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): March 1, 2022

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.)**

255 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 2.02 Results of Operations and Financial Condition.

On March 1, 2022, Pieris Pharmaceuticals, Inc. (the "Company") issued a press release announcing certain financial results for the fiscal year ended December 31, 2021. A copy of the press release issued by the Company is furnished as Exhibit 99.1 to this report.

The information set forth under this "Item 2.02. Results of Operations and Financial Condition," including Exhibit 99.1 furnished 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 7.01 Regulation FD Disclosure.

Furnished hereto as Exhibit 99.2 is the March 2022 Investor Presentation of the Company.

The information set forth under this "Item 7.01. Regulation FD Disclosure," including Exhibit 99.2 furnished 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 Press Release, dated March 1, 2022.

99.2 Investor Presentation, dated March 2022.

104 Cover Page Interactive Data File (embedded within the Inline XBRL document).

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: March 1, 2022

/s/ Tom Bures
Tom Bures
Chief Financial Officer

PRESS RELEASE

PIERIS PHARMACEUTICALS REPORTS FULL-YEAR 2021 FINANCIAL RESULTS AND PROVIDES CORPORATE UPDATE

COMPANY TO HOST AN INVESTOR CONFERENCE CALL ON
TUESDAY, MARCH 1, 2022 AT 8:00 AM EST

- **Initiated efficacy part of phase 2a study of PRS-060/AZD1402; expected topline readout this year**
- **Dosed first patient in phase 2 gastric study of cinrebafusp alfa; HER2-low arm data expected this year and HER2-high arm data expected in 2023**
- **Dosed first patient in phase 1/2 solid tumor study of PRS-344/S095012**
- **PRS-220 phase 1 initiation on track for this year**
- **Year-end cash and cash equivalents totaled $117.8 million**

BOSTON, MA, March 1, 2022 - ***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 reported financial results for the fiscal year ended December 31, 2021 and provided an update on the Company's recent and anticipated future developments.

"Last year was one of steady execution as we laid the groundwork for 2022, which we believe promises to be the most important catalyst year in the Company's history, including key efficacy data for cinrebafusp alfa and PRS-060/AZD1402. We announced a collaboration with R&D leader Genentech, reported data from several clinical and preclinical programs, and initiated multiple clinical trials. Later this year, we expect to report topline data from the phase 2a trial of PRS-060/AZD1402, which has recently cleared the safety gate for the 1 mg and 3 mg dose cohorts. Beyond PRS-060/AZD1402, we currently have two bispecific immuno-oncology programs in clinical development and plan on initiating clinical development for our proprietary inhaled-delivery idiopathic pulmonary fibrosis (IPF) drug program, PRS-220, later this year, with generous grant support from the Bavarian government," said Stephen S. Yoder, President and Chief Executive Officer of Pieris. "Through these initiatives, we have advanced our pipeline assets while strengthening our balance sheet through partnerships, grant funding, and focused utilization of our ATM facility, all with the focus of driving toward our key inflection point."

- **PRS-060/AZD1402 and AstraZeneca Collaboration:** Enrollment of part 2a (efficacy of 1 mg and 3 mg cohorts) and part 1b (safety of 10 mg cohort) has begun following successful completion of the sponsor safety review of part 1a (safety of 1 mg and 3 mg cohorts) of the multi-center, placebo-controlled phase 2a study of dry powder inhaler-formulated PRS-060/AZD1402. PRS-060/AZD1402 is an IL-4 receptor alpha inhibitor under development in collaboration with AstraZeneca for the treatment of moderate-to-severe asthma. Pieris and AstraZeneca expect to announce topline data from the phase 2a study this year, although the companies are actively evaluating the feasibility of study timelines in the current geopolitical environment and will update guidance in the orderly course of business, if needed. Upon completion of the study, which is being sponsored and funded by AstraZeneca, Pieris may choose to exercise its co-development option, which would be on a 25% cost-share basis with a cost cap or a 50% cost-share basis without a cost cap. Separately, Pieris will have a future option to co-commercialize PRS-060/AZD1402 in the United States.
- **Cinrebafusp Alfa (PRS-343):** In January 2022, the first patient was dosed in the phase 2 study of cinrebafusp alfa, a 4-1BB/HER2 Anticalin-based bispecific for the treatment of HER2-expressing gastric cancer. The two-arm, multicenter, open-label phase 2 study is evaluating the efficacy, safety, and tolerability of cinrebafusp alfa in combination with standard of care agents ramucirumab and paclitaxel in patients with HER2-high gastric cancer and in combination with tucatinib in patients with HER2-low gastric cancer. Pieris plans to report data from the HER2-low arm this year. Separately, the Company plans to disclose data from the HER2-high arm in 2023.

- **PRS-344/S095012 and Servier Collaboration:** The first patient was dosed in November 2021 in the phase 1/2 study of PRS-344/S095012, a 4-1BB/PD-L1 Anticalin-based bispecific for the

treatment of solid tumors, triggering an undisclosed milestone payment to Pieris. Pieris holds exclusive commercialization rights for PRS-344/S095012 in the United States and will receive royalties on any ex-U.S. sales for this program. Additionally, Servier is continuing development of PRS-352, an undisclosed Anticalin-based bispecific beyond 4-1BB.

- **PRS-220:** Pieris remains on track to begin a phase 1 trial this year for PRS-220, a proprietary inhaled Anticalin protein targeting connective tissue growth factor for the treatment of IPF.

Year End Financial Update:

Cash Position – Cash and cash equivalents totaled $117.8 million for the year ended December 31, 2021, compared to a cash and cash equivalents balance of $70.4 million for the year ended December 31, 2020. The increase since December 2020 is due to cash received from new and existing collaboration agreements, including milestone achievements. In addition, during 2021, the ATM program was utilized to raise a total of $38.5M in net proceeds at an average price of $4.85 per share. These increases were partially offset by cash used to fund operations in 2021.

R&D Expense - R&D expenses were $66.7 million for the year ended December 31, 2021, compared to $46.5 million for the year ended December 31, 2020. The increase reflects higher spending on preclinical and manufacturing activities for PRS-220, an increase in manufacturing costs across multiple immuno-oncology programs, higher clinical costs on cinrebafusp alfa and higher employee related costs. These increases were partially offset by lower manufacturing costs on PRS-060, which were fully reimbursed.

G&A Expense - G&A expenses were $16.5 million for the year ended December 31, 2021, compared to $16.7 million for the year ended December 31, 2020. Total G&A spending was consistent year-over-year as higher fixed and variable compensation and higher insurance costs in 2021 were offset by lower legal, accounting, and project management costs, along with lower one-time office and building equipment costs related to the move to the new R&D facility in Hallbergmoos, Germany in the prior year.

