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 30, 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 Boston, MA	02109
(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 30, 2021, Pieris Pharmaceuticals, Inc. (the "Company") issued a press release announcing certain financial results for the fiscal year ended December 31, 2020. 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 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference in such filing.

Item 7.01 Regulation FD Disclosure.

Attached hereto as Exhibit 99.2 and incorporated by reference herein is the March 2021 Investor Presentation of Pieris Pharmaceuticals, Inc.

The information set forth under this "Item 7.01. Regulation FD Disclosure," including Exhibit 99.2 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 Press Release Dated March 30, 2021.

99.2 Investor Presentation, Dated March 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: March 30, 2020

/s/ Tom Bures
Tom Bures
Vice President, Finance

PRESS RELEASE

PIERIS PHARMACEUTICALS REPORTS
FULL-YEAR 2020 FINANCIAL RESULTS AND PROVIDES CORPORATE UPDATE

COMPANY TO HOST AN INVESTOR CONFERENCE CALL ON
TUESDAY, MARCH 30, 2021 AT 8:00 AM EDT

- **Pieris achieves $13 million milestone from AstraZeneca for initiation of PRS-060/AZD1402 phase 2a study and AstraZeneca to purchase $10 million equity stake in Pieris common stock as part of an amended collaboration agreement**
- **$13 million equity investment by Seagen in Pieris, in addition to a clinical trial and supply agreement to evaluate cinrebafusp alfa (PRS-343) in combination with TUKYSA® (tucatinib) in HER2-low gastric cancer as part of an amended collaboration agreement**
- **Additional clinical benefit and safety data from the highest dose cohort and updated biomarker data across all active dose cohorts from cinrebafusp alfa phase 1 monotherapy study to be presented at American Association for Cancer Research Annual Meeting 2021**
- **Synergistic preclinical PRS-344 data to be presented at American Association for Cancer Research Annual Meeting 2021, including *in vitro* data evaluating potential effects of combining 4-1BB with PD-L1 and the effects of PRS-344 on CD8+ T cells, as well as dose-dependent anti-tumor response in *in vivo* preclinical models**

BOSTON, MA, March 30, 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 reported financial results for the fiscal year ended December 31, 2020 and provided an update on the Company's recent and anticipated future developments.

"We are pleased to announce the achievement of our second clinical milestone for PRS-060/AZD1402, triggered by the initiation of phase 2a by our partner, AstraZeneca, who further demonstrated their commitment to our respiratory-focused alliance with an equity investment," said Stephen S. Yoder, President and Chief Executive Officer of Pieris. "Within our immuno-oncology franchise, we look forward to presenting additional data for two of our 4-1BB-based bispecific programs at AACR, cinrebafusp alfa (PRS-343) and PRS-344, reinforcing our commitment to and leadership in the 4-1BB space. Following the generation of synergistic *in vitro* data for the combination of cinrebafusp alfa with TUKYSA® (tucatinib), we plan to pursue this combination in lower HER2-expressing gastric cancer patients with Seagen. Seagen has also recently made an equity investment in Pieris, further strengthening the alliance we signed in 2018. Partnerships are an important part of our corporate strategy, and our recent announcements reinforce the value our current alliances continue to bring."

- **PRS-060 & AstraZeneca Collaboration:** Pieris will receive a $13 million milestone payment from AstraZeneca for the initiation of patient enrollment in the phase 2a study of PRS-060/AZD1402, an inhaled IL-4 receptor alpha inhibitor the companies are developing for the treatment of moderate-to-severe asthma. The global phase 2a study of PRS-060/AZD1402 is a two-part, multi-center, placebo-controlled clinical study that will evaluate the drug candidate at up to three dose levels using a dry powder formulation administered twice daily on top of standard of care. Additionally, the companies amended their existing agreement to restructure certain commercial economics for PRS-060/AZD1402 by adjusting various milestones and royalty provisions, while fundamentally maintaining the overall value split between AstraZeneca and Pieris. In connection with the amendment, AstraZeneca will make a $10 million equity investment in Pieris through the purchase of 3,584,230 newly-issued shares of Pieris common stock at a price of $2.79 per share.

- **Cinrebafusp Alfa (PRS-343):** Pieris will present an updated dataset for 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 Annual Meeting 2021 (AACR) on April 10, 2021. The presentation will include additional clinical benefit and safety data from cohort 13b (18 mg/kg, administered Q2W), as well as biomarker data across all active dose cohorts. The Company is preparing for the phase 2 study of cinrebafusp alfa, expected to begin in the summer of 2021. The phase 2 study will evaluate cinrebafusp alfa in combination with ramucirumab and paclitaxel in high HER2-expressing gastric cancer and in combination with tucatinib in low HER2-expressing gastric cancer. Collaboration partners Lilly and Seagen will supply ramucirumab and tucatinib, respectively, for these study arms.

- **Seagen Collaboration Expansion:** Seagen made a $13 million equity investment in Pieris as part of an ongoing collaboration between the companies. Additionally, the companies have entered into a clinical trial and supply agreement to evaluate the safety and efficacy of combining Pieris' cinrebafusp alfa with Seagen's TUKYSA® (tucatinib), a small-molecule tyrosine kinase HER2 inhibitor, for the treatment of gastric cancer patients expressing lower HER2 levels (IHC2+/ISH- & IHC1+) as part of the upcoming phase 2 study to be conducted by Pieris. The companies have also amended their existing immuno-oncology collaboration whereby Pieris' option to co-develop and co-commercialize the second of three programs in the collaboration has been converted to a co-promotion option in the United States.

- **PRS-344 & Servier Collaboration:** Pieris and Servier will present preclinical data for PRS-344/S095012, a 4-1BB/PD-L1 bispecific, as part of a poster session at the AACR Annual Meeting 2021. The presentation will showcase synergistic data, including *in vitro* data evaluating potential effects of combining 4-1BB with PD-L1 and the effects of PRS-344 on CD8+ T cells, as well as dose-dependent anti-tumor response in *in vivo* preclinical models. PRS-344 in expected to enter phase 1 studies this year. Pieris holds exclusive commercialization rights for PRS-344 in the United States and will receive royalties on ex-U.S. sales by Servier for this program. Additionally, Pieris completed non-GLP preclinical work for PRS-352, a preclinical-stage program addressing undisclosed targets for immuno-oncology, last quarter; Servier is fully responsible for further development of that program.

- **Preclinical Respiratory Pipeline:** Pieris and AstraZeneca continue to advance each of the four programs in the collaboration beyond PRS-060/AZD140. Pieris also continues to advance several proprietary discovery-stage respiratory programs and expects to share data and rationale for advancement of one of its proprietary programs this year.

AACR Details:

Cinrebafusp Alfa Oral Presentation:

Title: *Clinical and biomarker activity of PRS-343, a bispecific fusion protein targeting 4-1BB and HER2, from a Phase 1 study in patients with advanced solid tumors*
Abstract: CT017
Session: CTMS01 - Early Clinical Trials with New Anticancer Agents
Date/Time: The presentation will take place at 2:05 PM EDT on Saturday, April 10, 2021 on Channel 08.

PRS-344 Poster:

Title: *Simultaneous costimulatory T cell engagement and checkpoint inhibition by PRS*

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

Abstract: LB135
Session: PO.ET01.08 - Targeting the Tumor Microenvironment in Drug Development
Date/Time: This poster will be available beginning at 8:30AM EDT on Saturday, April 10, 2021.

Fiscal Year Financial Update:

Cash Position - Cash, cash equivalents, and investments totaled $70.4 million for the year ended December 31, 2020, compared to a cash, cash equivalents, and investments balance of $104.2 million for the year ended December 31, 2019. The decrease was primarily due to funding operating and capital expenses in 2020, partially offset by ATM proceeds and milestone achievements during the year. The December 31, 2020 ending cash excludes the $13 million received from Seagen in March 2021 and the $23 million to be received from AstraZeneca in connection with phase 2a study initiation and equity investment.

