, Dated April 10, 2021.

99.4 Investor Presentation, Dated April 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.

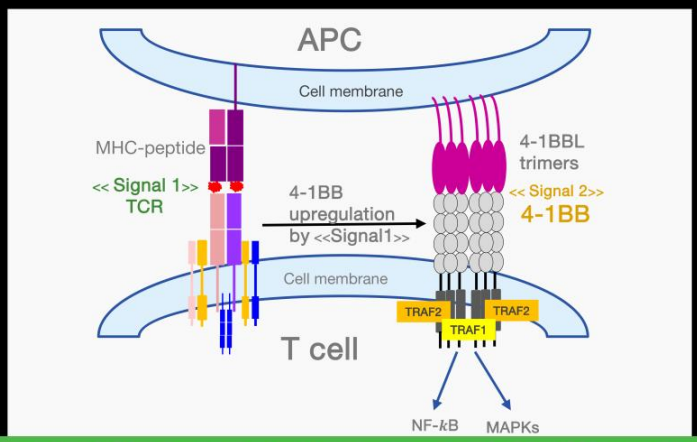
Dated: April 12, 2021

/s/ Tom Bures
Tom Bures
Vice President, Finance

Phase 1 Dose Escalation Study of PRS-343, a HER2/4-1BB Bispecific Molecule, in Patients with HER2+ Malignancies

Sarina Piha-Paul, MD
University of Texas, MD Anderson Cancer Center
Houston, TX


American Association



- Proliferation
- Cytotoxicity
- Cytokine Secretion
- Th1 Polarization
- Memory Formation
- T cell Survival
- Resistance to Exhaustion
- Metabolic Fitness

Pieris' 4-1BB bispecific strategy recognize that 4-1BB agonists have proven clinical potency, yet activity must be localized in order to minimize toxicity and ensure suitable therapeutic index

PRS-343 (Cinrebafusp alfa): HER2 x 4-1BB Bispecific

Drives 4-1BB Agonism in the Tumor Microenvironment of HER2+ Solid Tumors

American Association for Cancer Research®
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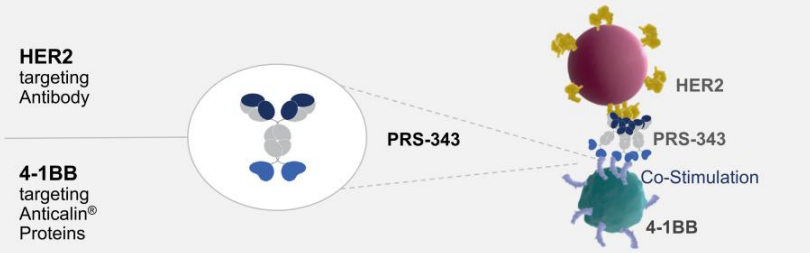
HER2-targeting moiety of the drug localizes to the tumor microenvironment and facilitates 4-1BB cross-linking

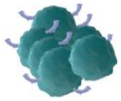
4-1BB cross-linking ameliorates T-cell exhaustion and is critical for T-cell expansion

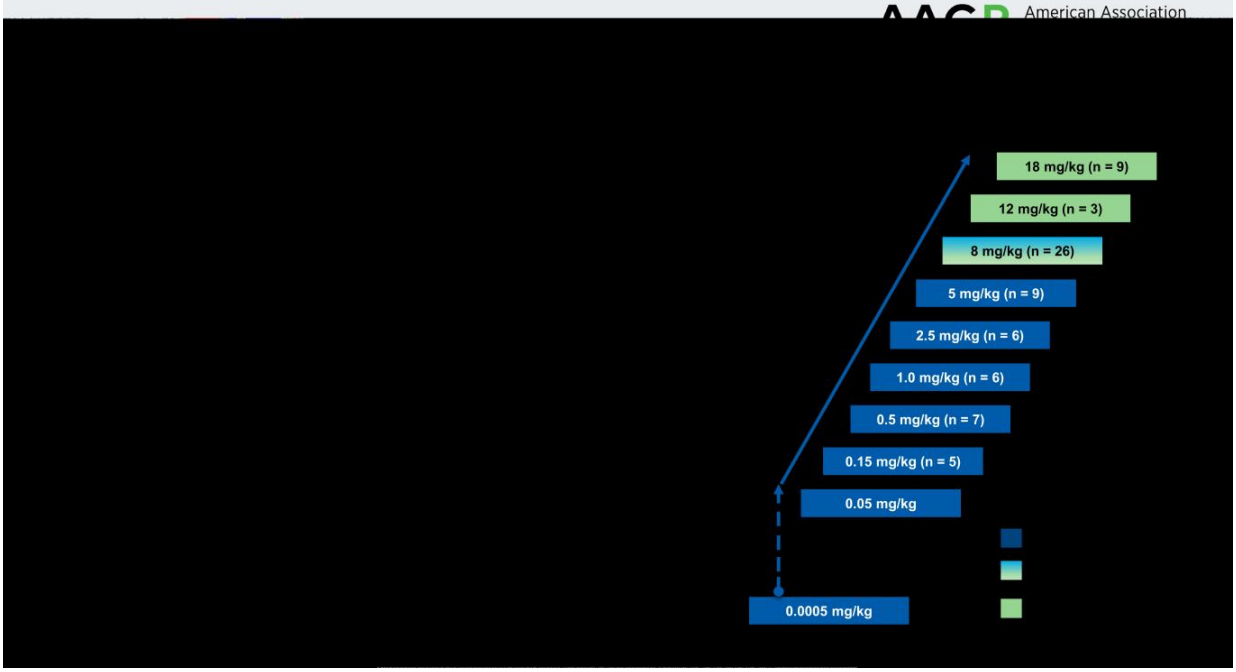


CLINICALLY-RELEVANT BIOMARKERS

4-1BB Pathway Activation
Soluble 4-1BB

T-cell Proliferation
$CD8^+$ and $CD8^+/Ki67^+$




18 mg/kg (n = 9)
12 mg/kg (n = 3)
8 mg/kg (n = 26)
5 mg/kg (n = 9)
2.5 mg/kg (n = 6)
1.0 mg/kg (n = 6)
0.5 mg/kg (n = 7)
0.15 mg/kg (n = 5)
0.05 mg/kg
0.0005 mg/kg

Characteristic	n (%)
Age, Median (range)	63 (24–92)
Gender	
F	46 (59%)
M	32 (41%)
ECOG PS	
0	19 (24%)
1	59 (76%)
Prior Therapy Lines	
1	11 (14%)
2	10 (13%)
3	16 (21%)
4	12 (15%)
5+	29 (37%)
Median # of anti-HER2 Tx	
Breast	6
Gastric	2

Primary Cancer Type	n (%)
Gastroesophageal	34 (44%)
Breast	16 (21%)
Colorectal	12 (15%)
Gynecological	9 (12%)
Bladder	2 (3%)
Pancreatic	1 (1%)
Other – Cancer of Unknown Origin	2 (3%)
Other – Salivary Duct	1 (1%)
Melanoma	1 (1%)

PRS-343 Treatment Related Adverse Events at Active Doses (≥ 2.5 mg/kg)

Treatment Related Adverse Events (TRAEs occurring in > 1 patient; n = 53)	All Grades n (%)	Grade 1-2 n (%)	Grade 3-4 n (%)
Infusion related reaction	13 (25%)	9 (17%)	4 (8%)
Nausea	7 (13%)	7 (13%)	
Chills	6 (11%)	6 (11%)	
Vomiting	6 (11%)	6 (11%)	
Dyspnoea	4 (8%)	4 (8%)	
Fatigue	4 (8%)	4 (8%)	
Arthralgia	3 (6%)	2 (4%)	1 (2%)
Decreased appetite	3 (6%)	3 (6%)	
Non-cardiac chest pain	3 (6%)	3 (6%)	
Asthenia	2 (4%)	2 (4%)	
Diarrhoea	2 (4%)	2 (4%)	
Dizziness	2 (4%)	2 (4%)	
Headache	2 (4%)	2 (4%)	
Paraesthesia	2 (4%)	1 (2%)	1 (2%)
Pruritus	2 (4%)	2 (4%)	
Pyrexia	2 (4%)	2 (4%)	
Rash	2 (4%)	2 (4%)	

1 Gr 3 Ejection Fraction dec and 1 Gr 3 Heart Failure; both events occurred in one patient and resolved w/o sequelae.

PRS-343 Efficacy Data Overview

AACR American Association for Cancer Research
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Cohort	13b	12b	11c	Obi	11b	11	10	9	Total
Best Response	18 mg/kg, Q2W	12 mg/kg, Q2W	8 mg/kg, QW	8 mg/Kg, Q2W	8 mg/kg, Q2W	8 mg/kg, Q3W	5 mg/kg, Q3W	2.5 mg/kg, Q3W	
Evaluable Patients	8	2	5	4	7	4	7	5	42
CR	1								1
PR	1				3				4
SD	3		1	2	3	3	3	2	17
ORR	25%	0%	0%	0%	43%	0%	0%	0%	12%
DCR	63%	0%	20%	50%	86%	75%	43%	40%	52%

PRS-343 Efficacy Data:
Analysis of Patients Treated at Active Doses

American Association for Cancer Research
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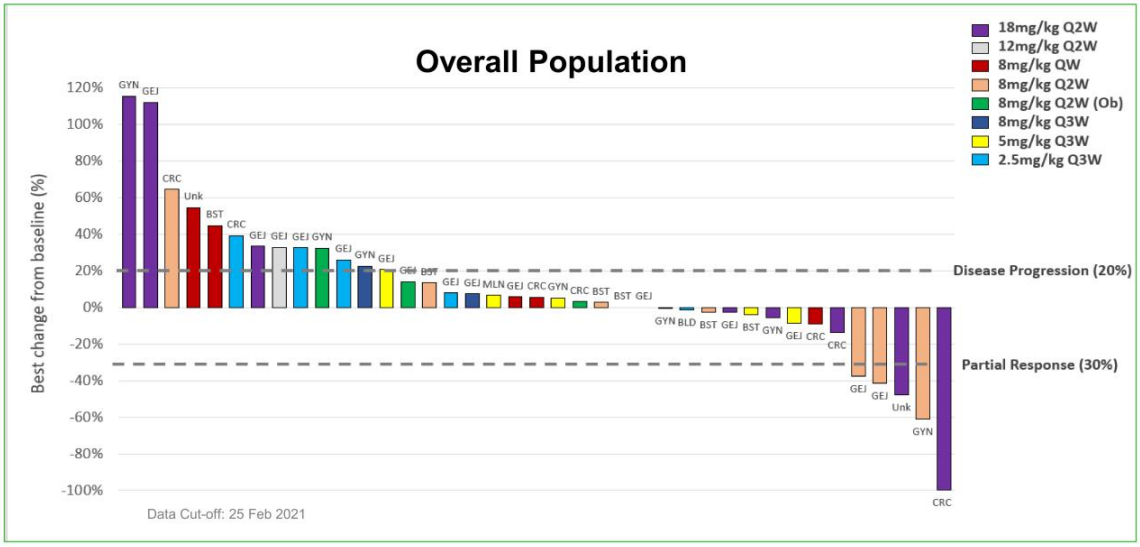
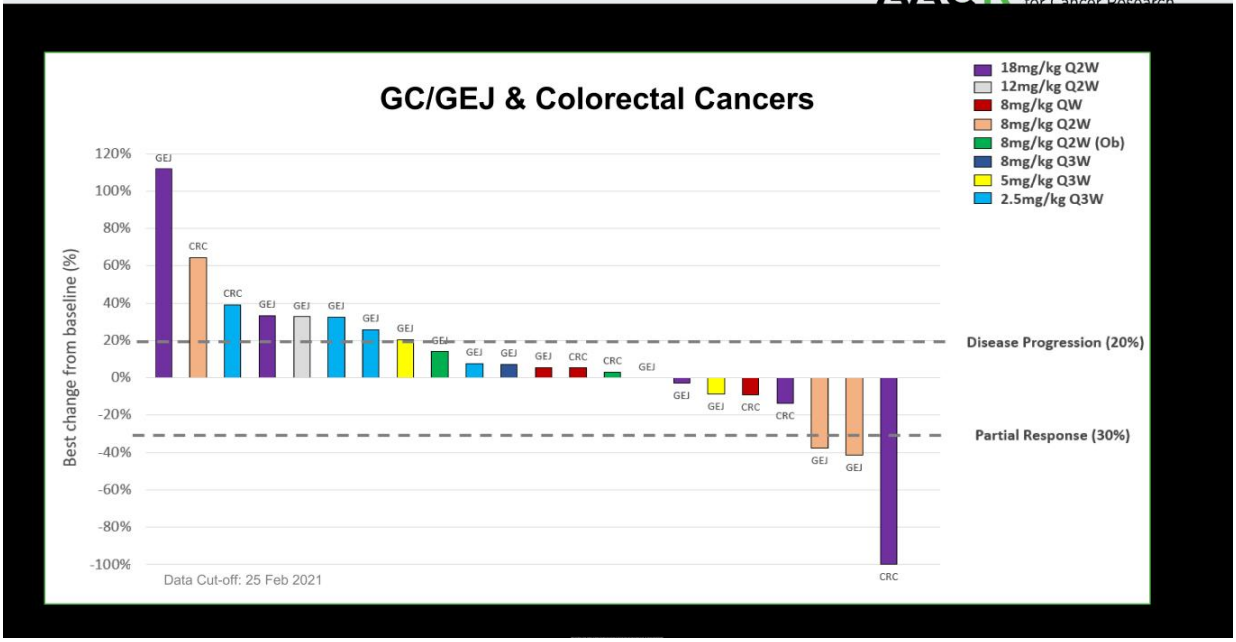