Other Income - For the year ended December 31, 2021, $3.7 million of other income was recorded for PRS-220 program costs that qualified for reimbursement under the Bavarian grant that was announced in June 2021. The Bavarian government reimburses these qualifying program costs as incurred over the PRS-220 development period.

Net Loss - Net loss was $45.7 million or $(0.71) per share for the year ended December 31, 2021, compared to a net loss of $37.2 million or $(0.68) per share for the year ended December 31, 2020.

Conference Call*:*
Pieris management will host a conference call beginning at 8:00 AM EST on Tuesday, March 1, 2022, to discuss the full-year financial results and provide a corporate update. Individuals can join the call by dialing +1-877-407-8920 (US & Canada) or +1-412-902-1010 (International). Alternatively, a listen-only audio webcast of the call can be accessed here.

For those unable to participate in the conference call or listen to the webcast, a replay will be available on the Investors section of the Company's website, www.pieris.com.

About Pieris Pharmaceuticals*:*

Pieris is a clinical-stage biotechnology company that combines leading protein engineering capabilities and deep understanding into molecular drivers of disease to develop medicines that drive local biology to produce superior clinical outcomes for patients. Our pipeline includes inhalable Anticalin proteins to treat respiratory diseases and locally-activated bispecifics for immuno-oncology. Proprietary to Pieris, Anticalin proteins are a novel class of therapeutics validated in the clinic and by respiratory and immuno-oncology focused partnerships with leading pharmaceutical companies. 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, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Statements in this press release that are not purely historical are forward-looking statements.

Such forward-looking statements include, among other things, the potential for Pieris' development programs such as PRS-060/AZD1402, cinrebafusp alfa, PRS-344/S095012 and PRS-220 to address our core focus areas such as respiratory diseases and immuno-oncology; 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/S095012 and PRS-220; the therapeutic potential of our Anticalin platform; our continued progress in the areas of co-stim bispecifics and inhaled therapeutics; and the advancement of our developmental programs generally. Actual results could differ from those projected in any forward-looking statement 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 or geo-political issues, including the conflict in Ukraine; 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 Securities and Exchange Commission available at www.sec.gov, including, without limitation, the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2021 and the Company's Quarterly Reports on Form 10-Q.

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PIERIS PHARMACEUTICALS, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS

(in thousands)

	December 31,	
	2021	2020
Assets:		
Cash and cash equivalents	$ 117,764	$ 70,436
Short term investments	—	—
Accounts receivable	3,313	1,706
Prepaid expenses and other current assets	6,548	3,579
Total current assets	127,625	75,721
Property and equipment, net	19,122	22,046
Operating lease right-of-use assets	3,909	3,934
Other non-current assets	2,904	3,309
Total Assets	$ 153,560	$ 105,010
Liabilities and stockholders' equity:		
Accounts payable	$ 8,609	$ 1,787
Accrued expenses	16,836	7,731
Deferred revenue, current portion	25,116	12,627
Total current liabilities	50,561	22,145
Deferred revenue, net of current portion	38,403	35,900
Operating lease liabilities	13,841	15,932
Other long-term liabilities	—	6
Total Liabilities	102,805	73,983
Total stockholders' equity	50,755	31,027
Total liabilities and stockholders' equity	$ 153,560	$ 105,010

PIERIS PHARMACEUTICALS, INC
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except per share data)

	Twelve Months Ended December 31, 2021	2020
Revenues	$ 31,418	$ 29,323
Operating expenses		
Research and development	66,656	46,531
General and administrative	16,593	16,713
Total operating expenses	83,249	63,244
Loss from operations	(51,831)	(33,921)
Interest income	4	511
Grant income	3,685	—
Other income (expense), net	2,404	(3,656)
Loss before income taxes	(45,738)	(37,066)
Provision for income tax	—	164
Net loss	$ (45,738)	$ (37,230)
Basic and diluted net loss per share	$ (0.71)	$ (0.68)
Basic and diluted weighted average shares outstanding	64,547	54,481

PIERIS PHARMACEUTICALS

CORPORATE PRESENTATION
March 2022

Forward-Looking Statements

This presentation contains forward-looking statements as that term is defined in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Statements in this presentation that are not purely historical are forward-looking statements. Such forward-looking statements include, among other things, the timing for initiation of clinical trials of PRS-220; whether PRS-220 will provide a clinical benefit in the treatment of IPF and PASC-related fibrosis, whether the combination of cinrebafusp alfa with other therapies could address a high medical need in HER2 gastric cancer patients who do not respond to traditional HER2-targeted therapies; whether the effects of the combination of cinrebafusp alfa with other therapies seen in preclinical studies will be observed in clinical trials; 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 Company's cash resources, 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; our ability to address the requests of the U.S. Food and Drug Administration; 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 presentation, 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 Securities and Exchange Commission available at www.sec.gov, including without limitation the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2021 and the Company’s subsequent Quarterly Reports on Form 10-Q.

Our Formula for Success

We combine leading protein engineering capabilities and deep insights into molecular drivers of disease to develop medicines that drive local biology to produce superior clinical outcomes for patients.

Executive Summary

Superior Medicines via Efficient Biology	• Protein therapeutics that exploit biology validated by mAbs yet are engineered for focused activity at disease locus • Improved activity, reduced side effects, increased convenience
Two Focus Areas	• Oral inhaled antagonists for respiratory disease • Locally activated immuno-oncology bispecifics • 2 POC readouts this year; several follow-on candidates
Supportive Partnerships	• ~$200M since 2017 in upfronts, milestones and equity investments • Several co-developed and out-licensed programs • Clinical supply for combination studies and development expertise

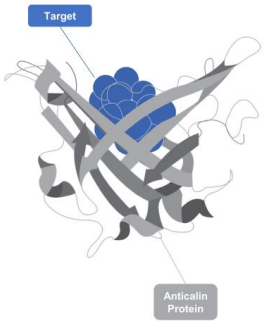
Anticalin® Proteins as Therapeutic Modalities

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

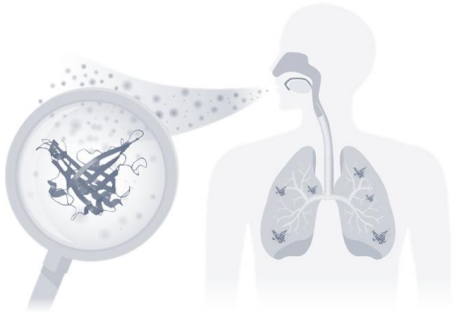
Translational Science Expertise to Deploy Platform in Meaningful Way