R&D Expense - R&D expenses were $46.5 million for the year ended December 31, 2020, compared to $55.0 million for the year ended December 31, 2019. The decrease in R&D expenses was primarily due to lower clinical and manufacturing costs on our immuno-oncology programs, in part due to the partial clinical hold on PRS-343, lower manufacturing spending on PRS-060 (which is fully reimbursed by AstraZeneca), and lower travel-related expenditures due to COVID-19 restrictions. The overall decrease was partially offset by an increase in allocated IT and facility costs due to the move to a new R&D facility in Hallbergmoos, Germany in early 2020.

G&A Expense – G&A expenses were $16.7 million for the year ended December 31, 2020, compared to $18.4 million for the year ended December 31, 2019. The decrease in G&A expenses was primarily due to lower personnel costs, lower audit and professional fees related to Sarbanes-Oxley readiness, and lower travel-related expenditures due to COVID-19 restrictions. These decreases were partially offset by higher allocated IT and facility costs due to the move to the new R&D facility.

Net Loss - Net loss attributable to common stockholders was $37.2 million or $(0.68) per share for the year ended December 31, 2020, compared to a net loss of $28.3 million or $(0.56) per share for the year ended December 31, 2019.

Conference Call:

Pieris management will host a conference call beginning at 8:00 AM EDT on Tuesday, March 30, 2021, 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). An archived replay of the call will be available by dialing +1-877-660-6853 (US & Canada) or +1-201-612-7415 (International) and providing the Conference ID #: 13661472.

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, including AstraZeneca, Seagen, and Servier. Anticalin® is a registered trademark of Pieris. For more information, visit www.pieris.com.

Forward Looking Statements:

This press release contains forward-looking statements as that term is defined in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Statements in this press

release that are not purely historical are forward-looking statements. Such forward-looking statements include, among other things, whether the combination of cinrebafusp alfa and TUKYSA could address a high medical need in HER2 low-expressing gastric cancer patients who do not respond to traditional HER2-targeted therapies; whether the effects of the combination of cinrebafusp alfa and TUKYSA 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 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 FDA; competition in the industry in which we operate; delays or disruptions due to COVID-19; and market conditions. These forward-looking statements are made as of the date of this press release, and we assume no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law. Investors should consult all of the information set forth herein and should also refer to the risk factor disclosure set forth in the reports and other documents we file with the SEC available at www.sec.gov, including without limitation the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and the Company's Quarterly Reports on Form 10-Q.

Investor Relations Contact:
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PIERIS PHARMACEUTICALS, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands)

	December 31, 2020	December 31, 2019
Assets:		
Cash and cash equivalents	$ 70,436	$ 62,260
Short term investments	—	41,894
Accounts receivable	1,706	6,787
Prepaid expenses and other current assets	3,579	4,072
Total current assets	75,721	115,013
Property and equipment, net	22,046	19,502
Operating lease right-of-use assets	3,934	3,436
Other non-current assets	3,309	3,146
Total Assets	$ 105,010	$ 141,097
Liabilities and stockholders' equity:		
Accounts payable	$ 1,787	$ 5,803
Accrued expenses	7,731	9,944
Deferred revenue, current portion	12,627	11,256
Total current liabilities	22,145	27,003
Deferred revenue, net of current portion	35,900	47,258
Operating lease liabilities	15,932	15,484
Other long-term liabilities	6	—
Total Liabilities	73,983	89,745
Total stockholders' equity	31,027	51,352
Total liabilities and stockholders' equity	$ 105,010	$ 141,097

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

	Twelve Months Ended December 31,	
	2020	2019
Revenues	$ 29,323	$ 46,279
Operating expenses		
Research and development	46,531	54,996
General and administrative	16,713	18,440
Total operating expenses	63,244	73,436
Loss from operations	(33,921)	(27,157)
Interest income	511	1,714
Other income (expense), net	(3,656)	(26)
Loss before income taxes	(37,066)	(25,469)
Provision for income tax	164	—
Net loss	$ (37,230)	$ (25,469)
Basic and diluted net loss per share	$ (0.68)	$ (0.56)
Basic and diluted weighted average shares outstanding	54,481	50,625

INVESTOR PRESENTATION

MARCH 2021

-pieris-

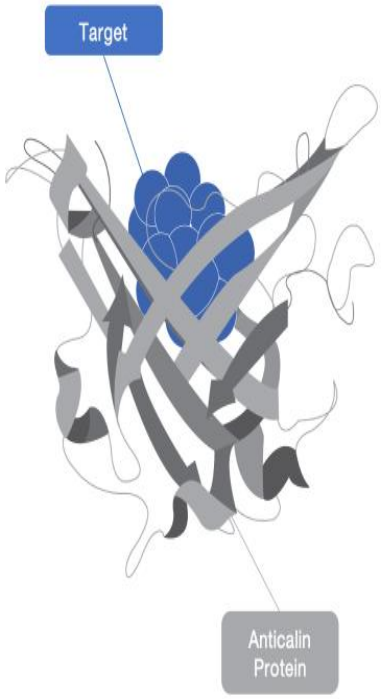
Forward Looking Statements

This presentation 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 presentation that are not purely historical are forward-looking statements. Such forward-looking statements include, among other things, whether the combination of cinrebafusp alfa and TUKYSA could address a high medical need in HER2 low-expressing gastric cancer patients who do not respond to traditional HER2-targeted therapies; whether the effects of the combination of cinrebafusp alfa and TUKYSA 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 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 FDA; 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 SEC available at www.sec.gov, including without limitation the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and the Company's Quarterly Reports on Form 10-Q.

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

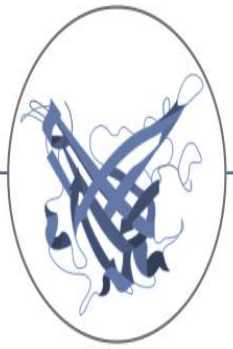
Translational Science Expertise to Deploy Platform in Meaningful Way

- 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

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

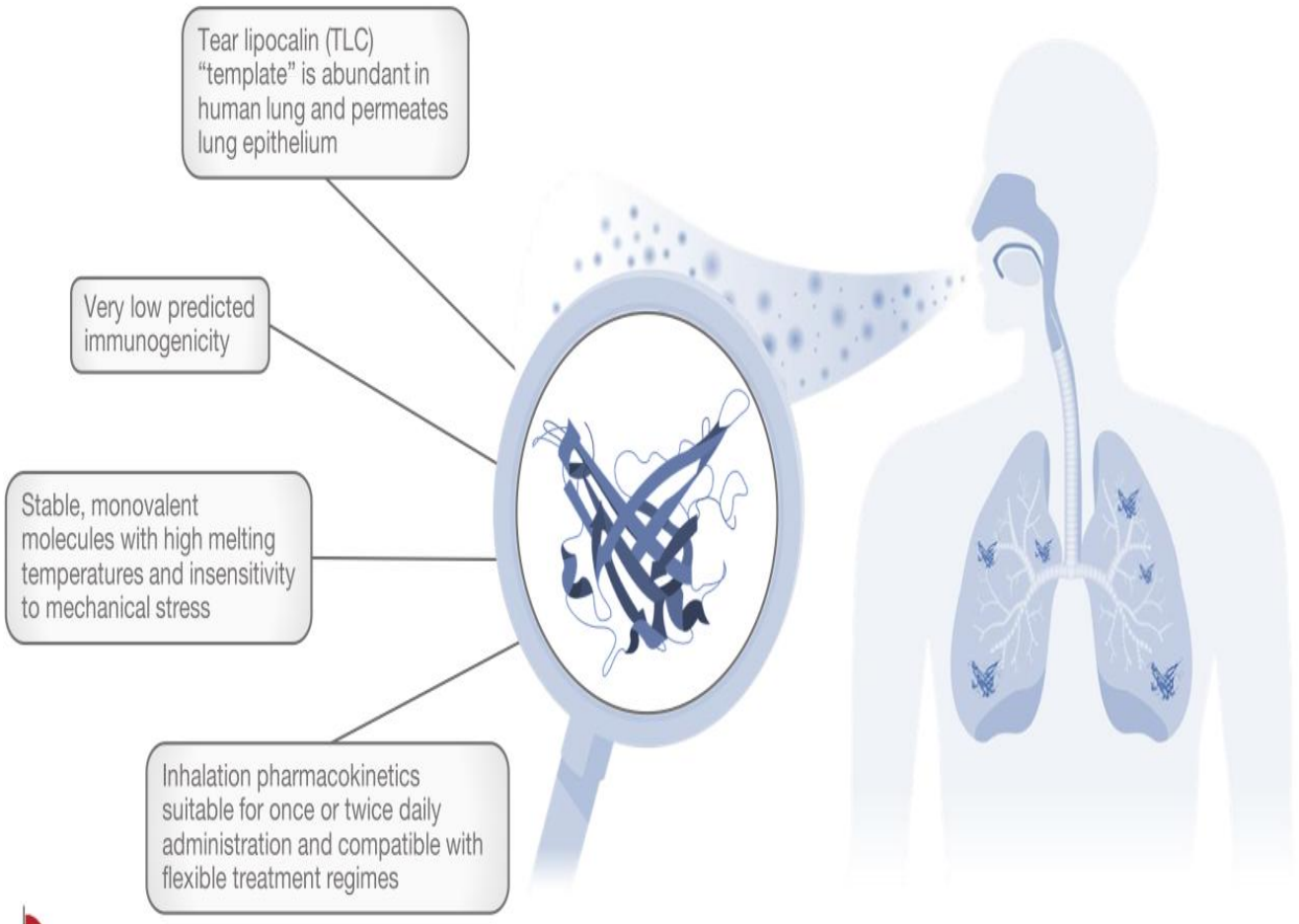
Strong Partners • Significant Cash Flow • Retained Commercial Rights