PRS-343 Efficacy Data:



Durable Responses with PRS-343 among Heavily Pre-treated Population

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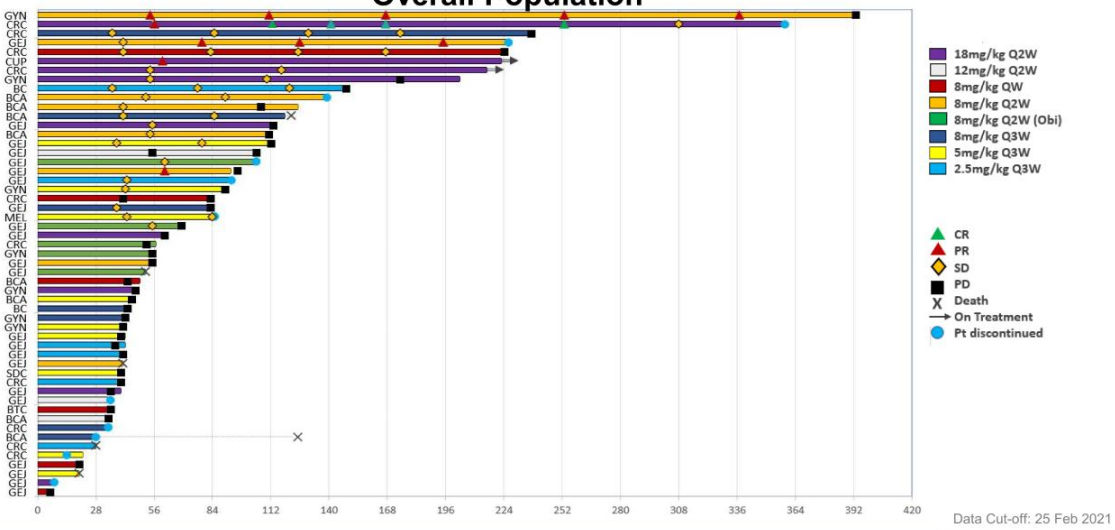
Overall Population



Data Cut-off: 25 Feb 2021

PRS-343 Generates Immunogenic Responses

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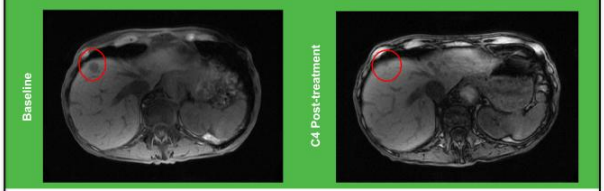
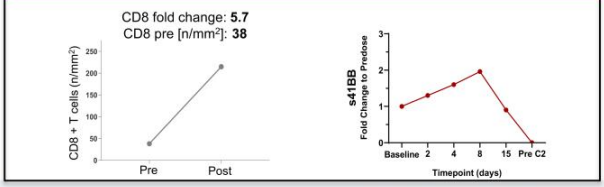
Gastric Cancer Patient with Partial Response
- 80-year-old woman; initial diagnosis in June 2017
- Gastric adenoca with mets to liver, LN and adrenals
- Treated with 8 mg/kg Q2W of PRS-343
- HER2 IHC 3+; PD-L1 positive (CPS=3) ; NGS: ERBB2 amplification

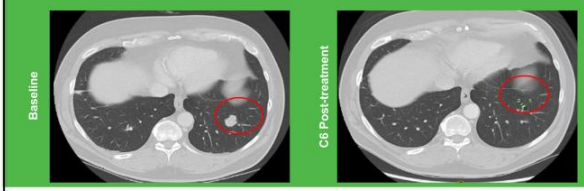
Prior Treatment includes:
- Trastuzumab, Pembrolizumab + Capecitabine/oxaliplatin
- Nivolumab with IDO1 inhibitor (investigational drug)

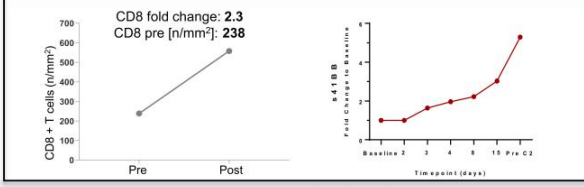




Rectal Cancer Patient with Complete Response
- 59-year-old male; initial diagnosis in March 2017
- Rectal cancer with cardiac and lung mets
- Treated with 18 mg/kg Q2W of PRS-343
- Foundation One Her2 amplification; verified in-house to be IHC 3+; MSS, TMB low

Prior Treatment includes:
- 5FU/Avastin maintenance
- Irinotecan/Avastin & SBRT





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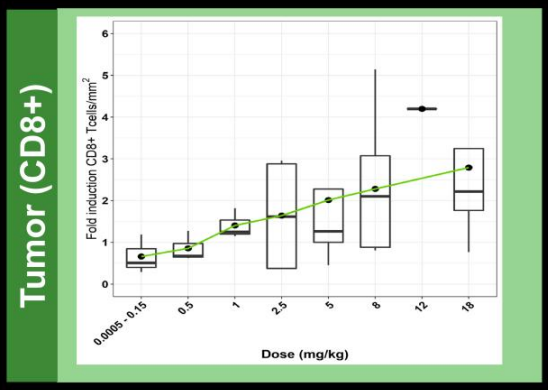
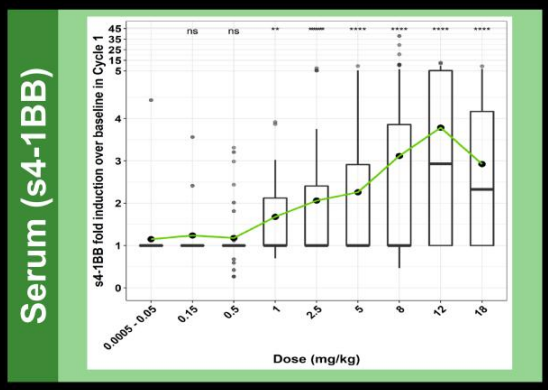
PRS-343 Shows Dose Dependent Activity





— Connects group averages Median Mann-Whitney U test Dose at 8 mg/kg incorporates patients treated at Q1W, Q2W or Q3W

PRS-343 Activates Adaptive and Innate Immunity in the Tumor

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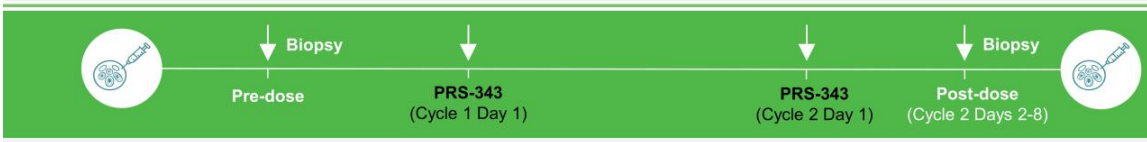
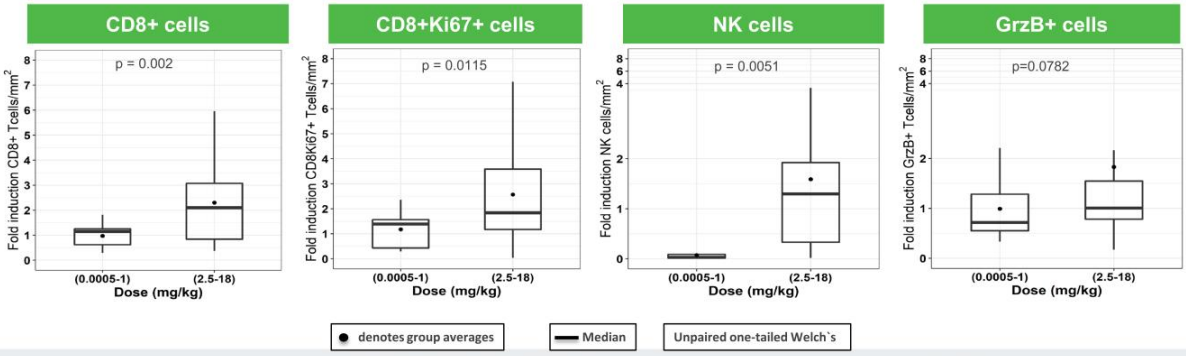


Based on preclinical and clinical data, serum concentration of > 20 µg/ml defines active dose range beginning at 2.5 mg/kg (Cohort 9)



AACR ANNUAL MEETING 2021: APRIL 10-15, 2021 AND MAY 17-21, 2021

PRS-343 Shows Clinical Activity in Both "Hot" and "Cold" Tumors

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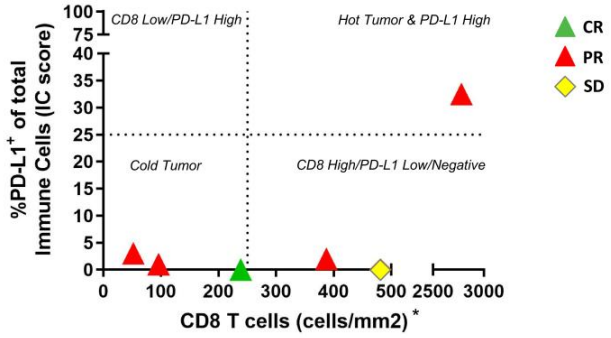
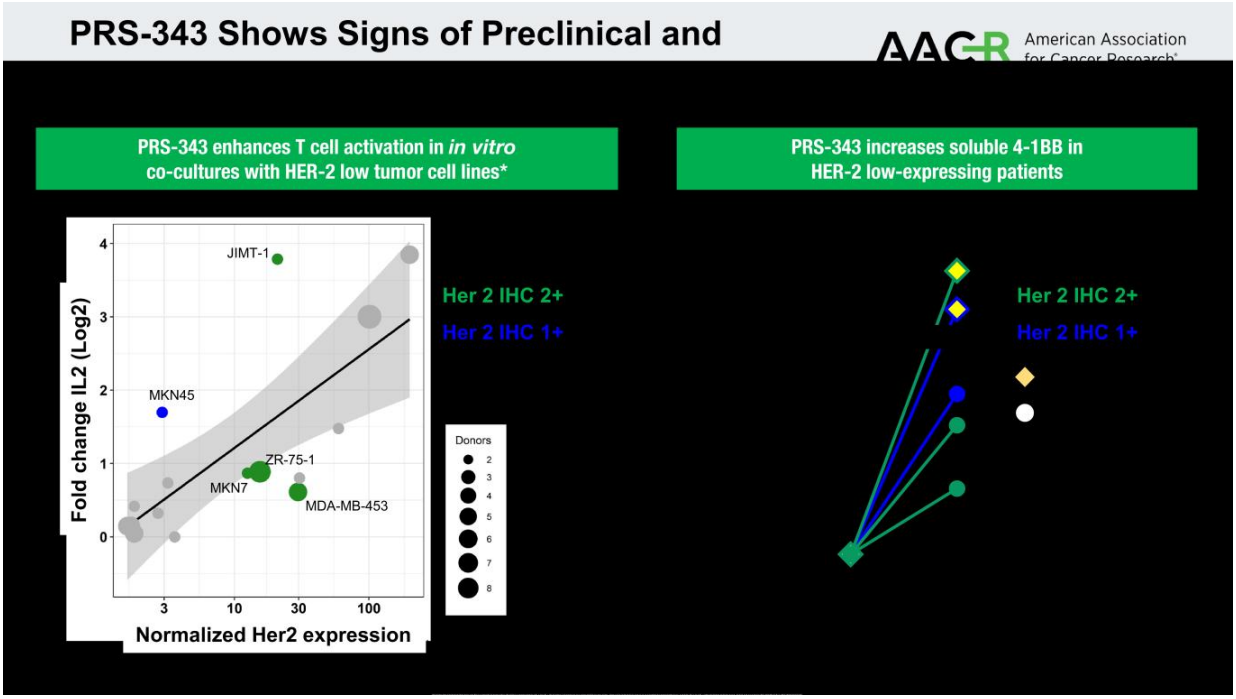
PD-L1 status and CD8+ T cells levels in tumor biopsies