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

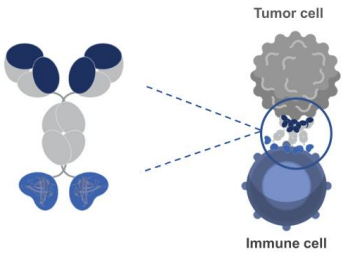


Two-fold Focus of Anticalin Platform Deployment

Inhalable formulations to treat respiratory diseases locally



Bispecifics for local immune agonism to treat cancer



Our Pipeline

RESPIRATORY

CANDIDATE	TARGETS	INDICATION	PARTNER	OUR COMMERCIAL RIGHTS	DISCOVERY	PRECLINICAL	Phase 1	Phase 2
PRS-060/AZD1402	IL4-Rα	Asthma	AstraZeneca	Worldwide Gross Margin Option				
PRS-220	CTGF	IPF, PASC-PF	n/a	Worldwide				
AstraZeneca Programs*	n.d.	n.d.	AstraZeneca	Worldwide Gross Margin Options				
Genentech Programs*	n.d.	n.d.	Genentech	Royalties				

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

*Collaboration includes 1 respiratory program and 1 ophthalmology program

IMMUNO-ONCOLOGY

CANDIDATE	TARGETS	INDICATION	PARTNER	OUR COMMERCIAL RIGHTS	DISCOVERY	PRECLINICAL	Phase 1	Phase 2
Cinrebafusp Alfa (PRS-343)	4-1BB/HER2	HER2-High GC**	n/a	Worldwide				
		HER2-Low GC**						
PRS-344/S095012	4-1BB/PD-L1	n.d.	Servier	US Rights; ex-US Royalties				
PRS-352	n.d.	n.d.	Servier	Royalties				
PRS-342/BOS-342	4-1BB/GPC3	n.d.	Boston Pharmaceuticals	Royalties				
Seagen Programs‡	Co-stim Agonist	n.d.	Seagen	US Co-Promotion Option; Royalties				

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

** Phase 2 study includes HER2-high arm in combination with ramucirumab and paclitaxel and HER2-low arm in combination with tucatinib; drug supply agreements with Lilly and Seagen, respectively

Validating Partnerships with Leading Companies

AstraZeneca

- PRS-060/AZD1402 + 4 additional programs
- Upfront & milestones to date: $70.5M
- $10M equity investment from AstraZeneca
- Eligible to receive over $5.4B in potential milestone payments plus royalties
- Retained co-development and co-commercialization (US) options on PRS-060 and up to 2 additional programs

BOSTON pharmaceuticals

- Boston Pharmaceuticals holds exclusive license for PRS-342/BOS-342
- Upfront & milestones to date: $10M
- Eligible to receive up to approximately $353M in potential milestone payments
- Entitled to tiered royalties

Genentech
A Member of the Roche Group

- 1 respiratory program + 1 ophthalmology program
- Upfront & milestones to date: $20M
- Eligible to receive over $1.4B million in potential milestone payments
- Entitled to tiered royalties
- Genentech has option to select additional targets in return for an option exercise fee

Seagen

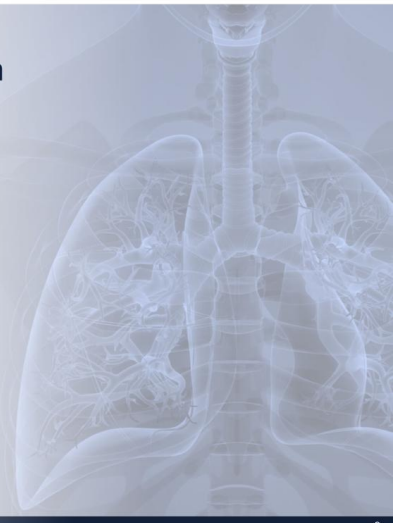
- 3-program IO bispecific partnership
- Upfront & milestones to date: $35M
- Eligible to receive up to approximately $1.2B in potential milestone payments plus royalties
- $13M equity investment from Seagen
- Tucatinib drug supply for phase 2 combination trial of cinrebafusp alfa in HER2-low gastric cancer

SERVIER

- PRS-344/S095012: PD-L1/4-1BB antibody-Anticalin bispecific, for which Pieris holds full U.S. rights
- Upfront & milestones to date: ~$41M
- Eligible to receive up to approximately $261M in potential milestone payments
- Entitled to tiered royalties

Anticalin Technology Advantages: Differentiated Respiratory Platform

- Lipocalin templates deployed by Pieris in respiratory programs are abundant in the human lung and can permeate lung epithelium
- Stable, monovalent molecules with high melting temperatures and insensitivity to mechanical stress
- Inhalation pharmacokinetics suitable for once or twice daily administration and compatible with flexible treatment regimens
- Control of particle size distribution in critical size range in both “wet” and “dry” formulations to enable tailored delivery to discrete lung regions



PRS-060/AZD1402: Inhaled IL-4Rα Antagonist

Candidate	PRS-060/AZD1402
Function/MoA	Inhibiting IL4-Rα (disrupts IL-4 & IL-13 signaling)
Indications	Moderate-to-severe asthma
Development	Phase 2a in moderate uncontrolled asthmatics
Commercial Rights	Co-development and U.S. co-commercialization options, including gross margin share

PRS-060/AZD1402

PRS-060/AZD1402 Progressed into Efficacy Portion of Phase 2a

Part 1 (Safety)	✓ Part 1a: 1mg + 3 mg Dose ❑ Part 1b: 10 mg Dose	**Participant Population:** Moderate asthmatics controlled on ICS/LABA **Primary Endpoint:** Safety and tolerability compared to placebo from baseline until follow-up (approximately 56 days) **# of Participants:** ~45 (randomized: 1:1:1 for part 1a; 2:1 for part 1b)
Part 2 (Efficacy)	❑ Part 2a: 1mg + 3 mg Dose ❑ Part 2b: 10 mg Dose	**Participant Population:** Moderate uncontrolled asthmatics on ICS/LABA with blood EO count of ≥ 150 cells/µL and FeNO ≥ 25 ppb at screening* **Primary Endpoint:** Improvement of FEV1 at four weeks relative to placebo **# of Participants:** ~300 (randomized: 1:1:1 for part 2a; 2:1 for part 2b)

Parts 1b & 2a initiated 1Q 2022

Dry powder formulation, administered b.i.d. over four weeks on top of standard-of-care therapy (medium dose ICS with LABA)

Up to three dose levels plus placebo

Study is sponsored, conducted, and funded by AstraZeneca

*In addition to uncontrolled asthmatics with threshold EO count and FeNO profile, there are other enrollment criteria associated with part 2 not in part 1, including FEV1, and a different ACQ score.