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

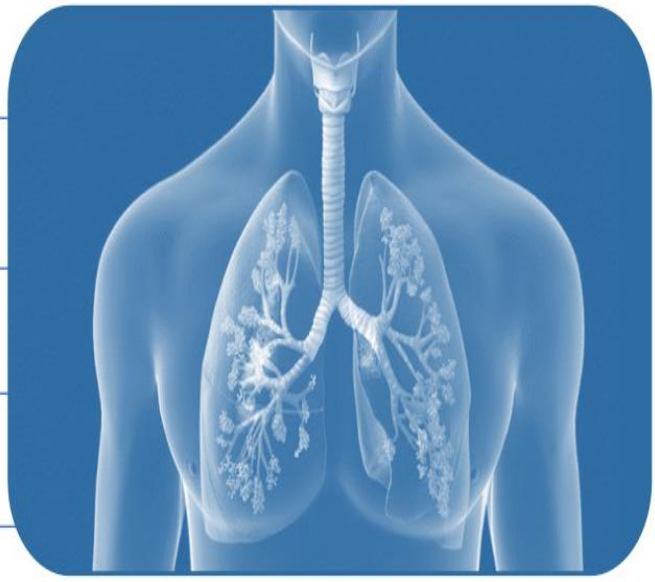
Candidate	PRS-060
Function/MoA	Inhibiting IL4-Rα (disrupts IL-4 & IL-13 signaling)
Indications	Moderate-to-severe asthma
Development	Phase 2a in moderate asthmatics
Commercial Rights	Co-development and U.S. co-commercialization rights, including gross margin share

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

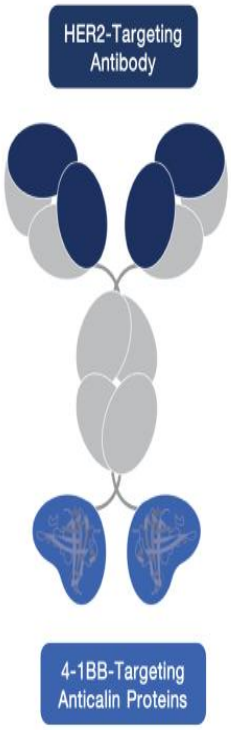
Unique Attributes of 4-1BB Agonism on Tumor-specific T Cells

- ✓ 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

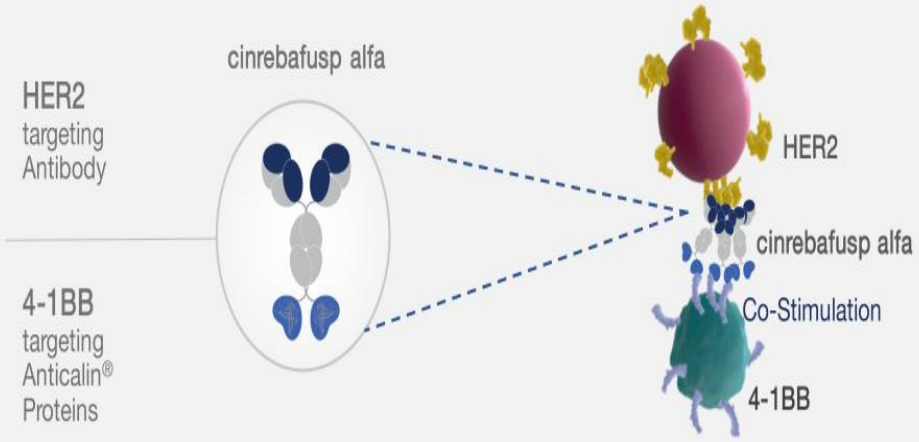


Cinrebafusp Alfa: 4-1B/HER2 Bispecific

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 $CD8^+/Ki67^+$

-pieris-

Improving Lives

Monotherapy and Combination Studies: Enabled Meaningful Clinical Characterization of Cinrebafusp Alfa

Snapshot

- Patients with HER2+ solid tumors
- Monotherapy and combination with atezolizumab
- Data updates presented at ESMO 2020

Primary Objectives

- Characterize safety profile
- Identify MTD or RP2D

Secondary Objectives

- Characterize PK profile
- Investigate dosing schedule
- Assess potential immunogenicity and PD effects
- Investigate efficacy

ACTIVE SCHEDULES	
	Schedule 1: Q3W dosing on day 1; 21-day cycle
	Schedule 2 (b): Q2W dosing on days 1, 15; 28-day cycle
	Schedule 3 (c): Q1W dosing on days 1, 8, 15; 21-day cycle
	In combination with atezolizumab: Q3W dosing on day 1; 21-day cycle

Mono Dose Cohort*	Combo Dose Cohort**	Dose (mg/kg)
1		0.0005
2		0.0015
3		0.005
4		0.015
5	1	0.05
6	2	0.15
7	3	0.5
8	4	1
9	5	2.5
10	6	5
11	7	8
11 (b)		8
11 (c)		8
12 (b)		12
13 (b)		18
Obinutuzumab + 11(b)		8

9-13b: active dose cohorts in mono study

*Additional dose cohorts enrolling in monotherapy study

**1200mg flat dose of atezolizumab

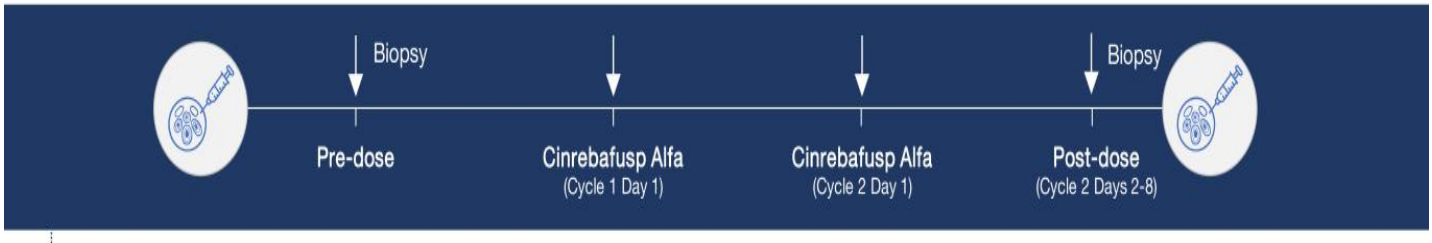
Summary of Responses of Cinrebafusp Alfa in Monotherapy