* Threshold informed by (Tumeh et al., 2014 and Blando et al., 2019)

Several patients with clinical benefit have low/negative PD-L1 status and low CD8 T cell numbers


PRS-343 Shows Signs of Preclinical and
American Association for Cancer Research
PRS-343 enhances T cell activation in *in vitro* co-cultures with HER-2 low tumor cell lines*
PRS-343 increases soluble 4-1BB in HER-2 low-expressing patients
Fold change IL2 (Log2)
Normalized Her2 expression
JIMT-1
MKN45
ZR-75-1
MKN7
MDA-MB-453
Donors
Her 2 IHC 2+
Her 2 IHC 1+
Her 2 IHC 2+
Her 2 IHC 1+


American Association


American Association
Patients, their families and caregivers
Investigators, as well as their site personnel
Pieris Pharmaceuticals Team

Simultaneous costimulatory T-cell engagement and checkpoint inhibition by PRS-344/S095012, a 4-1BB/PD-L1 bispecific compound for tumor-localized activation of the immune system

Aizea Morales-Kastresana[1*], Lucia Pattarini[2*], Marina Pavlidou[1*], Janet K. Peper-Gabriel[1*], Christian Barthels[1], Eva-Maria Hansbauer[1], Rachida Bel Aiba[1], Birgit Bossenmaier[1], Alix Scholer-Dahirel[2], Thomas Jaquin[1], Catherine Gallou[2], Véronique Blanc[2], Christine Rothe[1], Shane A Olwill[1]

[1]Pieris Pharmaceuticals GmbH, Zeppelinstrasse 3, 85399 Hallbergmoos - Germany
[2]Institut de Recherches Servier Oncology R&D Unit, Croissy Sur Seine, France
*Co-authors / equally contributing authors

INTRODUCTION

- 4-1BB (CD137) is a key co-stimulatory immunoreceptor and a promising oncology target.
- Peripheral immune activation by 4-1BB agonistic antibodies has been associated with on-target toxicity and a limited therapeutic window.
- To overcome 1st generation 4-1BB agonist safety and efficacy drawbacks, we have generated PRS-344/S095012, a 4-1BB/PD-L1 bispecific Anticalin® protein/mAb fusion protein (Figure 1) designed to have a 4-1BB localized activity, while also offering the benefit of checkpoint inhibition (Figure 2).
- Here we describe the preclinical in vitro and in vivo activity of PRS-344/S095012.

This program is part of the strategic alliance between Pieris and Servier.

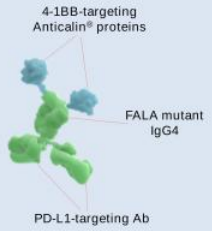


Figure 1. Structure of PRS-344/S095012

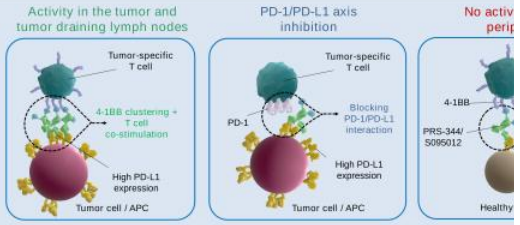


Figure 2. PRS-344/S095012 dual MoA: selective activation of 4-1BB+ T cells in F and/or antigen-presenting cells in the tumor microenvironment or tumor-draining ly and blocking of the PD-1 / PD-L1 interaction. No clustering of 4-1BB is expected ir

PRS-344/S095012 is capable of dual target engagement

- PRS-344/S095012 binds to 4-1BB and PD-L1 in a comparable way to the respective single building blocks and can bind both targets simultaneously.
- PRS-344/S095012 effectively blocks the PD-1/PD-L1 binding and shares an overlapping 4-1BB-binding epitope with a clinically active anti-4-1BB benchmark mAb.

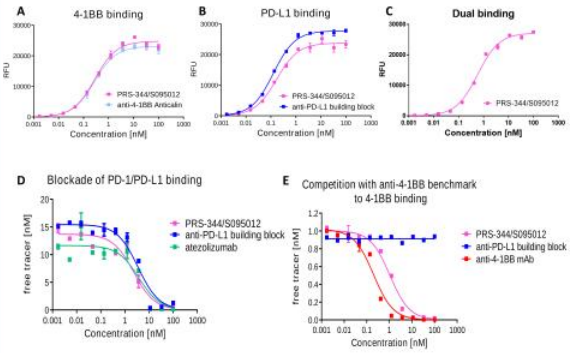


Figure 3. Binding A,B) Direct binding to human recombinant 4-1BB and PD-L1 C) Simultaneous binding of PRS-344/S095012 to 4-1BB and PD-L1. D) Blockade of PD-1/PD-L1 interaction. E) Competition with an anti-4-1BB benchmark mAb. All experiments were conducted with an ELISA-based approach

PRS-344/S095012 stimulates activated T cells in a PD-L1-dependent fashion and enhances their proinflammatory and cytotoxic potential

- PRS-344/S095012-mediated co-stimulation is strictly PD-L1 dependent and only occurs upon TCR engagement, reducing the risk of periph
- PRS-344/S095012 stimulates the release of cytotoxic molecules and cytokines from activated antigen-specific CD8 T cells or polyclonal T
- The in vitro functional activity of PRS-344/S095012 is superior to single agent anti-PD-L1 or benchmark anti-4-1BB mAb.
- Engagement of PDL1 and 4-1BB through PRS-344/S095012 bispecific is superior to combination of PD-L1 and 4-1BB mAbs.

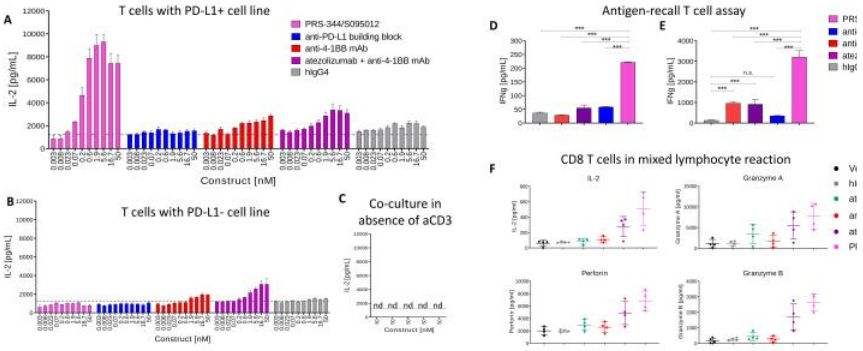
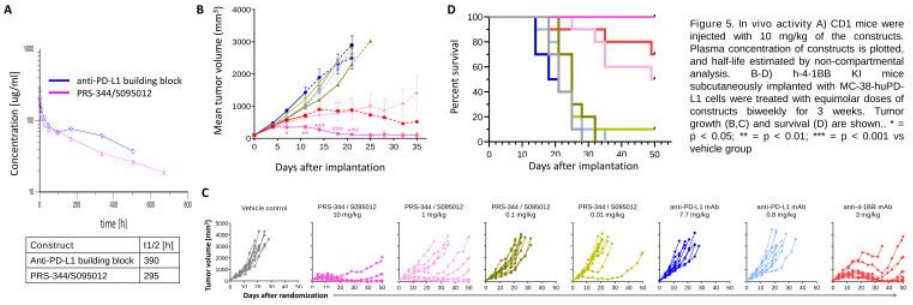


Figure 4. In vitro activity A-C) Co-culture assay: human T cells with coated anti-CD3 mAb and tested constructs co-cultured with A) hPD-L1 positive CHO cells or B) control CHO c CD3 as a negative control. n.d., not detected. D-E) Recall assay of human PBMCs stimulated with a peptide pool with the indicated constructs or (D), pre-expanded with a peptide p with the peptide pool plus the indicated constructs (E). Data is shown as mean ± SEM, n.s= non-significant, ***, P < 0.01. F) Mixed lymphocyte reaction: CD8 T cells from healthy bloc with monocyte-derived dendritic cells from another healthy blood donor.

PRS-344/S095012 displays Ab-like PK in mice and drives a strong anti-tumoral activity superior to anti-PD-L1 mAb

- The mAb-like half-life of the anti-PD-L1 mAb building block is preserved within PRS-344/S095012.
- PRS-344/S095012 triggers a dose-dependent antitumoral response that leads to a significant extension of survival in a humanized KI model.
- Complete regression of implanted tumors is observed in 5 out of 10 mice treated with the highest dose of PRS-344/S095012.
- PRS-344/S095012 is superior to equimolar doses of anti-PD-L1 mAb treatment alone.



Construct	t1/2 [h]
Anti-PD-L1 building block	390
PRS-344/S095012	295

Figure 5. In vivo activity A) CD1 mice were injected with 10 mg/kg of the constructs. Plasma concentration of constructs is plotted, and half-life estimated by non-compartmental analysis. B-D) h-4-1BB KI mice subcutaneously implanted with MC-38-huPD-L1 cells were treated with equimolar doses of constructs biweekly for 3 weeks. Tumor growth (B,C) and survival (D) are shown.. * = p < 0.05; ** = p < 0.01; *** = p < 0.001 vs vehicle group

Conclusions

- PRS-344/S095012 is a 4-1BB / PD-L1 bispecific, generated b fusion of a 4-1BB-binding Anticalin® protein and an anti-PD-L1 m
- PRS-344/S095012-mediated 4-1BB activation is PD-L1-depende reducing the risk of peripheral toxicity. Furthermore, 4-1BB co-st occurs in combination with simultaneous TCR signaling, stimulation to antigen-specific T cells.
- PRS-344/S095012 induces an effective CD8 T cell respons secretion of inflammatory cytokines and cytotoxic molecules.
- PRS-344/S095012 displays mAb-like pharmacokinetics in mice.
- PRS-344/S095012 induces a dose-dependent anti-tumor respons model setup refractory to anti-PD-L1 and significantly extends t mice.
- Preclinical data support clinical evaluation of PRS-344/S095012.

ACKNOWLEDGEMENTS - We would like to especially thank to the scientis assistants that performed these experiments: Maximilien Grandclaudon, Celine Sa Riviere, Christina Grasmüller, Nicole Andersen, Linda Schnapp, Markus Rehle and well as Marlon Hinner and Louis Matis for their support with original concept.

April 10, 2021

Pieris Pharmaceuticals Presents Updated Phase 1 Monotherapy Data for 4-1BB/HER2 Bispecific Cinrebafusp Alfa and Preclinical Data for 4-1BB/PD-L1 Bispecific PRS-344/S095012 at 2021 AACR Annual Meeting

- **Additional, ongoing confirmed durable partial response and three additional patients with stable disease as best response at the highest dose cohort of cinrebafusp alfa**
- **Durable anti-tumor activity in heavily pre-treated patient population including "cold" and HER2-low expressing tumors**
- **Dose-dependent immune activation and 4-1BB modulation in both HER2-high and HER2-low expressing patients**
- **PRS-344/S095012 preclinical data show that the drug candidate induces a dose-dependent anti-tumor response in an anti-PD-L1-resistant mouse model**

BOSTON, MA / ACCESSWIRE / April 10, 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, today presented a clinical data update from the phase 1 monotherapy study of cinrebafusp alfa (PRS-343), a 4-1BB/HER2 bispecific for the treatment of HER2-expressing solid tumors, in an oral presentation at the American Association for Cancer Research (AACR) Virtual Congress 2021. The Company also presented preclinical data for PRS-344/S095012, a 4-1BB/PD-L1 bispecific the Company is developing with Servier, at a poster session at the congress.