DPI Formulation of PRS-060/AZD1402 Passed Safety Review

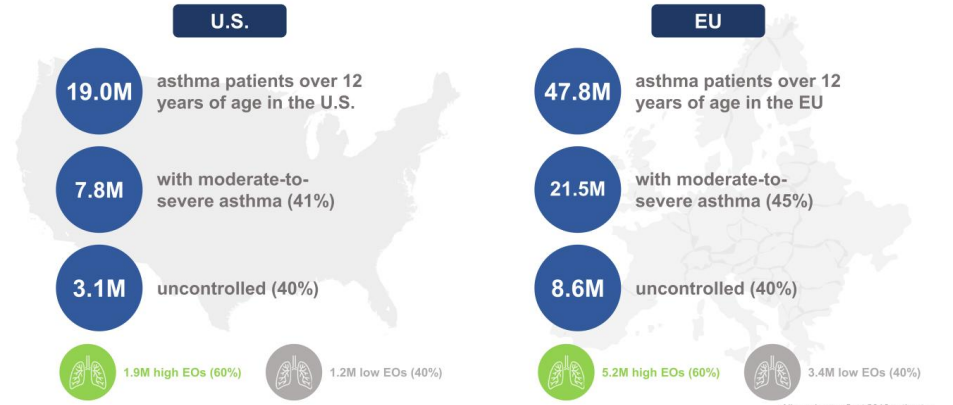
31 moderate asthmatics controlled on standard-of-care (medium dose ICS with LABA) asthma therapy were dosed twice daily over four weeks randomized across two dose levels and placebo arm (1:1:1)

Safety review successfully completed for two different dose levels that will now be explored for efficacy in participants with asthma uncontrolled on medium dose ICS-LABA

Safety review performed of the following (compared to placebo):

- ☑ Incidence of adverse events
- ☑ Changes in laboratory markers (immune biomarkers, clinical chemistry, and hematology)
- ☑ Forced expiratory volume in 1 second (FEV1)
- ☑ Pharmacokinetics

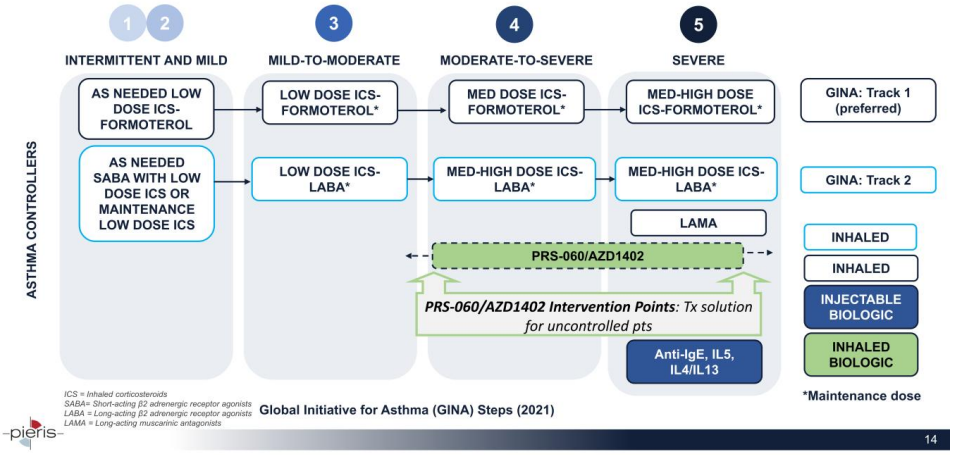
Moderate-to-Severe Asthma Market Opportunity



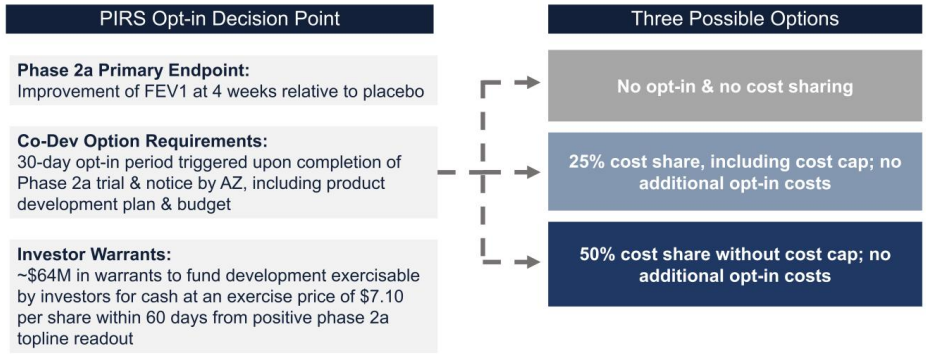
All numbers reflect 2016 estimates.

Source: Artisan Healthcare Consulting analysis (2016), including the following: CDC, Eurostat, Rabe (2004), Cazzoletti (2007), Colice (2012), Hekking (2015).

Potential Large Market Opportunity in Moderate-to-Severe Asthma not Addressed by ICS/LABA before Injectable Biologics



Co-Development Options for PRS-060/AZD1402



PRS-220: Inhaled CTGF Antagonist

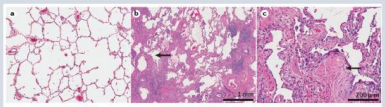
Candidate	PRS-220
Function/MoA	Inhibiting CTGF/CCN2
Indications	IPF and PASC-PF*
Development	Entering phase 1 in healthy subjects this year
Commercial Rights	Fully proprietary

PRS-220

*Idiopathic pulmonary fibrosis and post-acute sequelae of SARS-CoV-2 infection (PASC) pulmonary fibrosis

IPF: High Unmet Medical Need and Significant Commercial Opportunity

IPF is a chronic, progressive, and ultimately fatal lung disease of unknown cause characterized by chronic lung inflammation and progressive scarring (fibrosis) of the tissues between the alveoli of the lung



Martinez, Nature Rev Dis Primer, 2017

3 to 5 million people affected worldwide with increasing global incidence, with ~130K affected in the US each year[1,2]

2 to 5 years mean survival from the time of diagnosis[2]

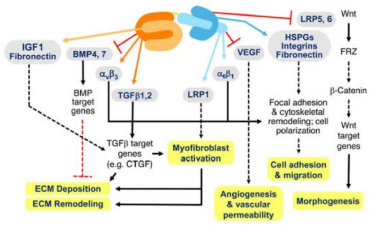
>$3B current market in sales

Currently approved treatments provide modest benefit, in addition to having side effects that require management

1 – Glassberg, AJMC 2019
2 - Meltzer, Orphanet Journal of Rare Diseases 2008

CTGF: Clinically Validated Intervention for IPF

- Connective tissue growth factor (CTGF), or CCN2, a protein localized in the extracellular matrix, is a driver of fibrotic remodeling as consequence of an aberrant wound healing process
- Over-expression of the protein in lung tissue is observed in patients suffering from IPF
- Competitor clinical data indicate inhibition of CTGF reduces the decline in lung function among patients with IPF
- Competitor compound requires high-dose infusions to effectively target lung-resident CTGF



CTGF affects multiple signaling pathways and processes important in pathophysiology. CTGF interacts with a variety of molecules, including cytokines and growth factors, receptors and matrix proteins. These interactions alter signal transduction pathways, either positively or negatively, which results in changes in cellular responses.