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

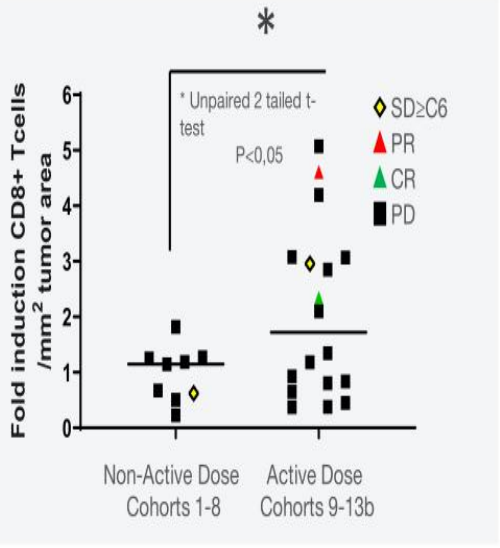
Cohort	13b	12b	11c	Obi	11b	11	10	9	Total
Best Response	18 mg/kg, Q2W	12 mg/kg, Q2W	8 mg/kg, QW	8 mg/Kg, Q2W	8 mg/kg, Q2W	8 mg/kg, Q3W	5 mg/kg, Q3W	2.5 mg/kg, Q3W	
Evaluable Patients	3	2	4	2	7	4	6	5	33
CR	1	-	-		-	-	-	-	1
PR	-	-	-		3	-	-	-	3
SD	-	-	1	1	3	3	3	2	13
ORR	33%	0%	0%	0%	43%	0%	0%	0%	12%
DCR	33%	0%	25%	50%	86%	75%	50%	40%	52%

Data cut-off: 27-Jul-20

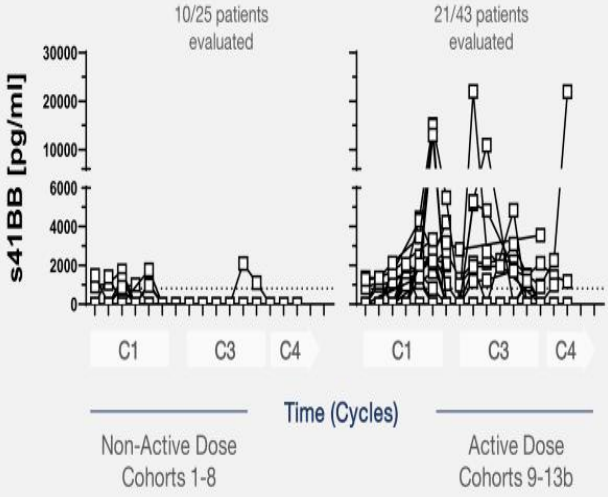
Increase in CD8+ T Cells and Circulating Soluble 4-1BB Support 4-1BB Engagement by Cinrebafusp Alfa



Tumor



Serum



Data cut-off: 27-Jul-20

Cinrebafusp Alfa (PRS-343) – AACR Presentation: April 10th

Clinical and biomarker activity of PRS-343, a bispecific fusion protein targeting 4-1BB and HER2, from a Phase 1 study in patients with advanced solid tumors

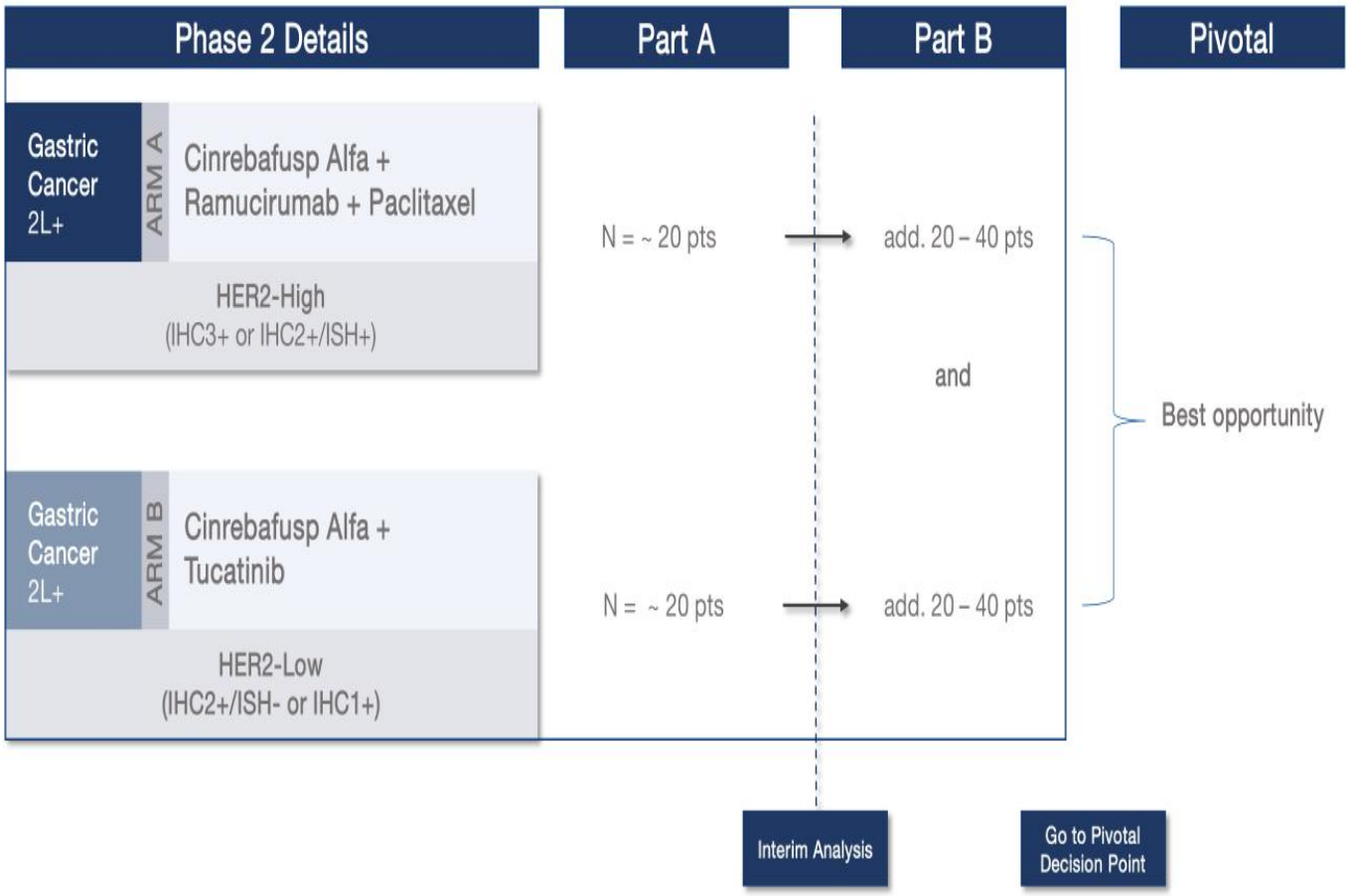
Sarina Piha-Paul, MD MD Anderson Cancer Center, Houston, TX