Cinrebafusp Alfa (PRS-343):

Presented data demonstrated additional clinical benefit at the highest dose, including an additional, ongoing confirmed durable partial response, three additional patients with stable disease as best response, and overall durable benefit. Based on clinical benefit and pharmacodynamic correlates, cinrebafusp alfa showed a clear dose response and a 4-1BB-driven mechanism of action. Additionally, clinical benefit was observed in patients with "cold" tumors as well as those with HER2-low expressing tumors. Cinrebafusp alfa continues to be well-tolerated. The Company plans to initiate a phase 2 study in gastric cancer this summer that will evaluate both HER2-high and HER2-low patient settings.

As of the cut-off date of February 25, 2021, 8 patients in the monotherapy trial were

evaluable for a response at the highest dose cohort (cohort 13b; 18 mg/kg Q2W) out of a total of 42 response-evaluable patients enrolled in the predicted active dose cohorts (cohort 9 and higher; ≥2.5 mg/kg) in the study.

- In cohort 13b, one additional patient (cancer of unknown primary) achieved an ongoing confirmed durable partial response, for an updated overall response rate (ORR) of 25% in that cohort as compared to an ORR of 12% across active dose levels.
- In cohort 13b, three additional patients experienced stable disease as best response, for an updated disease control rate (DCR) of 63% in that cohort as compared to a DCR of 52% across active dose levels.
- Cinrebafusp alfa activates adaptive and innate immunity in the tumor microenvironment, consistent with intended mode of action as evidenced by post-treatment increases in CD8+ T cells, NK cells and cytotoxic activity.
- Dose-dependent increases of CD8+ T cells in the tumor and soluble 4-1BB in the blood of patients demonstrate target engagement and a 4-1BB-driven mode of action.
- Cinrebafusp alfa shows preliminary evidence of activity among "cold" tumor types as well as "hot" tumor types.
- Activity in HER2-low expressing patients supports continued development of cinrebafusp alfa in that population, which the Company will evaluate in its phase 2 gastric cancer study.
- Cinrebafusp alfa monotherapy appeared to be well-tolerated up to 18 mg/kg, with no significant specific anti-HER2 or anti-4-1BB safety signal and no dose limiting toxicity identified.

The cinrebafusp alfa data presented at AACR can be found in an updated corporate presentation at https://ir.pieris.com.

PRS-344S095012:

The synergistic preclinical data presented for PRS-344/S095012 demonstrate PRS-344/S095012 is superior to the combination of PD-L1- and 4-1BB-targeting molecules. In an anti-PD-L1-resistant mouse model, the drug candidate induces a dose-dependent anti-tumor response and significantly extends survival. *In vitro*, PRS-344/S095012 enhances effective CD8+ T cell response and proinflammatory cytokine release.

PRS-344/S095012-mediated 4-1BB activation is strictly PD-L1 dependent, reducing the risk of peripheral toxicity. Furthermore, 4-1BB co-stimulation only occurs in combination with simultaneous TCR signaling, restricting its activity to antigen-specific T cells. PRS-344/S095012 also displays mAb-like pharmacokinetics in mice.

These data support further development of PRS-344/S095012, for which the phase 1 study is expected to begin this year.

A copy of the poster is available atthis link.

"The matured data from the highest dose cohort of cinrebafusp alfa demonstrate a clear dose-dependent response that supports our recommended phase 2 dose, and the biomarker data generated across all active dose cohorts demonstrate that cinrebafusp alfa activity is 4-1BB-driven and that the drug candidate is active not only in HER2-high expressing tumors, but also HER2-low expressing tumors - a significant opportunity and

unmet medical need that we are excited to pursue in our upcoming phase 2 study," said Stephen S. Yoder, President and Chief Executive Officer of Pieris. "Separately, we are pleased with the clear evidence of dose-dependent synergistic anti-tumor effects of PRS-344/S095012, as well as further evidence for its tumor-localized mechanism of action, and we look forward to moving this asset into the clinic this year. By its design, this bispecific has best-in-class potential in the 4-1BB/PD-L1 arena."

About Cinrebafusp Alfa:

Cinrebafusp alfa (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. Based on encouraging phase 1 study results, which demonstrated clinical benefit as single agent and biomarker data indicative of a 4-1BB-driven mechanism of action, the Company is actively working towards initiating a phase 2 study of cinrebafusp alfa in combination with ramucirumab and paclitaxel for the treatment of HER2-high expressing gastric cancer and in combination with tucatinib in HER2-low expressing gastric cancer.

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, 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 cinrebafusp alfa 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, 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; 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, 2020 and the Company's Quarterly Reports on Form 10-Q.

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View source version on accesswire.com:
https://www.accesswire.com/639834/Pieris-Pharmaceuticals-Presents-Updated-Phase-1-Monotherapy-Data-for-4-1BBHER2-Bispecific-Cinrebafusp-Alfa-and-Preclinical-Data-for-4-1BBPD-L1-Bispecific-PRS-344S095012-at-2021-AACR-Annual-Meeting

INVESTOR PRESENTATION

APRIL 2021

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Forward Looking Statements

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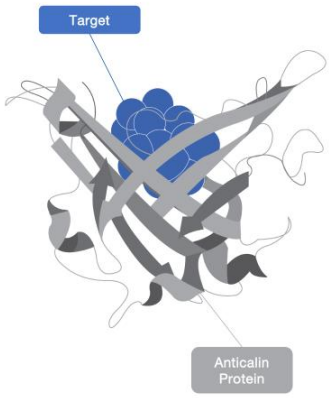
The Anticalin® Protein Platform

A Novel Therapeutic Class with Favorable Drug-Like Properties

- **Human** – Derived from lipocalins (human extracellular binding proteins)
- **Small** – Monomeric, monovalent, small size (~18 kDa vs 150kDa mAbs)
- **Stable** – Inhalable delivery
- **Simple** – Bi/multispecific constructs
- **Proprietary** – Broad IP position on platform and derived products



Powerful Drug Discovery Platform

- Highly diverse libraries
- Automated screening
- Protein engineering know-how

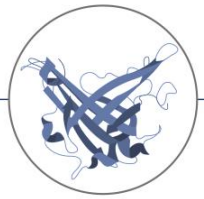
Translational Science Expertise to Deploy Platform in Meaningful Way

- Immunology expertise underpins IO and respiratory focus
- A leader in 4-1BB-related efforts
- Patient phenotyping efforts for improved stratification and novel intervention points in, e.g., asthma

Company Snapshot

Pipeline Highlights

- **PRS-060:** Inhaled IL4-Rα antagonist for moderate-to-severe asthma (partnered with AstraZeneca)
- **Cinrebafusp alfa (PRS-343):** 4-1BB/HER2 bispecific for solid tumors
- **Next-generation respiratory:** Includes 6 discovery-stage inhaled therapeutics programs (2 proprietary, 4 partnered with AstraZeneca)
- **4-1BB-based bispecifics:** Multiple proprietary and partnered 4-1BB-based programs for IO



Anchor Partnerships

- Validation through three anchor partnerships
- $160+M in upfront payments, milestones and strategic equity investment since January 2017
- Each partnership includes options for co-development & US-focused commercialization rights
- Value-driving opt-in for PRS-060 after phase 2a completion

Catalysts

- **Respiratory:**
  - ✓ PRS-060 phase 2a trial initiation and milestone
  - ❑ Data and rationale for advancement into IND-enabling studies for wholly-owned inhaled program
- **IO:**
  - ❑ Cinrebafusp alfa monotherapy data for cohort 13b at AACR
  - ❑ Cinrebafusp alfa phase 2 initiation
  - ❑ Preclinical data for PRS-344 at AACR
  - ❑ PRS-344 IND submission

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Anchor Partnerships

AstraZeneca

- PRS-060 + 4 additional novel inhaled Anticalin protein programs
- Retained co-development and co-commercialization (US) options on PRS-060 and up to 2 additional programs
- Upfront & milestones to date: $70.5M
- $2B+ in milestone potential, plus double-digit royalties
- AZ funds all PRS-060 development costs through post-phase 2a co-development opt-in decision
- Access to complementary formulation and device know-how for inhaled delivery
- $10M equity investment from AstraZeneca

SERVIER

- Immuno-oncology partnership based on antibody-Anticalin bispecific protein fusions
- PRS-344: PD-L1/4-1BB antibody-Anticalin bispecific
  - Pieris holds full U.S. rights
- PRS-352: n.d. antibody-Anticalin bispecific
  - ✓ Pieris completed non-GLP preclinical work
  - Pieris to receive tiered royalties up to low double digits
- ~$31M upfront payment with significant milestone potential
  - ✓ Two preclinical milestones achieved for PRS-344

SeattleGenetics

- 3-program partnership based on tumor-localized costimulatory bispecific fusion proteins
- Pieris retains opt-in rights for US co-promotion on one of the programs with increased royalties
- Upfront & milestones to date: $35M upfront payment
- ~$1.2B milestone potential, plus up to double-digit royalties on non-co-developed products
- $13M equity investment from Seagen
- Clinical trial and supply agreement for tucatinib to be evaluated in combination with cinrebafusp alfa

Strong Partners • Significant Cash Flow • Retained Commercial Rights

Pipeline

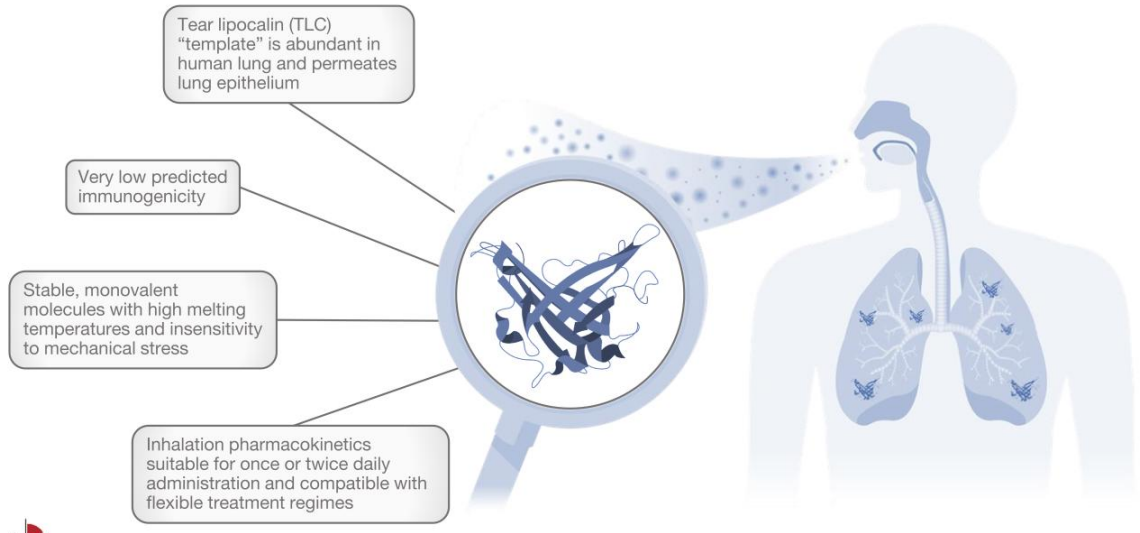
RESPIRATORY							
CANDIDATE	TARGETS	PARTNER	PIERIS' COMMERCIAL RIGHTS	DISCOVERY	PRECLINICAL	PHASE I	PHASE II
PRS-060/AZD1402	IL4-Rα	AstraZeneca	Worldwide Profit-Share Option				
Proprietary Programs	n.d.	n/a	Worldwide				
AstraZeneca Programs*	n.d.	AstraZeneca	Worldwide Profit-Share Option				

*4 respiratory programs in collaboration with AstraZeneca, 2 of which carry co-development and co-commercialization options for Pieris