(Lipson, Fibrogenesis & Tissue Repair, 2012)

PRS-220: Inhaled Solution

The only CTGF inhibitor in clinical trials for IPF is a monoclonal antibody administered by IV infusion, 30 mg/kg every three weeks

The objective of PRS-220 is to more efficiently engage a clinically validated target via oral inhalation directly to the lung epithelium and interstitium

Benefits of inhaled administration:

- Inhaled administration eliminates the need for additional clinic visits required for systemic drug administration
- Direct administration into the lungs may result in more efficient CTGF inhibition in the site of the disease
- Patients with IPF frequently take inhaled medications and thus no additional training required
- This approach supports add-on to SOC, whereas patients on SOC are excluded from current studies of reference mAb

Grant from Bavarian Government to Support Program Acceleration and Evaluation of Efficacy in PASC-PF

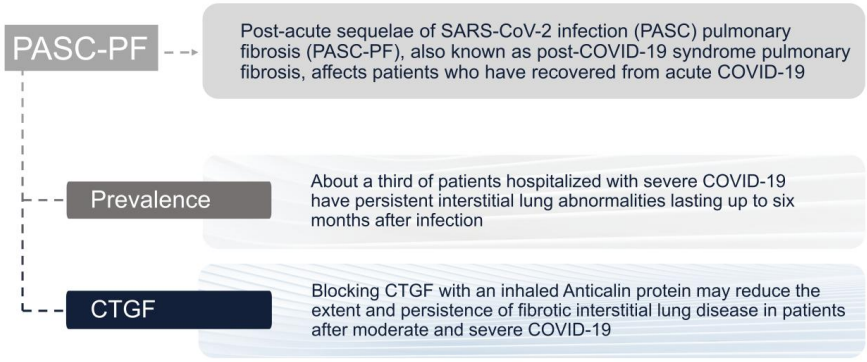
~$17M

approximately 14 million euro grant from the Bavarian government for the research and development of PRS-220 for post-acute sequelae of SARS-CoV-2 infection (PASC) pulmonary fibrosis (PASC-PF)

Grant will:

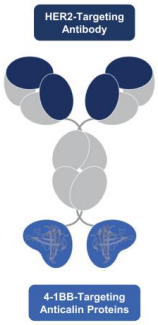
- Allow Pieris to accelerate development of the program – IND planned 2022
- Support clinical-readiness activities and initial clinical development for the program, including GLP tox studies, GMP manufacturing, and phase 1 clinical development
- Broaden scope of the program beyond the original IPF indication by including the evaluation of PRS-220 for the treatment of post-COVID-19-related pulmonary fibrosis

PRS-220 for PASC-PF



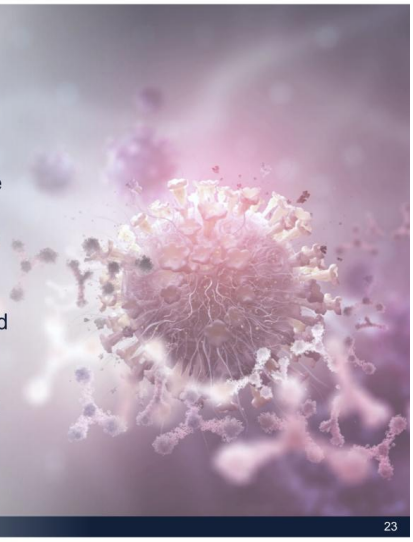
Cinrebafusp Alfa (PRS-343): Lead IO Asset

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



Cinrebafusp Alfa Phase 1 Summary

- Acceptable profile observed at all doses tested with no dose-limiting toxicities
- Clinical benefit at active dose levels (≥ 2.5 mg/kg), including confirmed complete response and several confirmed partial responses
- Dose-dependent immune activation and 4-1BB modulation in both HER2-high and HER2-low expressing patients
- Durable anti-tumor activity in heavily pre-treated patient population, including "cold" tumors
- As lead IO program, cinrebafusp alfa provides key validation of 4-1BB franchise and follow-on programs, including PRS-344 and PRS-342



Cinrebafusp Alfa Phase 1 Monotherapy Study

Study Objectives

Primary: Characterize safety profile
Identify MTD or RP2D

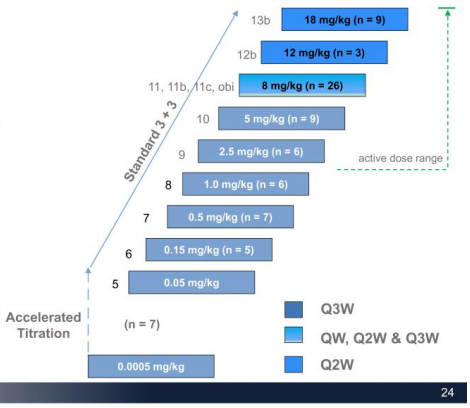
Secondary: Characterize PK/PD & immunogenicity
Preliminary anti-tumor activity

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 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%)	
Dyspnea	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%)	
Diarrhea	2 (4%)	2 (4%)	
Dizziness	2 (4%)	2 (4%)	
Headache	2 (4%)	2 (4%)	
Paresthesia	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.