Date/Time: April 10, 2021 at 2:05 PM EDT
Abstract Number: CT017

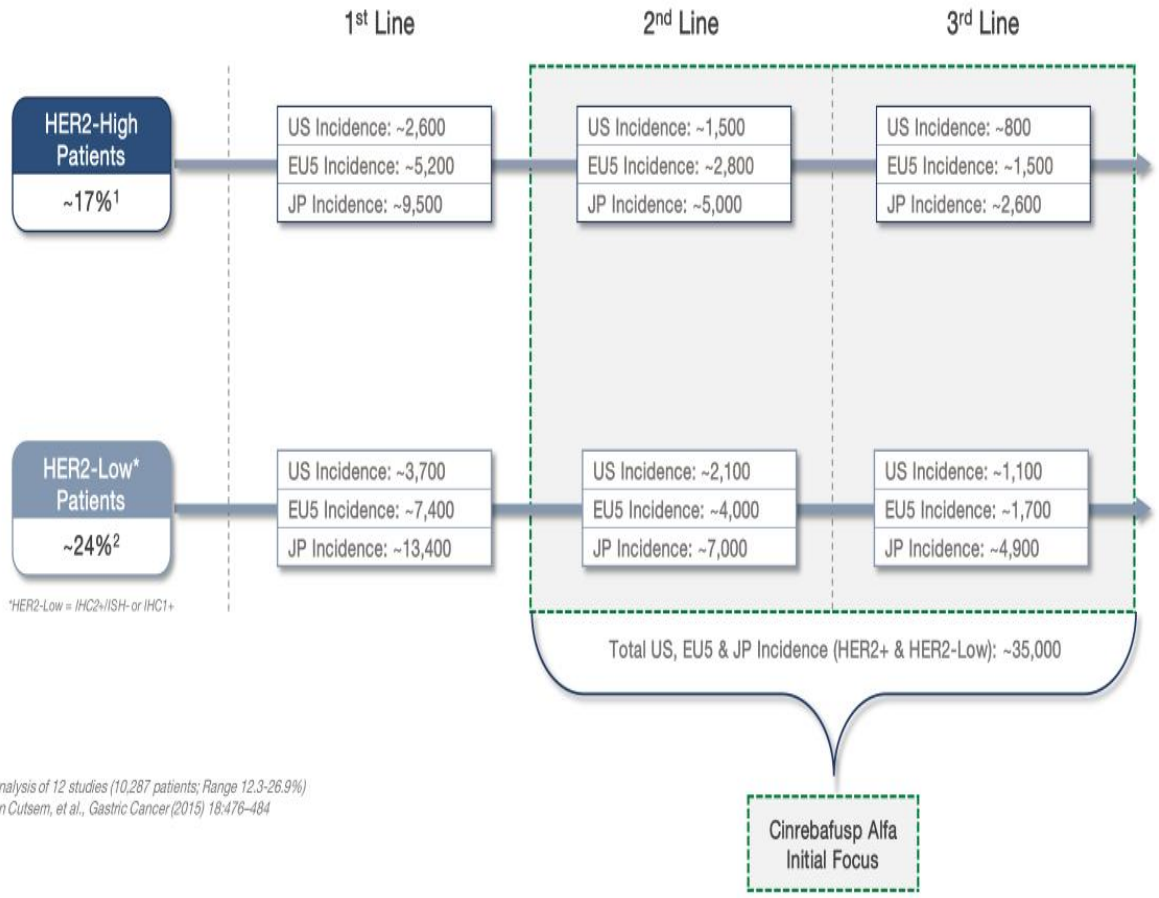
Topics Covered:

- Safety and tolerability profile
- Additional and maintained clinical benefit; pharmacodynamic correlates
- Observations that support RP2D and phase 2 development plans

Cinrebafusp Alfa (PRS-343) Clinical Development Plan



Cinrebafusp Alfa (PRS-343) Opportunity in High-HER2 & Low-HER2 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

Paclitaxel – Chemotherapy

- Reduce tumor bulk
- Antigen release
- Improve T cell: tumor target ratio

Ramucirumab – Anti-Angiogenic[1-3]

- Normalizes vascularization
- Alters tumor barrier to T cell penetration
- Reduces Tregs & inhibits TAMs
- Multiple αVEGF / IO combos approved

Cinrebafusp Alfa – 4-1BB Agonist

- Increase T cell survival and metabolic fitness in the TME
- Induce T cell memory
- Drive T cell expansion
- Induce anti-tumor cytolytic activity

1 - Allen et al., Science Translational Medicine 2017
2 - Juang et al. Front Immunology 2018
3 - Tada et al., Joumal 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]
- Increased clustering of cinrebafusp alfa on the tumor cell surface to drive 4-1BB cross-linking and enhanced activation of tumor-specific T cells & NK cells

Cinrebafusp Alfa – Dual MoA

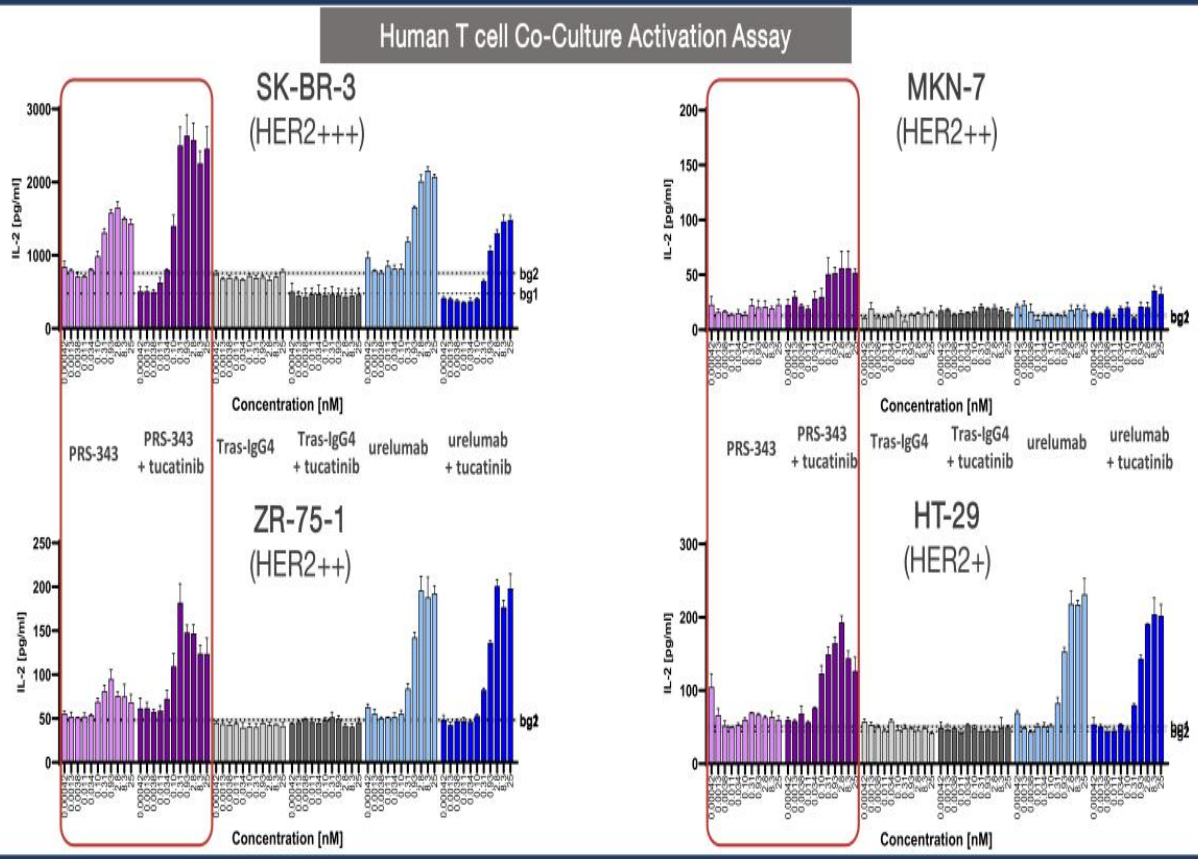
- Inhibition of HER2 signaling AND activation of tumor-specific T cells in tumor microenvironment

Complements Both MoAs

- Enhanced inhibition of HER2 signaling by concurrent binding to HER2 on the tumor cell surface and small molecule 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