IMMUNO-ONCOLOGY							
CANDIDATE	TARGETS	PARTNER	PIERIS' COMMERCIAL RIGHTS	DISCOVERY	PRECLINICAL	PHASE I	PHASE II
Cinrebafusp Alfa (PRS-343)	HER2/4-1BB	n/a	Worldwide				
PRS-344	PD-L1/4-1BB	SERVIER	US Rights; ex-US Royalties				
PRS-352	n.d.	SERVIER	Royalties				
Proprietary IO Programs	n.d.	n/a	Worldwide				
Seattle Genetics Program‡	co-stim agonist	SeattleGenetics	US Co-Promotion Option; Royalties				

‡3 bispecific programs in collaboration with Seattle Genetics, with Pieris retaining a US co-promotion option for the second program

Anticalin Technology Advantages: Differentiated Respiratory Platform



PRS-060: IL-4Rα Antagonist

Candidate	PRS-060
Function/MoA	Inhibiting IL4-Rα (disrupts IL-4 & IL-13 signaling)
Indications	Moderate-to-severe asthma
Development	Phase 2a in moderate asthmatics
Commercial Rights	Co-development and U.S. co-commercialization rights, including gross margin share

PRS-060

PRS-060 Phase 2a Trial

Part 1	**Patient Population:** Moderate controlled asthmatics **Primary Endpoint:** Safety and tolerability **Number of Patients:** ~45
Part 2	**Patient Population:** Moderate uncontrolled asthmatics with blood eosinophil count of ≥ 150 cells/µL and FeNO ≥ 25 ppb at screening **Primary Endpoint:** Improvement of FEV1 over four weeks relative to placebo **Number of Patients:** ~360

- Enrollment initiated 1Q2021
- Dry powder formulation, administered b.i.d. over four weeks
- Up to three dose levels plus placebo
- Study is sponsored and funded by AstraZeneca

4-1BB Agonism Offers Promise of Material Clinical Benefit

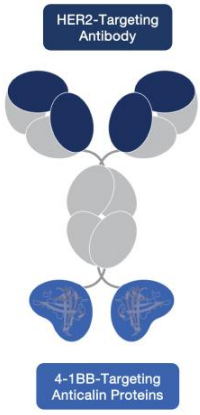
Unique Attributes of 4-1BB Agonism on Tumor-specific T Cells

- ✓ Increases T-cell proliferation to bolster immune repertoire
- ✓ Enhances cytotoxicity for tumor killing
- ✓ Improves metabolic fitness for increased survival of T cells
- ✓ Drives T-cell memory phenotype for increased durability

Pieris' 4-1BB bispecifics recognize that 4-1BB agonists have proven clinical potency, yet must be kept out of the liver to ensure suitable therapeutic index

Cinrebafusp Alfa (PRS-343): Proprietary Lead IO Asset

Candidate	Cinrebafusp alfa (PRS-343)
Function/MoA	Tumor-targeted 4-1BB agonism and HER2 antagonism
Indications	HER2-high and HER2-low gastric cancer
Development	Initiating phase 2
Commercial Rights	Fully proprietary

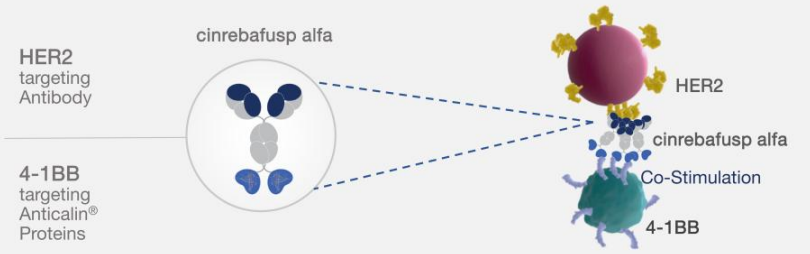


Cinrebafusp Alfa: 4-1B/HER2 Bispecific

Cinrebafusp alfa drives 4-1BB agonism in the tumor microenvironment of HER2+ solid tumors

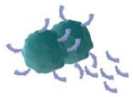
HER2-targeting moiety of the drug localizes to the tumor microenvironment and facilitates 4-1BB cross-linking

4-1BB cross-linking ameliorates T-cell exhaustion and is critical for T-cell expansion

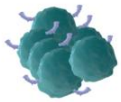


CLINICALLY-RELEVANT BIOMARKERS

4-1BB Pathway Activation
Soluble 4-1BB



T-cell Proliferation
$CD8^+$ and $CD8^+/Ki67^+$



Cinrebafusp Alfa Phase 1 Monotherapy Study

Study Objectives

Primary: Characterize Safety Profile
Identify MTD or RP2D

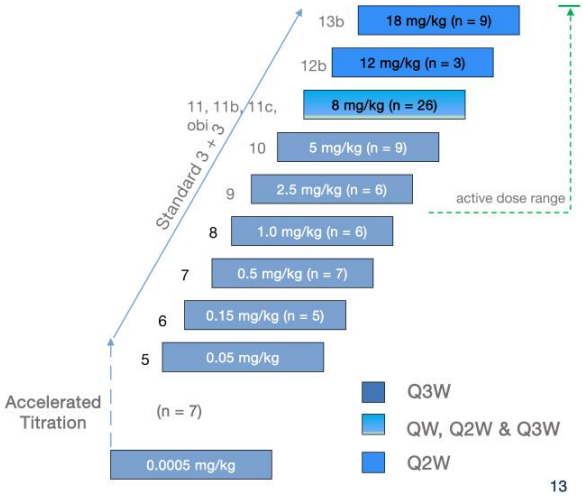
Secondary: Characterize PK/PD & Immunogenicity
Preliminary anti-tumor activity

Key Eligibility Criteria

Inclusion: Metastatic HER2+ solid tumors
Breast & Gastric/GEJ ≥ 1 prior anti-HER2 Tx
Measurable disease (RECIST v1.1)
ECOG 0 or 1

Exclusion: Symptomatic or unstable brain metastasis
Abnormal cardiac EF (< 45%)

Dose Escalation Study Design



Phase 1 Monotherapy Baseline Characteristics (N = 78)

Characteristic	n (%)
Age, Median (range)	63 (24–92)
Gender	
F	46 (59%)
M	32 (41%)
ECOG PS	
0	19 (24%)
1	59 (76%)
Prior Therapy Lines	
1	11 (14%)
2	10 (13%)
3	16 (21%)
4	12 (15%)
5+	29 (37%)
Median # of anti-HER2 Tx	
Breast	6
Gastric	2

Primary Cancer Type	n (%)
Gastroesophageal	34 (44%)
Breast	16 (21%)
Colorectal	12 (15%)
Gynecological	9 (12%)
Bladder	2 (3%)
Pancreatic	1 (1%)
Other – Cancer of Unknown Origin	2 (3%)
Other – Salivary Duct	1 (1%)
Melanoma	1 (1%)

Data cut-off: 25-Feb-21

Phase 1 Monotherapy Treatment Related Adverse Events at Active Doses (≥ 2.5 mg/kg)

Treatment Related Adverse Events (TRAEs occurring in > 1 patient; n = 53)	All Grades n (%)	Grade 1-2 n (%)	Grade 3-4 n (%)
Infusion related reaction	13 (25%)	9 (17%)	4 (8%)
Nausea	7 (13%)	7 (13%)	
Chills	6 (11%)	6 (11%)	
Vomiting	6 (11%)	6 (11%)	
Dyspnoea	4 (8%)	4 (8%)	
Fatigue	4 (8%)	4 (8%)	
Arthralgia	3 (6%)	2 (4%)	1 (2%)
Decreased appetite	3 (6%)	3 (6%)	
Non-cardiac chest pain	3 (6%)	3 (6%)	
Asthenia	2 (4%)	2 (4%)	
Diarrhoea	2 (4%)	2 (4%)	
Dizziness	2 (4%)	2 (4%)	
Headache	2 (4%)	2 (4%)	
Paraesthesia	2 (4%)	1 (2%)	1 (2%)
Pruritus	2 (4%)	2 (4%)	
Pyrexia	2 (4%)	2 (4%)	
Rash	2 (4%)	2 (4%)	

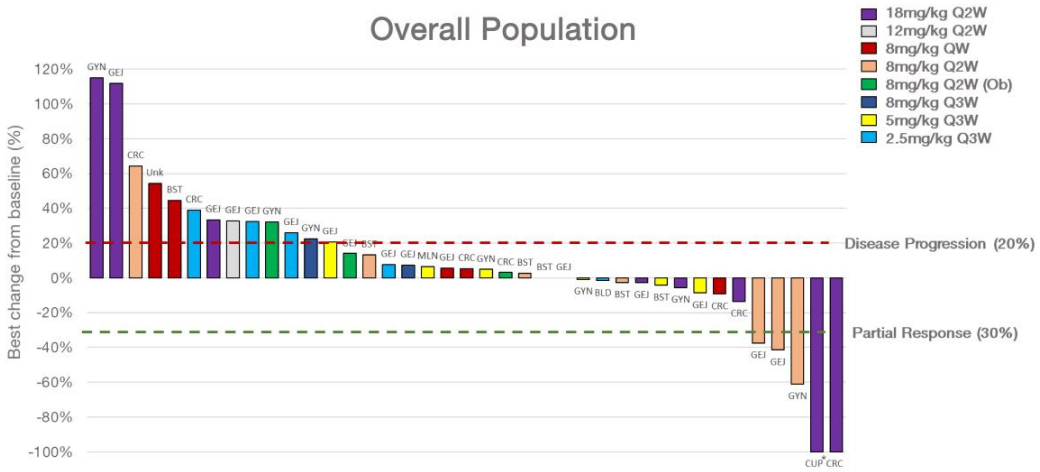
1 Gr 3 Ejection Fraction dec and 1 Gr 3 Heart Failure; both events occurred in one patient and resolved w/o sequelae.

Summary of Responses in Phase 1 Monotherapy Study

Cohort	13b	12b	11c	Obi	11b	11	10	9	Total
Best Response	18 mg/kg, Q2W	12 mg/kg, Q2W	8 mg/kg, QW	8 mg/Kg, Q2W	8 mg/kg, Q2W	8 mg/kg, Q3W	5 mg/kg, Q3W	2.5 mg/kg, Q3W	
Evaluable Patients	8	2	5	4	7	4	7	5	42
CR	1	-	-	-	-	-	-	-	1
PR	1	-	-	-	3	-	-	-	4
SD	3	-	1	2	3	3	3	2	17
ORR	25%	0%	0%	0%	43%	0%	0%	0%	12%
DCR	63%	0%	20%	50%	86%	75%	43%	40%	52%

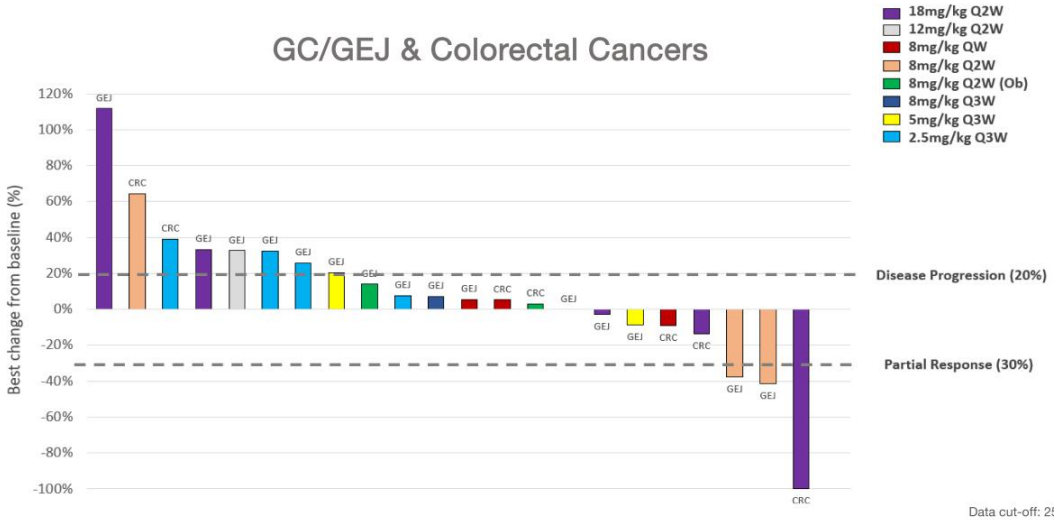
Data cut-off: 25-Feb-21

Cinrebafusp Alfa Phase 1 Monotherapy Efficacy Data: Analysis of Patients Treated at Active Doses