Data cut-off: 25-Feb-21

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%

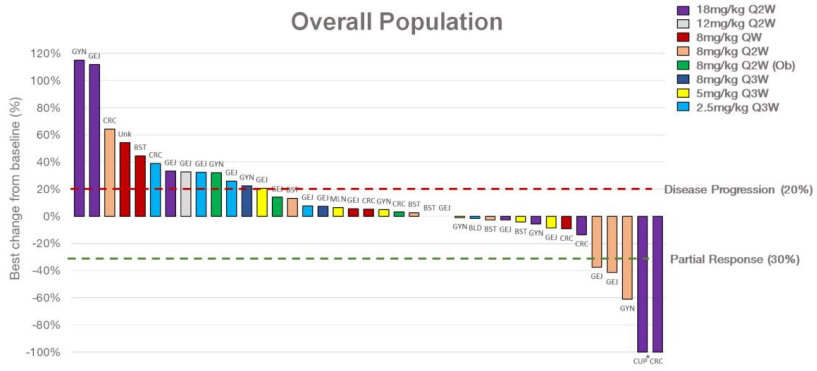
Data cut-off: 25-Feb-21

Summary of Responses in 4-1BB Bispecific Phase 1 Monotherapy Study

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

Data cut-off: 25-Feb-21

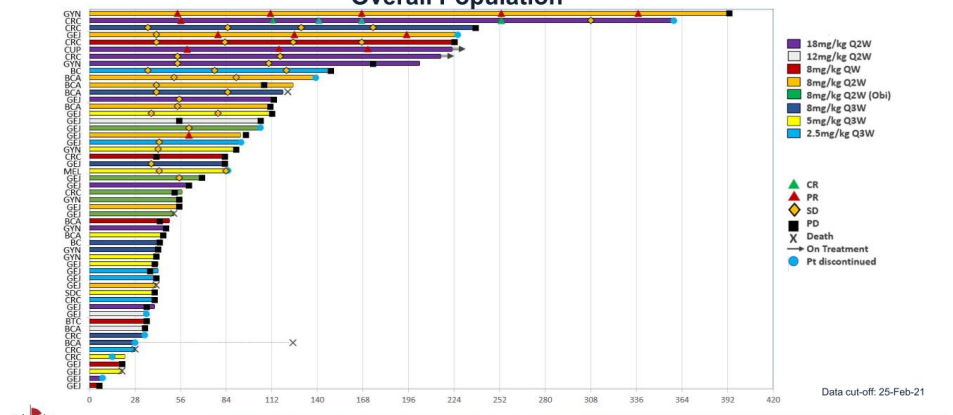
Cinrebafusp Alfa Phase 1 Monotherapy Efficacy Data: Analysis of Patients Treated at Active Doses



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

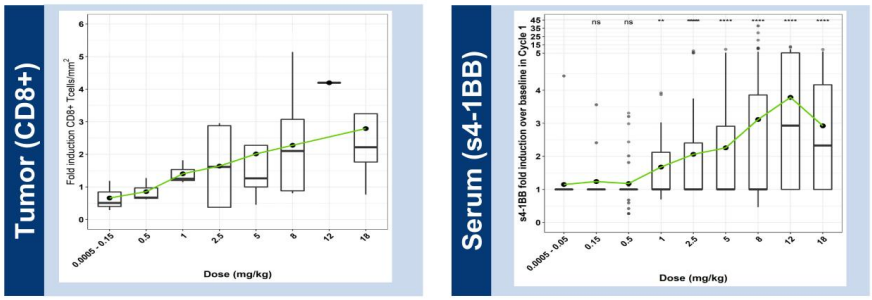
Durable Responses with Cinrebafusp Alfa Among Heavily Pre-treated Population

Overall Population



Data cut-off: 25-Feb-21

Cinrebafusp Alfa Shows Dose-dependent Activity Across Key Pharmacodynamic Parameters



Connects group averages

Median

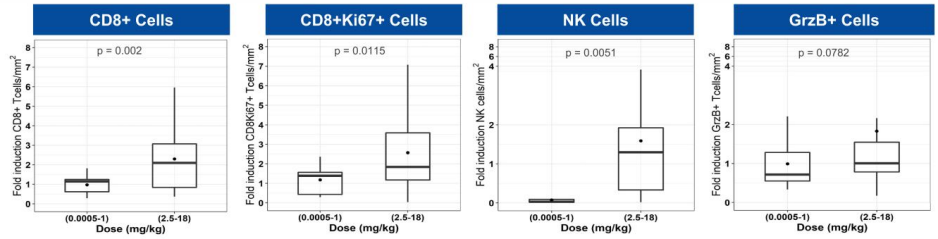
Mann-Whitney U Test

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)



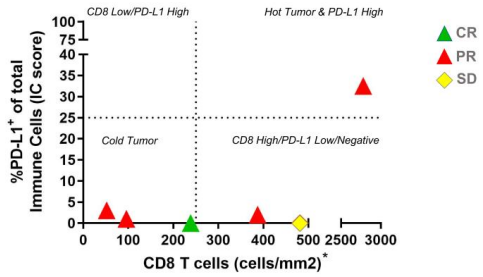
Denotes group averages
Median

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



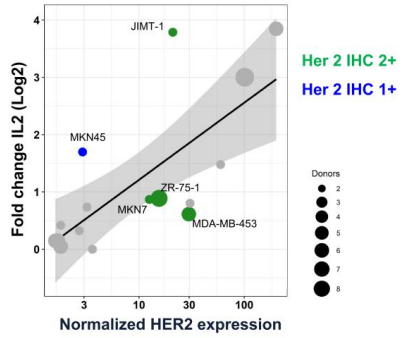
* Threshold informed by (Tumeh et al., 2014 and Blando et al., 2019)

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

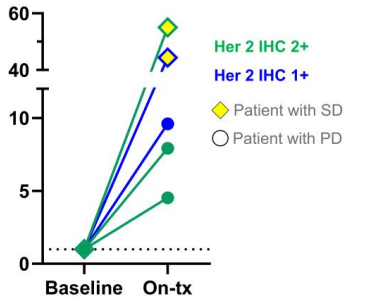
Data cut-off: 25-Feb-21

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

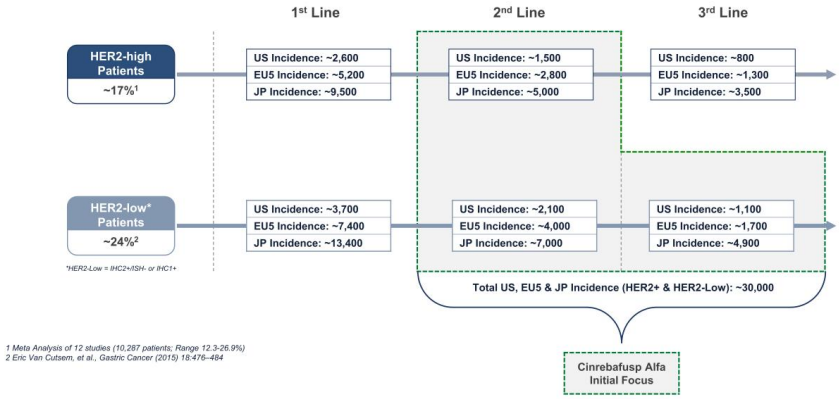


Data cut-off: 25-Feb-21

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

Cinrebafusp Alfa Clinical Development Plan

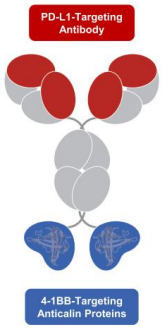
Cinrebafusp Alfa Opportunity in HER2-High & HER2-Low Gastric Cancer



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

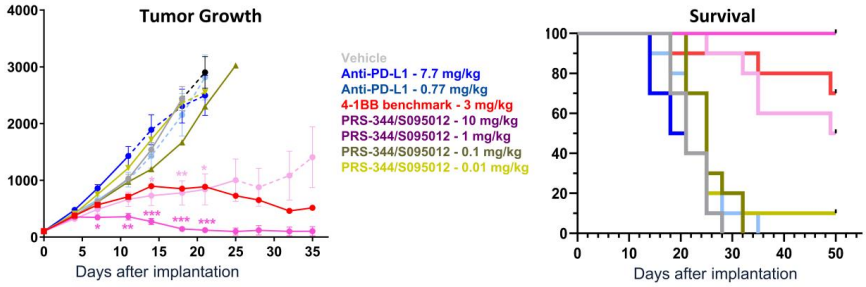
PRS-344/S095012: Meaningfully Building on Localized MoA of Cinrebafusp Alfa