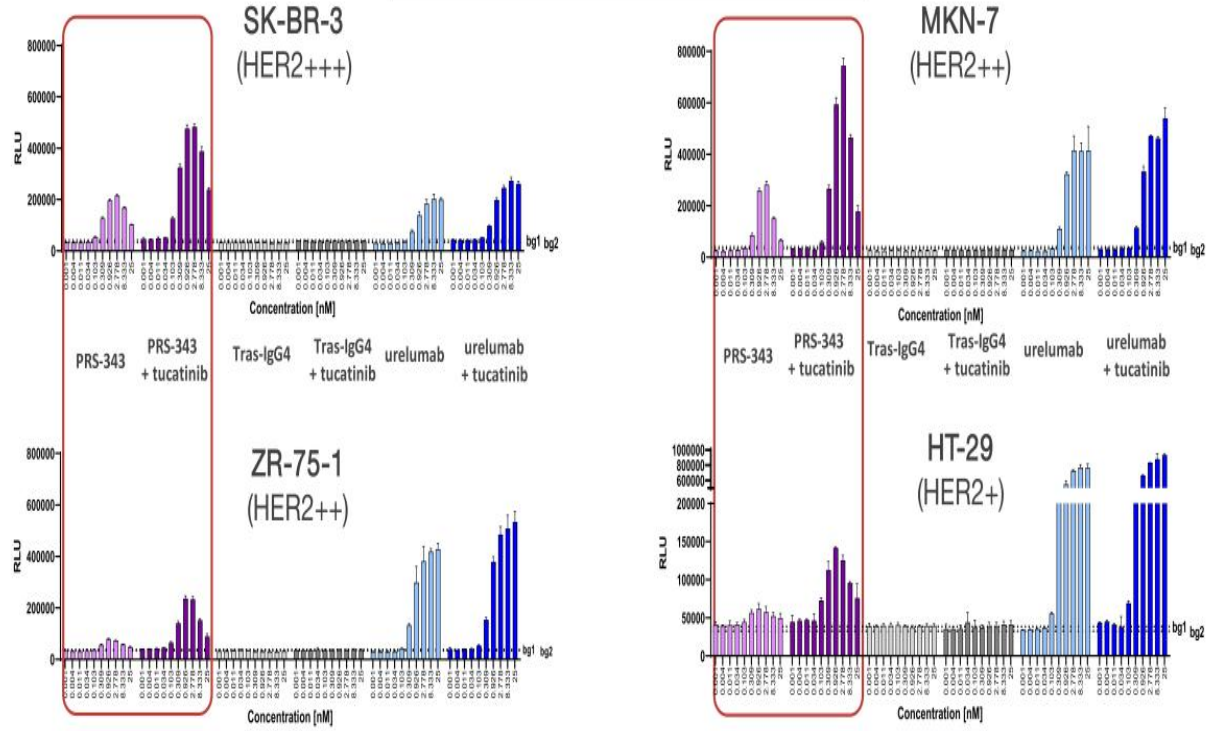
Cinrebafusp Alfa and Tucatinib Combination Enhances T-cell Activation



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

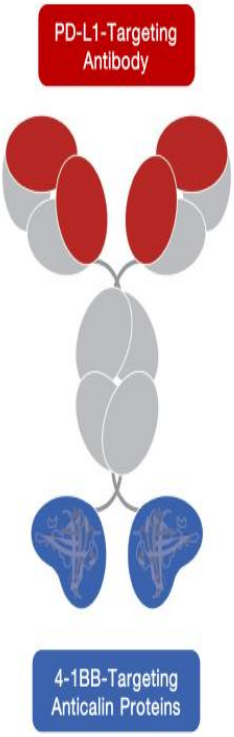
(4-1BB Reporter Cell Assay)



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 – AACR Poster: April 10th

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

Date/Time: April 10, 2021 at 8:30AM EDT
Abstract Number: LB135

Synergistic data, including :

- *In vitro* data evaluating potential synergistic effects of combining 4-1BB with PD-L1
- *In vitro* data evaluating effects of PRS-344 on CD8+ T cells
- Dose-dependent anti-tumor response in *in vivo* preclinical models

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

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

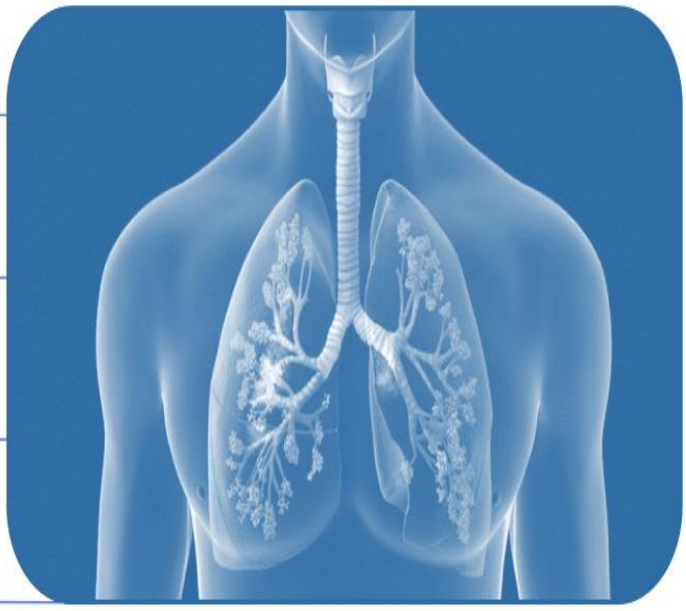
*q.d. on Day 10

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



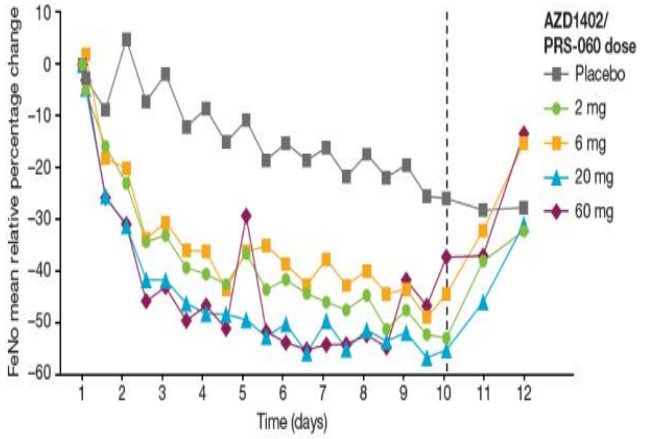
Phase 1b Interim Results: Favorable Safety Profile

- 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

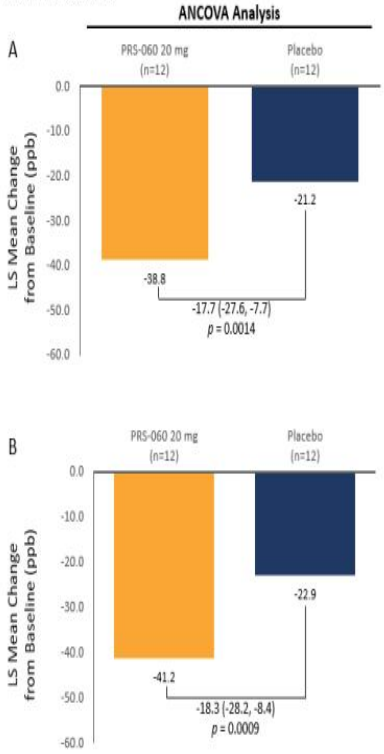
PRS-060 Relative FeNO Reduction (Emax Analysis)