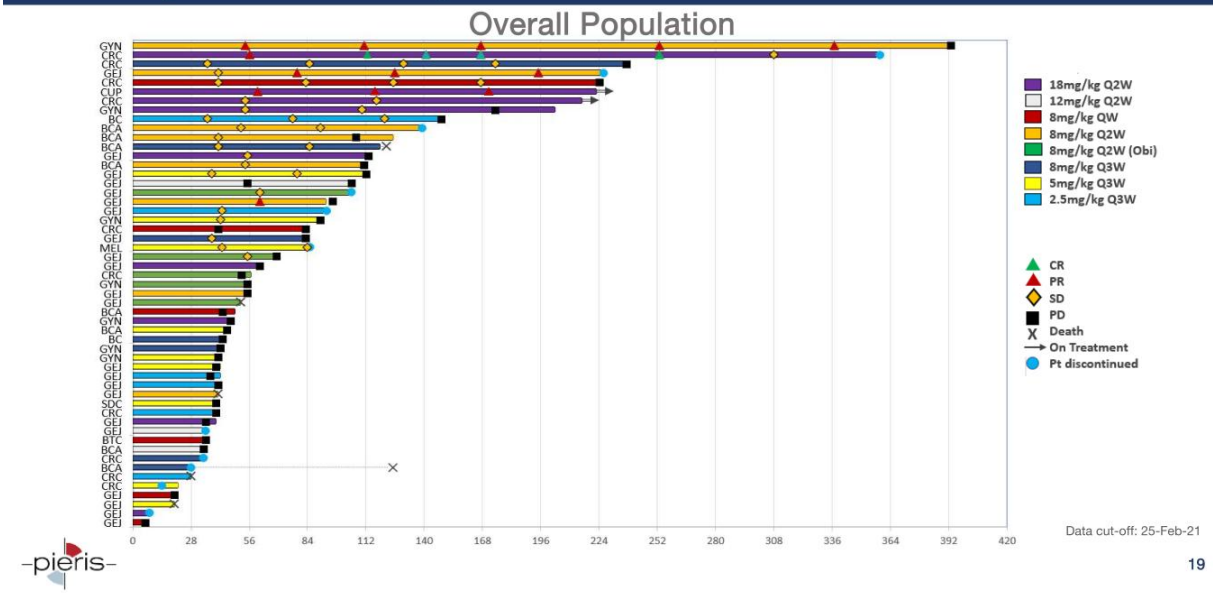
Data cut-off: 25-Feb-21
*Manual update for CUP patient from Medidata 9-Apr-21

Cinrebafusp Alfa Phase 1 Monotherapy Efficacy Data: Analysis of Patients Treated at Active Doses



Data cut-off: 25-Feb-21

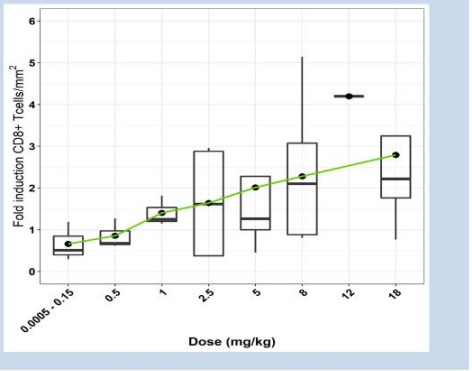
Durable Responses with Cinrebafusp Alfa Among Heavily Pre-treated Population



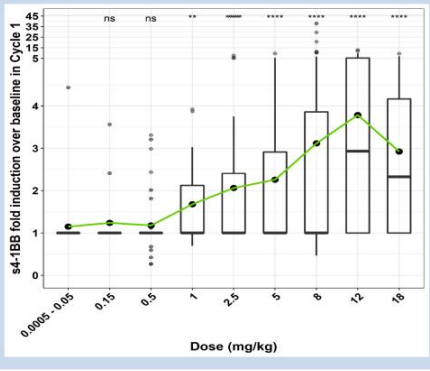
Data cut-off: 25-Feb-21

Cinrebafusp Alfa Shows Dose-dependent Activity Across Key Pharmacodynamic Parameters

Tumor (CD8+)



Serum (s4-1BB)



Connects group averages

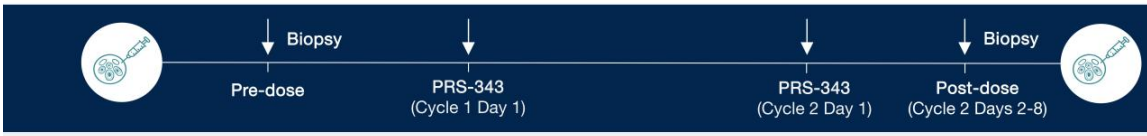
Median

Mann-Whitney U Test

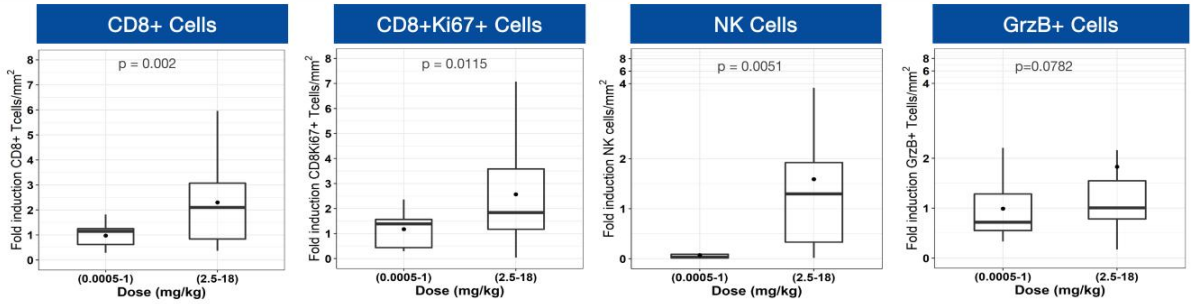
Dose at 8 mg/kg incorporates patients treated at Q1W, Q2W, or Q3W

Data cut-off: 25-Feb-21

Cinrebafusp Alfa Activates Adaptive and Innate Immunity in the Tumor



Based on preclinical and clinical data, serum concentration of > 20 µg/ml defines active dose range beginning at 2.5 mg/kg (Cohort 9)



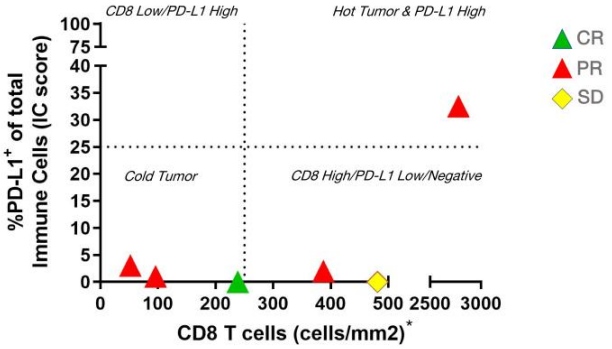
Denotes group averages
Median

Unpaired One-Tailed Welch`s

Data cut-off: 25-Feb-21

Single-Agent Activity in Both “Hot” and “Cold” Tumors

PD-L1 status and CD8+ T cells levels in tumor biopsies



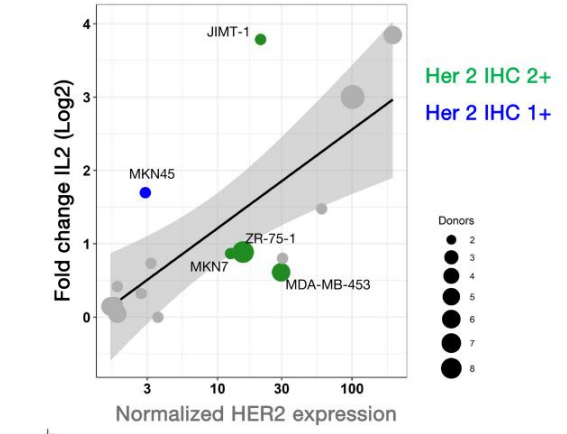
* Threshold informed by (Tumeh et al., 2014 and Blando et al., 2019)

Several patients with clinical benefit have low/negative PD-L1 status and low CD8 T cell numbers

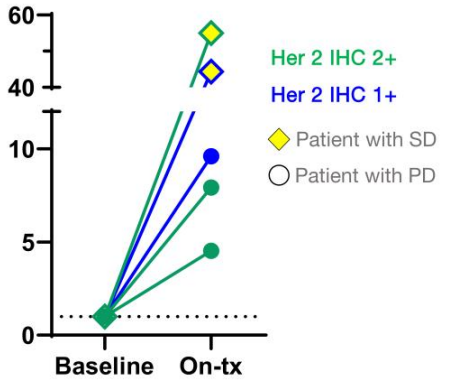
Data cut-off: 25-Feb-21

Signs of Preclinical and Clinical Activity in the HER2-Low Setting

PRS-343 enhances T cell activation in *in vitro* co-cultures with HER2-low tumor cell lines[1]



PRS-343 increases soluble 4-1BB in HER2-low-expressing patients



Data cut-off: 25-Feb-21

[1]*Hinner et al Clin Can Res 2019*

Case Studies: PR in Gastric Cancer and CR in Rectal Cancer

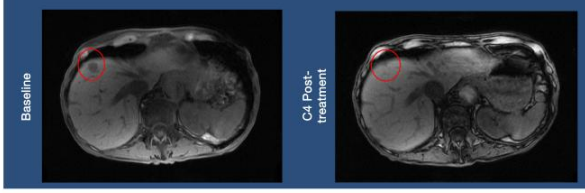
Patient Profile, Treatment History and Treatment Outcome

Gastric Cancer Patient with Partial Response

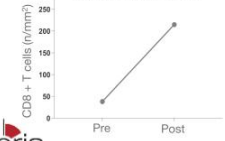
- 80-year-old woman; initial diagnosis in June 2017
- Gastric adenoca with mets to liver, LN and adrenals
- Treated with 8 mg/kg Q2W of PRS-343
- HER2 IHC 3+; PD-L1 positive (CPS=3) ; NGS: ERBB2 amplification

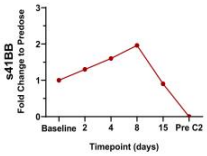
Prior Treatment includes:

- Trastuzumab, Pembrolizumab + Capecitabine/oxaliplatin
- Nivolumab with IDO1 inhibitor (investigational drug)



CD8 fold change: **5.7**
CD8 pre [n/mm²]: **38**



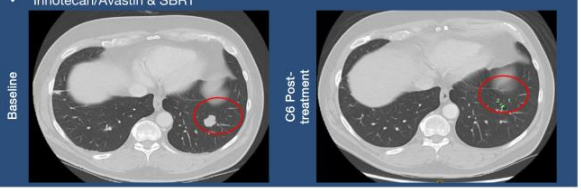


Rectal Cancer Patient with Complete Response

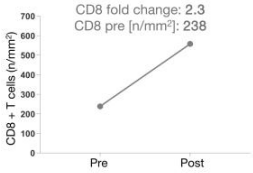
- 59-year-old male; initial diagnosis in March 2017
- Rectal cancer with cardiac and lung mets
- Treated with 18 mg/kg Q2W of PRS-343
- Foundation One Her2 amplification; verified in-house to be IHC 3+; MSS, TMB low

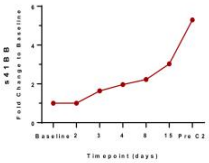
Prior Treatment includes:

- Folfiri/Avastin
- 5FU/Avastin maintenance
- Irinotecan/Avastin & SBRT



CD8 fold change: **2.3**
CD8 pre [n/mm²]: **238**





Case Study: PR in Cancer of Unknown Primary

Patient Profile, Treatment History and Treatment Outcome

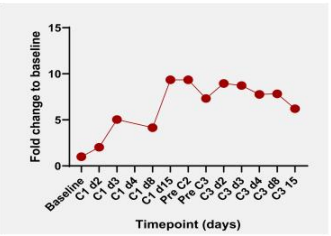
Patient Profile

82-year-old male
Initial diagnosis October 2019
Carcinoma of Unknown Primary
Stage 4
HER2 amplification via MD Anderson
NGS; MSS- stable; TMB unknown