Candidate	PRS-344/S095012
Function/MoA	Localized 4-1BB agonism with PD-L1 antagonism
Indications	N.D.
Development	Phase 1 (in co-dev with Servier)
Commercial Rights	Co-development with full U.S. commercial rights; royalty on ex-U.S. sales



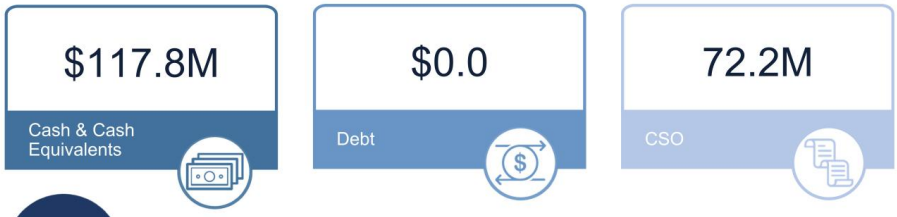
PRS-344 Drives Strong Anti-tumor Activity in Anti-PD-L1 mAb-resistant Mouse Model

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

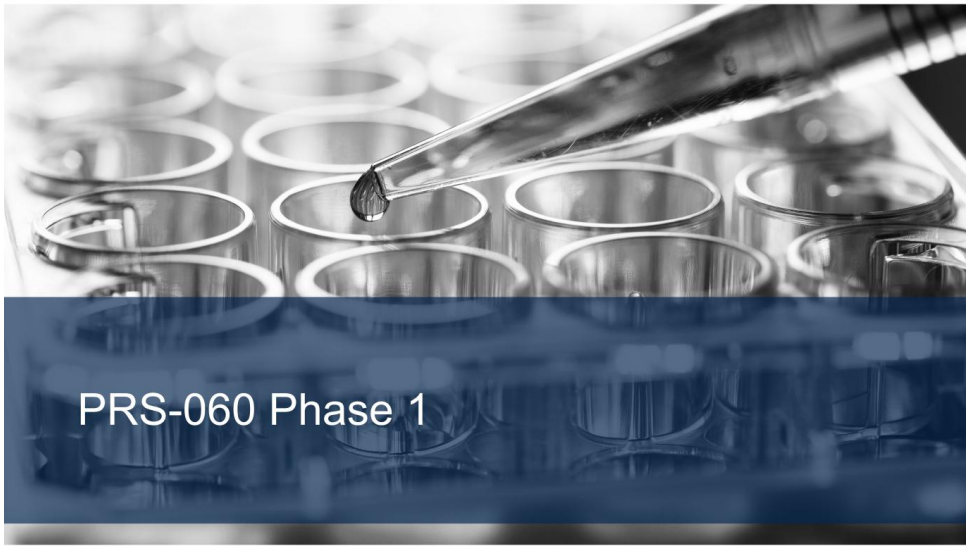
Financial Overview (as of 12/31/21)



>$175M non-dilutive capital from partnerships since 2017

>$17M grant announced in 2021

Appendix

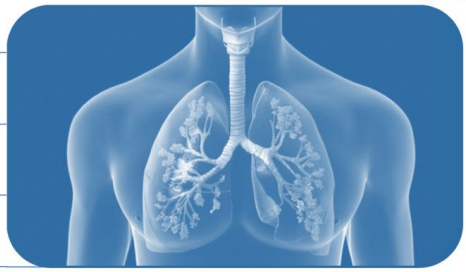

PRS-060 Phase 1

PRS-060 Phase 1 Multiple Ascending Dose Trial

Strategic Objectives	Ascertain PK/PD with a reliable biomarker to confirm local target engagement and inform Phase 2 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, and 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



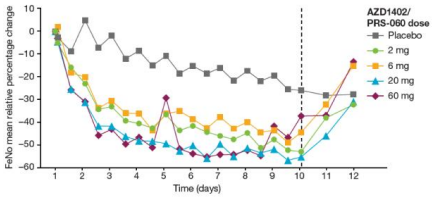
Phase 1b Interim Results: Favorable Safety Profile

- 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

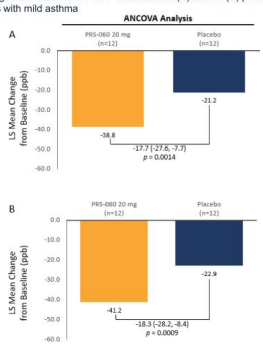
PRS-060 Relative FeNO Reduction (Emax Analysis)



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		

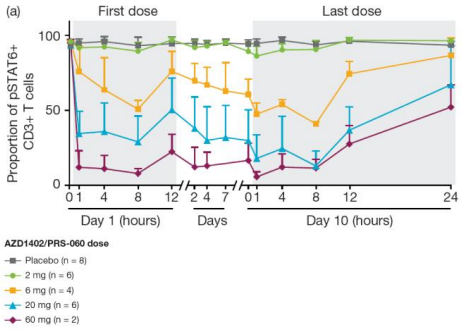
PRS-060 Relative FeNO Reduction (ANCOVA Analysis)

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 2 mg 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 – Phase 1 Monotherapy

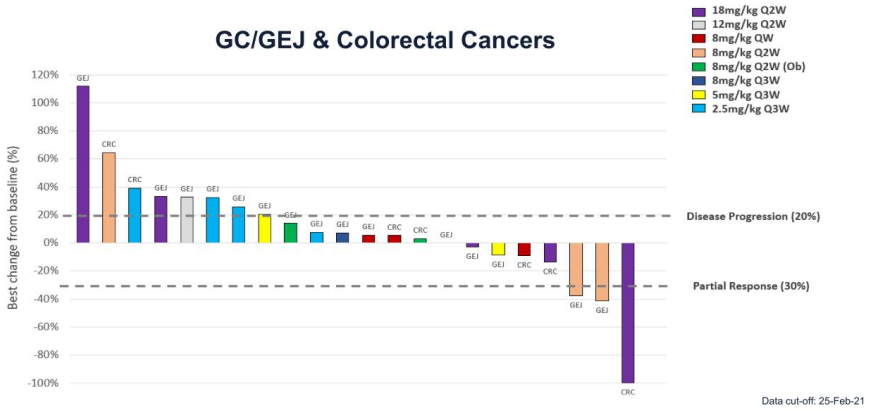
Phase 1 Monotherapy Baseline Characteristics (N = 78)