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		

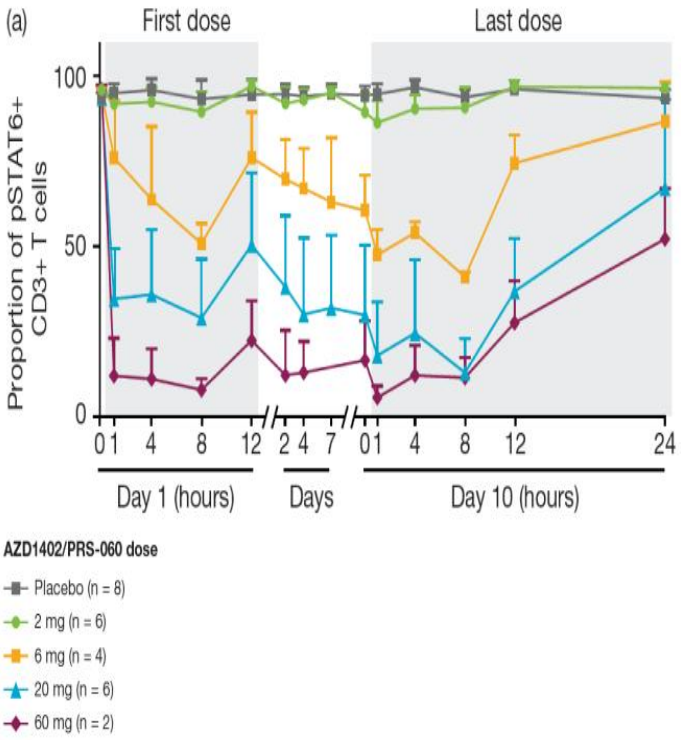
PRS-060 Relative FeNO Reduction (ANCOVA Analysis)

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 Phase I

Baseline Characteristics for Cinrebafusp Alfa Phase I Studies: Monotherapy and Combination with Atezolizumab

All Subjects (n = 74, 41)

Characteristic	Monotherapy; n (%)	In Combination with Atezolizumab; n (%)
Age, Median (range)	63 (24–92)	59 (26-87)
Gender		
F	44 (59%)	23 (56%)
M	30 (41%)	18 (44%)
ECOG PS*		
0	19 (26%)	12 (29%)
1	55 (74%)	18 (44%)
Prior Therapy Lines		
1	9 (12%)	5 (12%)
2	10 (14%)	7 (17%)
3	15 (21%)	6 (15%)
4	11 (15%)	6 (15%)
5+	28 (38%)	17 (41%)
Median no. of anti-HER2 Treatments		
Breast	7	3-4
Gastric	3	1

Primary Cancer Type	Monotherapy; n (%)	In Combination with Atezolizumab; n (%)
Gastroesophageal	27 (36%)	7 (17%)
Breast	16 (22%)	12 (29%)
Colorectal	10 (14%)	5 (12%)
Gynecological	9 (12%)	4 (10%)
Biliary Tract	7 (9%)	6 (15%)
Non-Small Cell Lung	-	4 (10%)
Bladder	2 (3%)	1 (2%)
Pancreatic	1 (1%)	1 (2%)
Other – Cancer of Unknown Origin	1 (1%)	1 (2%)
Other – Salivary Duct	1 (1%)	-

*Combination trial enrolled ECOG 2 patients as well (not shown on this chart)

Data cut-off: 27-Jul-20

Cinrebafusp Alfa – Monotherapy

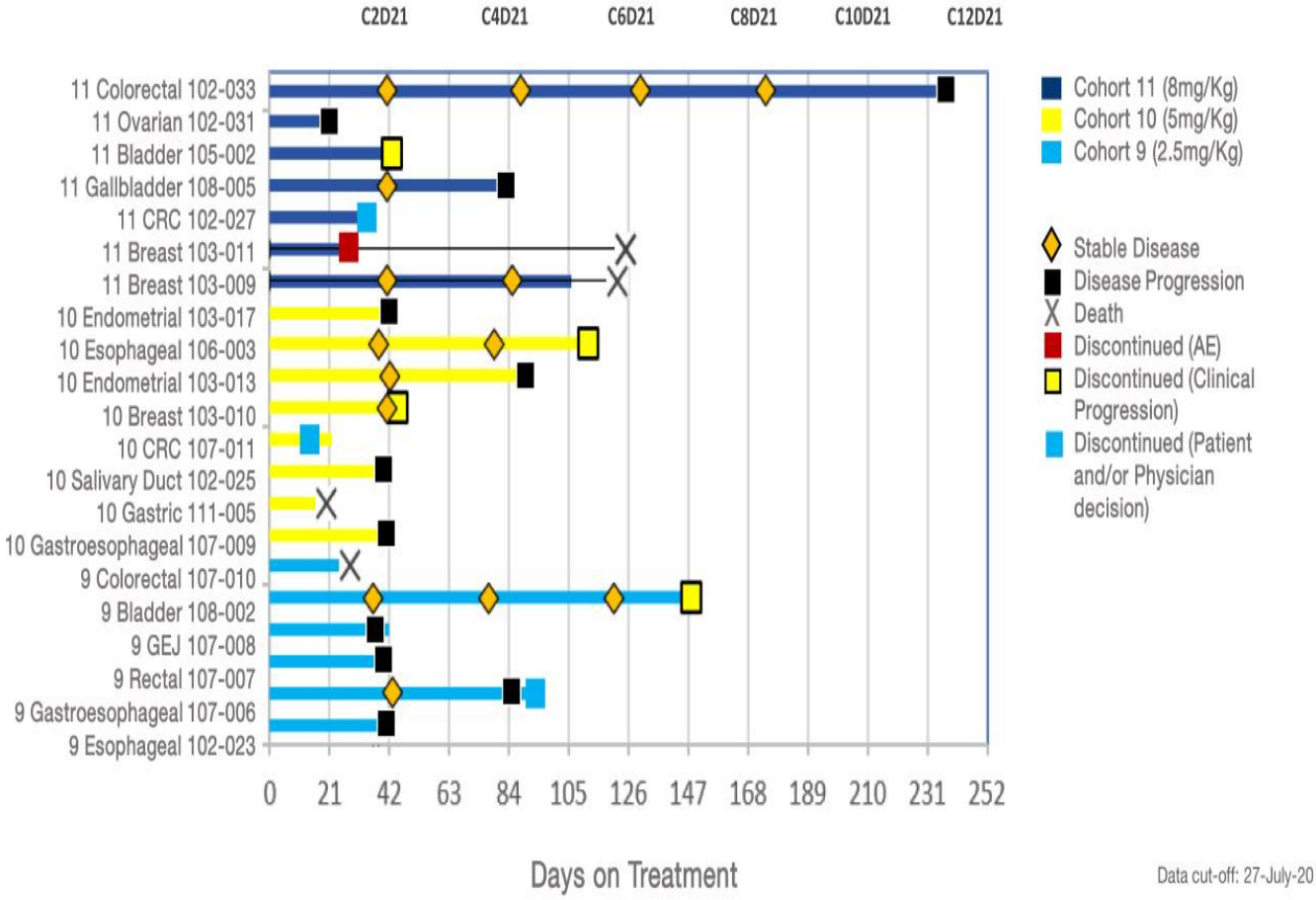
Treatment-Related Adverse Events (Monotherapy Trial)
All Subjects

Occurred in > 1 Patient	Monotherapy	
	n = 145 (%)	% Grade 3
Infusion Related Reaction	27 (19%)	3 (2%)
Fatigue	11 (8%)	1 (1%)
Nausea	11 (8%)	
Vomiting	8 (6%)	
Chills	8 (6%)	
Anemia	2 (1%)	1 (1%)
Arthalgia	2 (1%)	
Asthenia	2 (1%)	
Cough	2 (1%)	
Decreased appetite	2 (1%)	
Diarrhea	6 (4%)	
Dizziness	2 (1%)	
Dyspnoea	3 (2%)	
Flushing	5 (3%)	2 (1%)
Non-cardiac chest pain	4 (3%)	
Paraesthesia	3 (2%)	1 (1%)
Pruritis	3 (3%)	
Rash	2 (1%)	

One TRAE above Grade 3: Grade 4 Infusion Related Reaction in cohort 10 (5mg/kg cinrebafusp alfa, Q3W).