Treatment History

Open Radical
Prostatectomy
Radiation
Carboplatin + gemcitabine

s4-1BB Serum



Lesions	Lesion Site	Lesion Size (mm)			
		Pre-treatment	Post-treatment		
			Cycle 2	Cycle 4	Cycle 6
Target 1	Lung, right lower lobe mass	25	13	0	0
	Total	25	13	0	0
	% Change from Baseline		-48%	-100%	-100%
Non-target 1	Lung, bilateral pulmonary masses	Present	Not assessed	Present	Present
Non-target 2	Lymph nodes, mediastinal and hilar	Present	Not assessed	Present	Present
Overall Response			PR	PR	PR

Data cut-off: 25-Feb-21

Case Study: SD in Colorectal Cancer

Patient Profile, Treatment History and Treatment Outcome

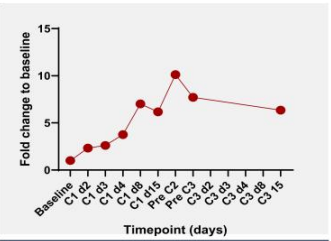
Patient Profile

56-year-old female
Initial diagnosis Jan 2009
Stage 4 Colorectal Adenocarcinoma Cancer
Archival HER2 3+
MSI stable; KRAS, NRAS, BRAF wt

Treatment History

9 prior lines of therapy, including:
Folfiri
Folfox + Avastin
5-FU + bevacizumab
trastuzumab/pertuzumab
Investigational agent (immune stimulator antibody conjugate (ISAC) with antibody similar to trastuzumab

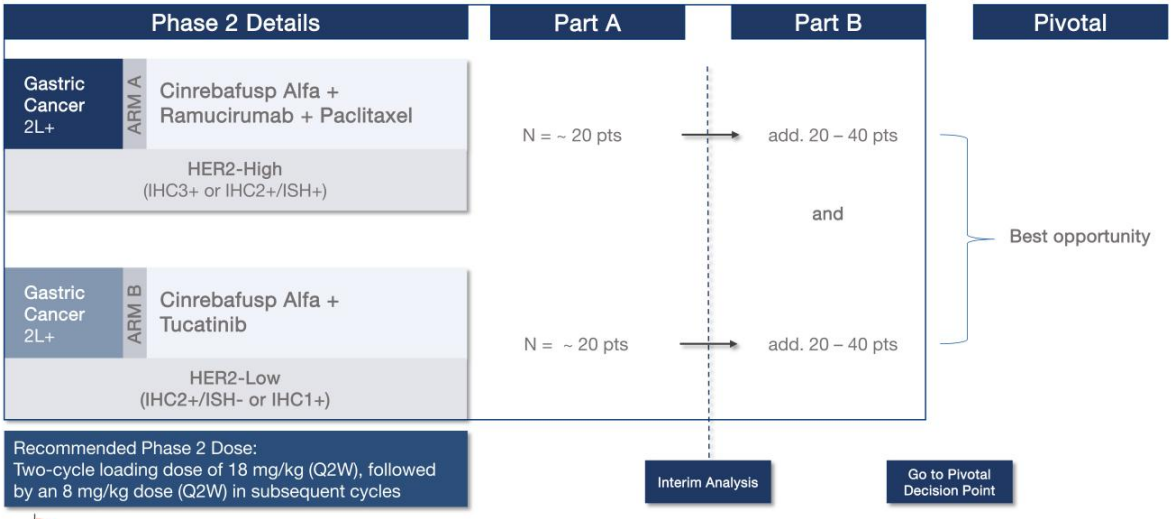
s4-1BB Serum



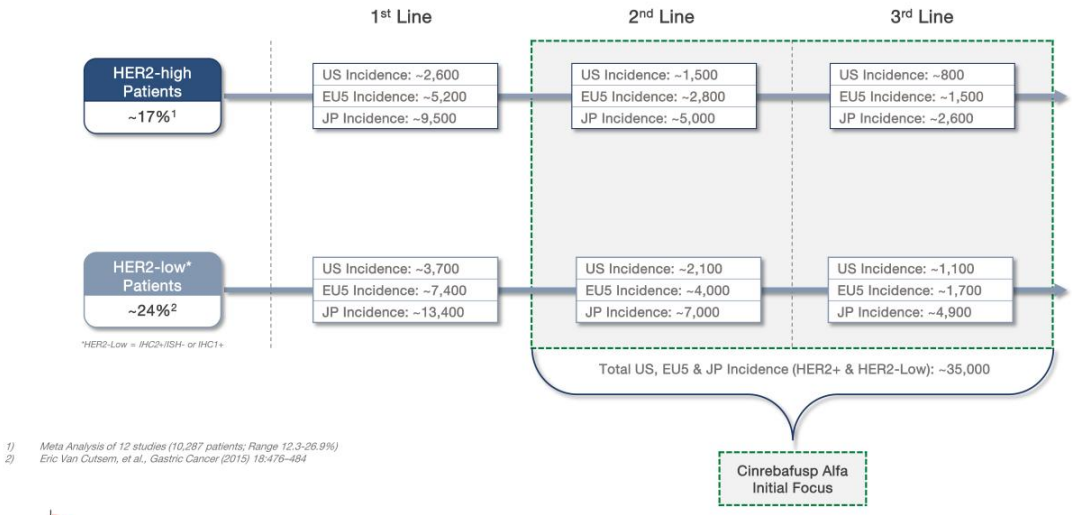
Lesions	Lesion Site	Lesion Size (mm)			
		Pre-treatment	Post-treatment		
			Cycle 2	Cycle 4	Cycle 6*
Target 1	Lung, right upper lobe pulmonary nodule	10	8	8	-
Target 2	Lung, right lower lobe pulmonary nodule	12	11	11	-
	Total	22	19	19	-
	% Change from Baseline		-14%	-14%	-
Non-target 1	Lung, multiple pulmonary nodules	Present	Present	Present	-
CEA		<1.9	1.1	1.3	-

Data cut-off: 25-Feb-21
*Data not yet available due to COVID-related delays

Cinrebafusp Alfa Clinical Development Plan

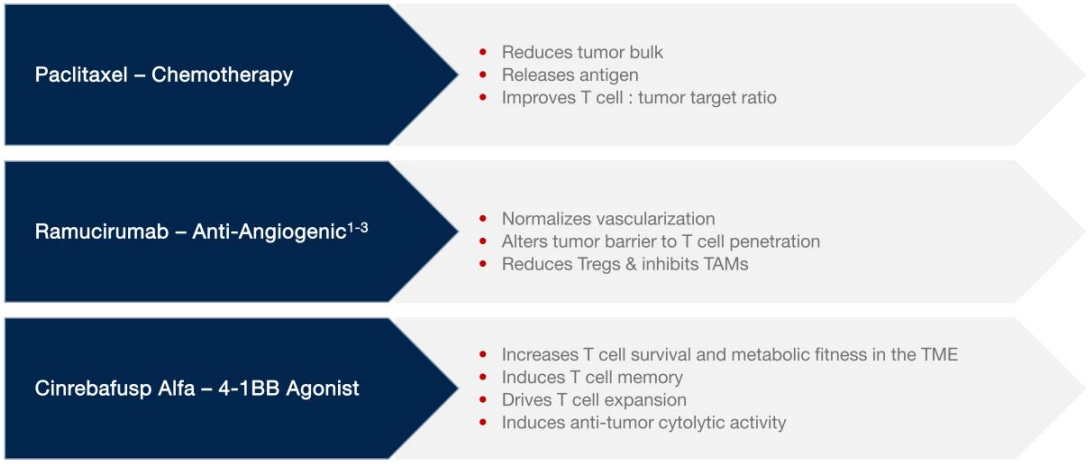


Cinrebafusp Alfa Opportunity in HER2-high & HER2-low Gastric Cancer



1) *Meta Analysis of 12 studies (10,287 patients; Range 12.3-26.9%)*
2) *Eric Van Cutsem, et al., Gastric Cancer (2015) 18:476–484*

Scientific Rationale for Combining Cinrebafusp Alfa & SoC



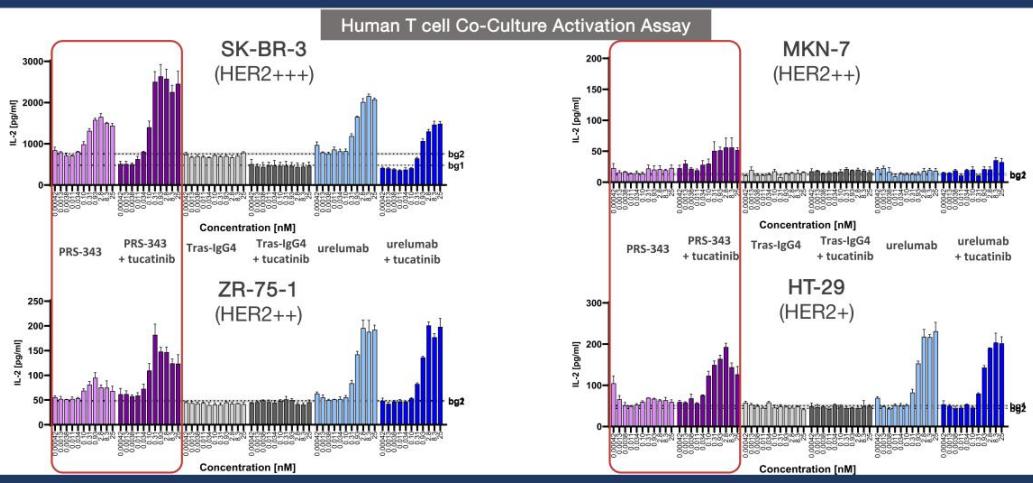
1 - Allen et al., Science Translational Medicine 2017
2 - Juang et al. Front Immunology 2018
3 - Tada et al., Journal for Immunotherapy of Cancer 2018

Scientific Rationale for Combining Cinrebafusp Alfa & Tucatinib

Tyrosine kinase inhibitors (tucatinib)	• Upregulates or stabilizes tumor cell surface HER2 expression[2,3,4] • Increases clustering potential of cinrebafusp alfa on tumor cells to drive enhanced 4-1BB cross-linking
Cinrebafusp Alfa – Dual MoA	• Inhibits HER2 signaling AND activates tumor-specific T cells in tumor microenvironment
Complements Both MoAs	• Enhances inhibition of HER2 signaling by concurrent binding to HER2 on the tumor cell surface and TKI inhibition of the internal kinase signaling domain[1] • *In vitro*, combination leads to significantly increased T cell activation in the presence of HER2-Low cell lines

1 - Baselga J., Lancet, 2012;
2 - Maruyama T., et al, Anticancer Res., 2011
3 - Scaltriti M., et al, Oncogene, 2009
4 - Hartmans, et al, Oncotarget,, 2017

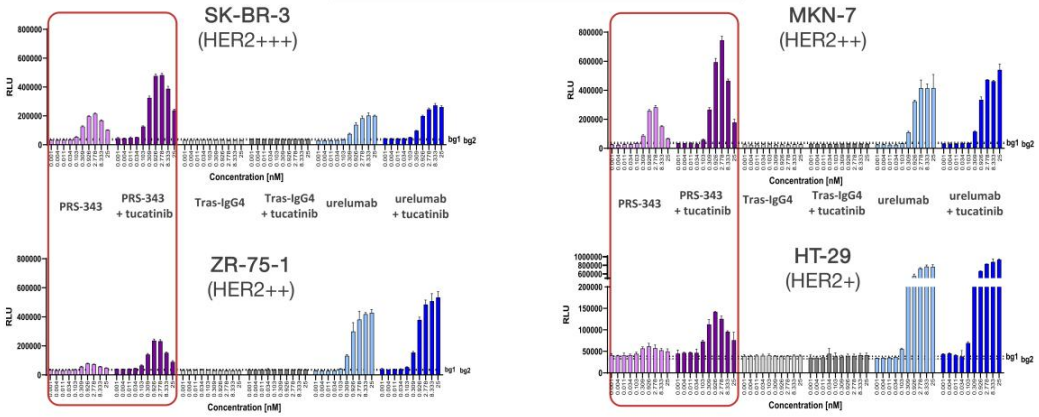
Cinrebafusp Alfa and Tucatinib Combination Enhances T-cell Activation