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

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



Data cut-off: 25-Feb-21

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

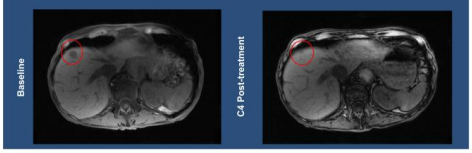
Patient Profile, Treatment History and Treatment Outcome

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)

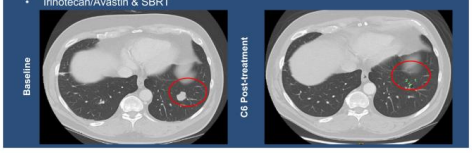


Rectal Cancer Patient with Complete Response

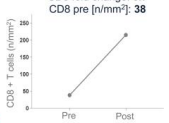
- 59-year-old male; initial diagnosis in March 2017
- Rectal cancer with cardiac and lung mets
- Treated with 18 mg/kg Q2W of PRS-343
- Foundation One Her2 amplification; verified in-house to be IHC 3+; MSS, TMB low

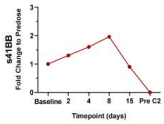
Prior Treatment includes:

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

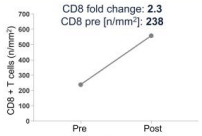


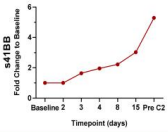
CD8 fold change: **5.7**
CD8 pre [n/mm²]: **38**





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





pieris

Case Study: PR in Cancer of Unknown Primary

Patient Profile, Treatment History and Treatment Outcome

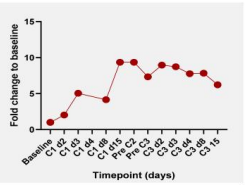
Patient Profile

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

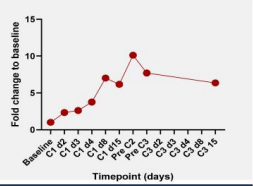
Patient Profile

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 – Biomarkers

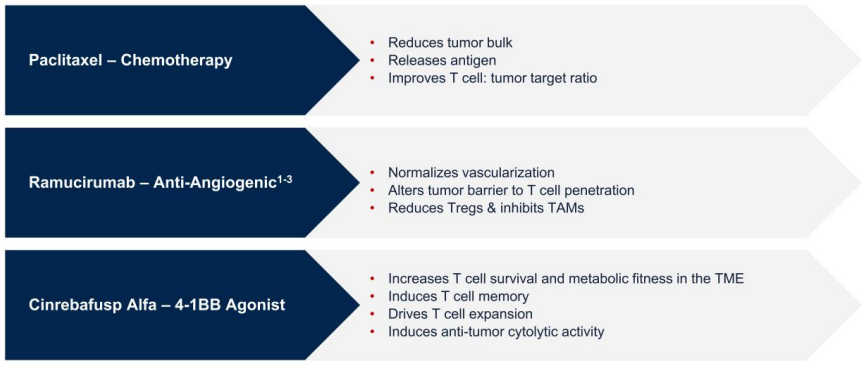
Soluble 4-1BB (s4-1BB): Blood-based Biomarker of Cinrebafusp Alfa Engagement

- 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 as a negative regulator, keeping 4-1BB-mediated co-stimulation in check

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

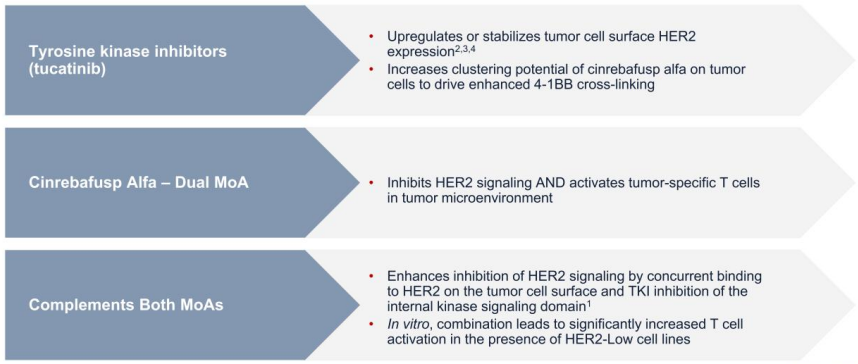
Cinrebafusp Alfa – Phase 2 Rationale

Scientific Rationale for Combining Cinrebafusp Alfa & SoC



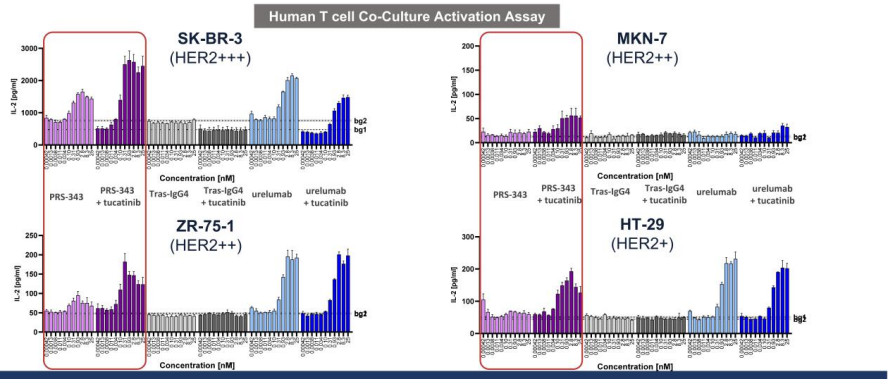
1 - Allen et al., Science Translational Medicine 2017
2 - Juang et al., Front Immunology 2018
3 - Tada et al., Journal for Immunotherapy of Cancer 2018

Scientific Rationale for Combining Cinrebafusp Alfa & Tucatinib



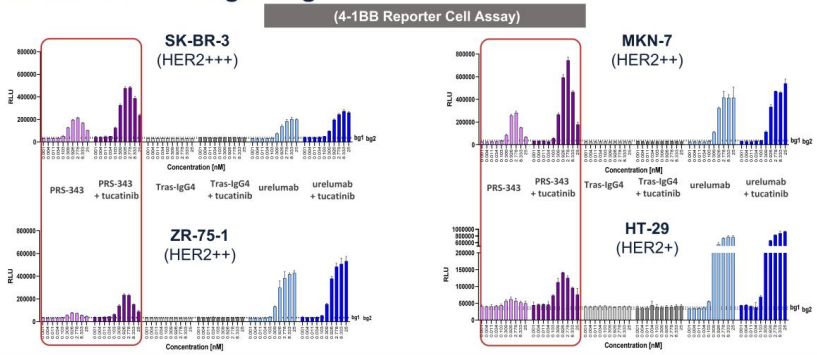
1 - Baselga J., Lancet, 2012
2 - Maruyama T., et al, Anticancer Res., 2011
3 - Scaltriti M., et al, Oncogene, 2009
4 - Hartmans, et al, Oncotarget., 2017

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



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

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