Increased IL-2 secretion observed when cinrebafusp alfa was combined with fixed dose tucatinib in a co-culture assay with SK-BR-3 (high HER2), MKN-7, ZR-75-1 (medium HER2) and HT-29 (low HER2) tumor cell lines

Cinrebafusp Alfa and Tucatinib Combination Leads to Enhanced 4-1BB Signaling

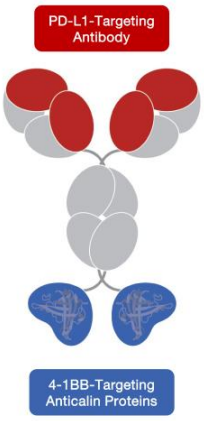
(4-1BB Reporter Cell Assay)



Increased 4-1BB signaling observed when cinrebafusp alfa was combined with fixed dose tucatinib in a reporter assay with SK-BR-3 (high HER2), MKN-7, ZR-75-1 (medium HER2) and HT-29 (low HER2) tumor cell lines

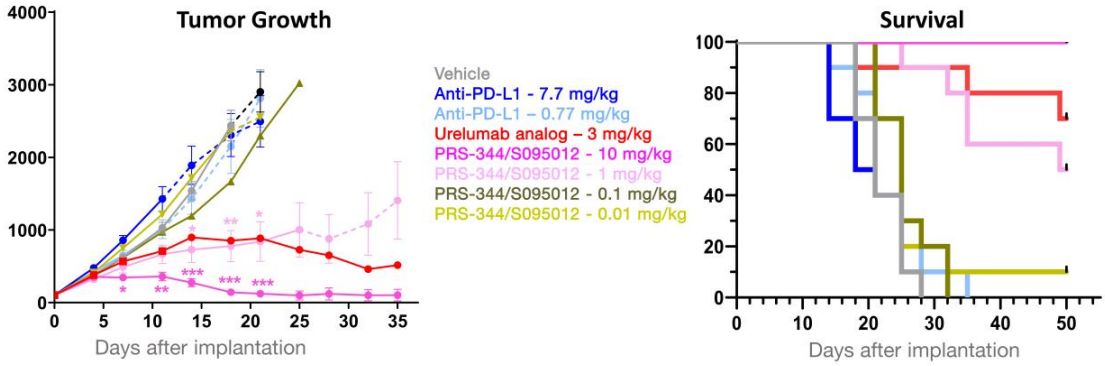
PRS-344: Meaningfully Building on Localized MoA of Cinrebafusp Alfa

Candidate	PRS-344
Function/MoA	Localized 4-1BB agonism with PD-L1 antagonism
Indications	N.D.
Development	2021 IND expected (in co-dev with Servier)
Commercial Rights	Opt-in for co-development with full U.S. commercial rights; royalty on ex-U.S. sales



PRS-344 Drives Strong Anti-tumor Activity in Anti-PD-L1 mAb-resistant Mouse Model

h-4-1BB knock-in mice subcutaneously implanted with MC-38-huPD-L1 cells



- Dose-dependent anti-tumor response that leads to significant extension of survival
- Superior to equimolar doses of anti-PD-L1 mAb treatment alone

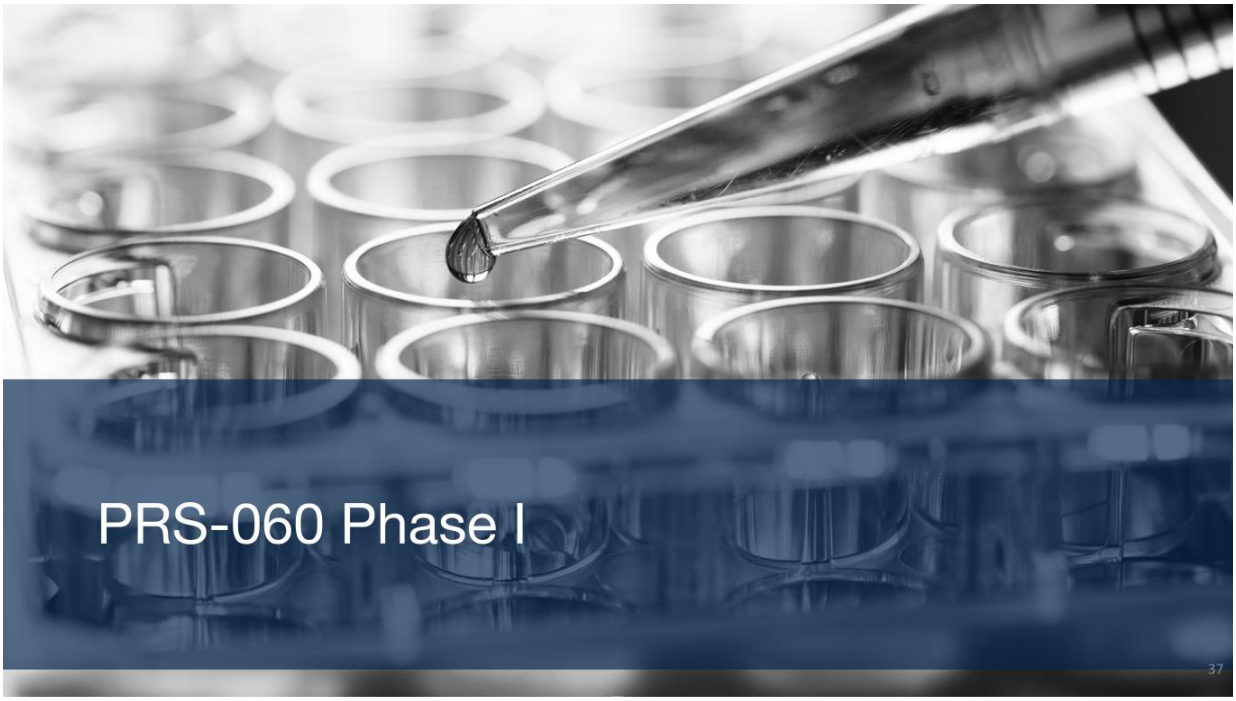
Financial Overview (As of 12/31/20)

$70.4* M	$0.0	56.0* M
Cash & Cash Equivalents	Debt	CSO

$135+ M non-dilutive capital from anchor partnerships

*Excludes $36M from PRS-060 phase 2a milestone and Seagen and AstraZeneca equity investments (along with ~7.3M common shares issued)

Appendix


PRS-060 Phase I

PRS-060 Phase I Multiple Ascending Dose Trial

Strategic Objectives	Ascertain PK/PD with a reliable biomarker to confirm local target engagement and inform Phase II dosage regimen
Trial Design Highlights	Dosing patients with mild asthma with elevated FeNO levels (≥35 ppb), to receive inhaled PRS-060 or pbo b.i.d.* over a 10-day period

*q.d. on Day 10

Initiated in July 2018

Evaluating safety, tolerability, PK, PD and will also evaluate FeNO reduction vs. placebo

Measuring safety, tolerability and FeNO changes days 1-10,17, and 40

Pieris is sponsoring the trial, AstraZeneca is reimbursing Pieris for all associated costs

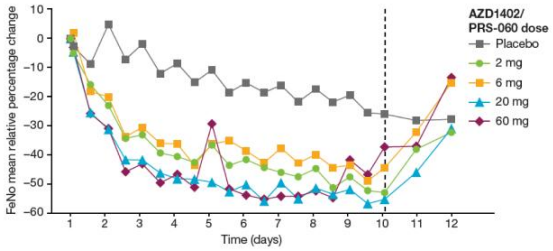
Phase 1b Interim Results: Favorable Safety Profile

- All doses of AZD1402/PRS-060 tested in the study were well tolerated
- No treatment-related serious AEs were observed

System organ class AE Preferred Terms[b]	Placebo (N = 12) n (%) m	AZD1402/PRS-060[c] (N = 30) n (%) m	Overall (N = 42) n (%) m
Gastrointestinal disorders	4 (33.3) 4	13 (43.4) 14	17 (40.5) 18
Dry mouth	1 (8.3) 1	2 (6.7) 2	3 (7.1) 3
Nausea	1 (8.3) 1	3 (10.0) 3	4 (9.5) 4
Infections and infestations	1 (8.3) 1	7 (23.3) 8	8 (19.0) 9
Upper respiratory tract infection	1 (8.3) 1	3 (10.0) 4	4 (9.5) 5
Nervous system disorders	5 (41.7) 9	13 (43.4) 18	18 (42.9) 27
Headache	3 (25.0) 6	5 (16.7) 7	8 (19.0) 13
Presyncope	0	4 (13.3) 6	4 (9.5) 6
Respiratory, thoracic and mediastinal disorders	6 (50.0) 6	14 (46.7) 15	20 (47.6) 21
Cough	1 (8.3) 1	4 (13.3) 4	5 (11.9) 5
Rhinorrhoea	2 (16.7) 2	1 (3.3) 1	3 (7.1) 3
Wheezing	2 (16.7) 2	4 (13.3) 5	6 (14.3) 7

Phase 1b Interim Results: Robust FeNO Reduction

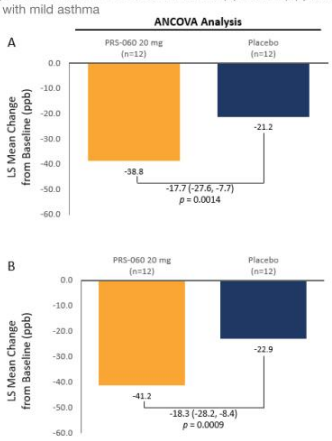
PRS-060 Relative FeNO Reduction (Emax Analysis)



PRS-060, mg (delivered)	n	Reduction vs. placebo, % (95% CI)	p-value
2	6	24.0 (1.8–41)	0.04
6	6	24.3 (2.7–41)	0.03
20	12	36.4 (22–48)	<0.0001
60	6	30.5 (10–46)	0.005
Placebo	12		

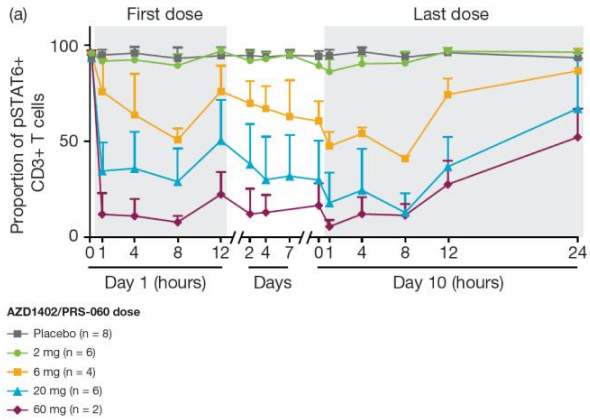
PRS-060 Relative FeNO Reduction (ANCOVA Analysis)

Mean change from baseline in FeNO levels at 0.5h (A) and 2h (B) post-dose on Day 10 in participants with mild asthma



Phase 1b Interim Results: Pharmacological Versatility

pSTAT6 levels over time following inhalation of PRS-060



No systemic target engagement and minimal systemic exposure was observed at the 2mg dose, suggesting that local target engagement by the drug is sufficient to reduce airway inflammation

Pharmacological versatility, given low-dose FeNO reduction with no observed systemic activity (pSTAT6) versus high-dose FeNO reduction with systemic activity

Cinrebafusp Alfa – Biomarkers

Soluble 4-1BB (s4-1BB): Blood-based Biomarker of PRS-343 Target Engagement

- s4-1BB is an alternatively spliced form of 4-1BB receptor lacking the transmembrane encoding exon (Setareh et al., 1995; Shao et al., 2008)
- s4-1BB is **released by leukocytes in an activation-dependent manner** (Michel et al., 2000; Salih et al., 2001; Schwarz et al., 1996)
- s4-1BB is **produced with a slightly delayed kinetic to pathway activation**. Hypothesized role is as a negative regulator, keeping 4-1BB-mediated co-stimulation in check

s4-1BB utility as a pathway specific biomarker provides ability to track PRS-343 target engagement and activity using serum samples

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