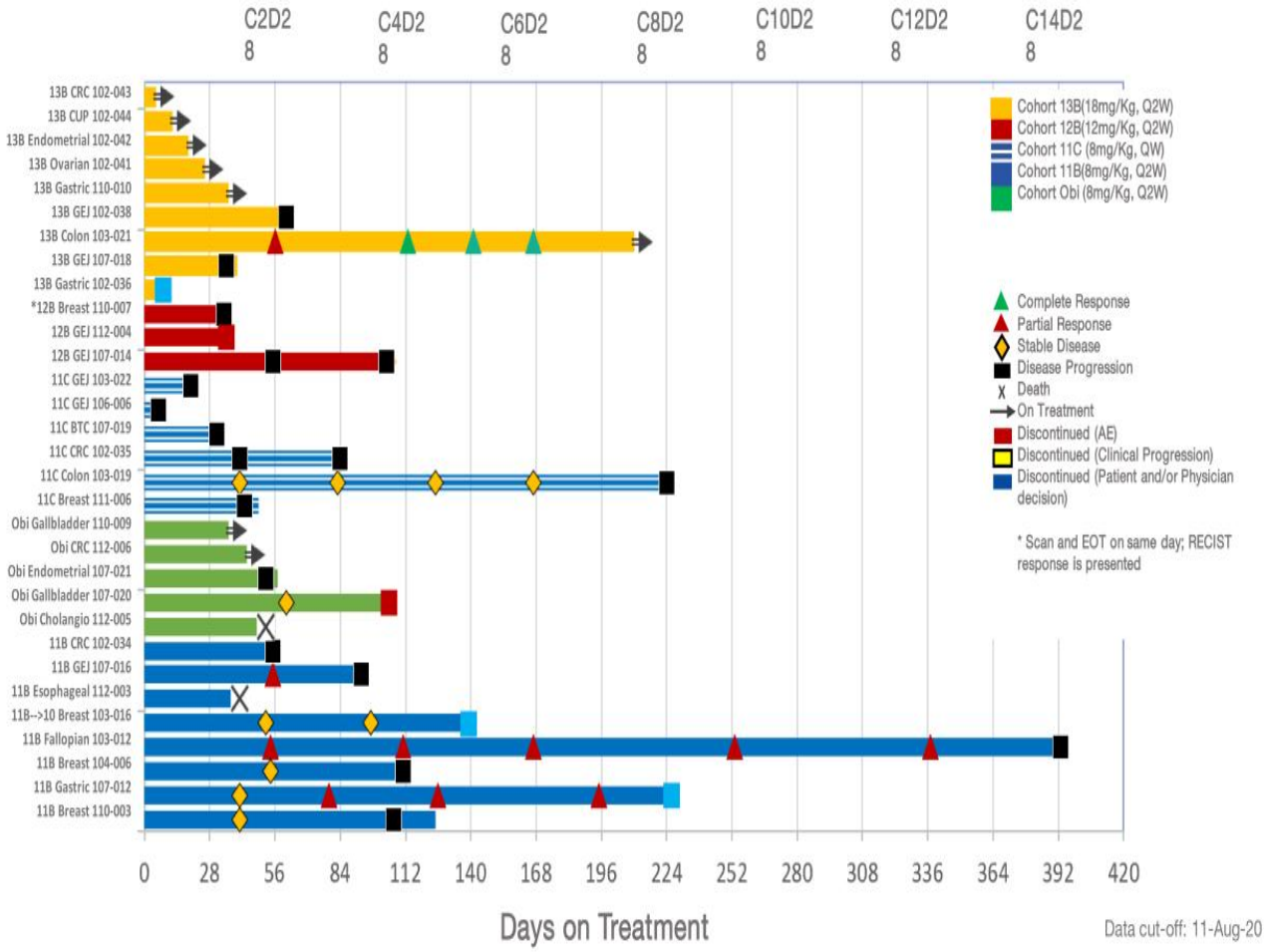
Data cut-off: 27-Jul-20

Average Time on Treatment with Cinrebafusp Alfa
Cohorts 9-11a



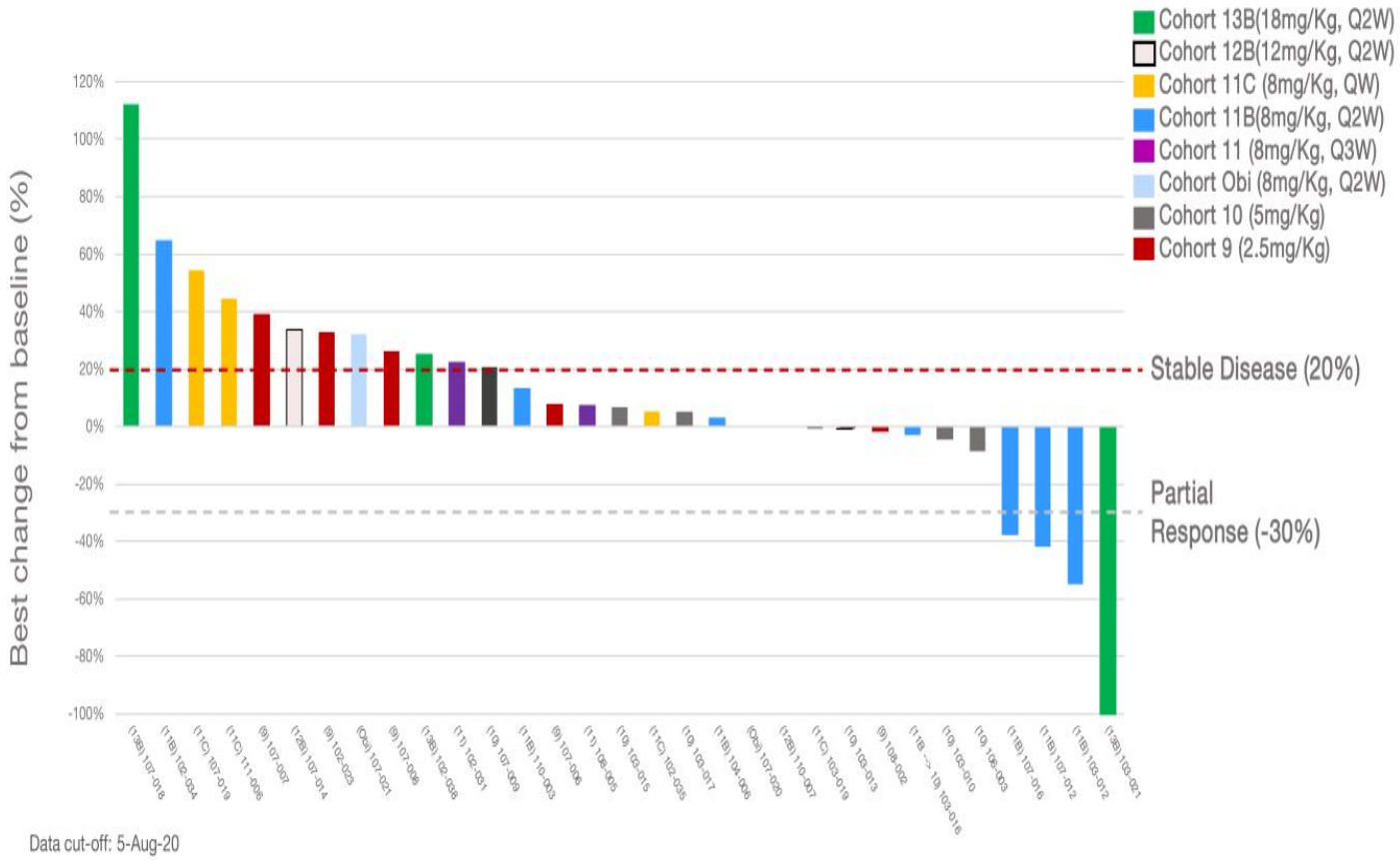
Data cut-off: 27-July-20

Average Time on Treatment with Cinrebafusp Alfa
Cohorts 11b-13b



Data cut-off: 11-Aug-20

Best Response in Target Lesions (Monotherapy Trial)
Cohorts 9-13b



Data cut-off: 5-Aug-20

Case Study: Gastric Cancer Patient with Confirmed Partial Response

Patient Profile, Treatment History and Treatment Outcome

Patient Profile

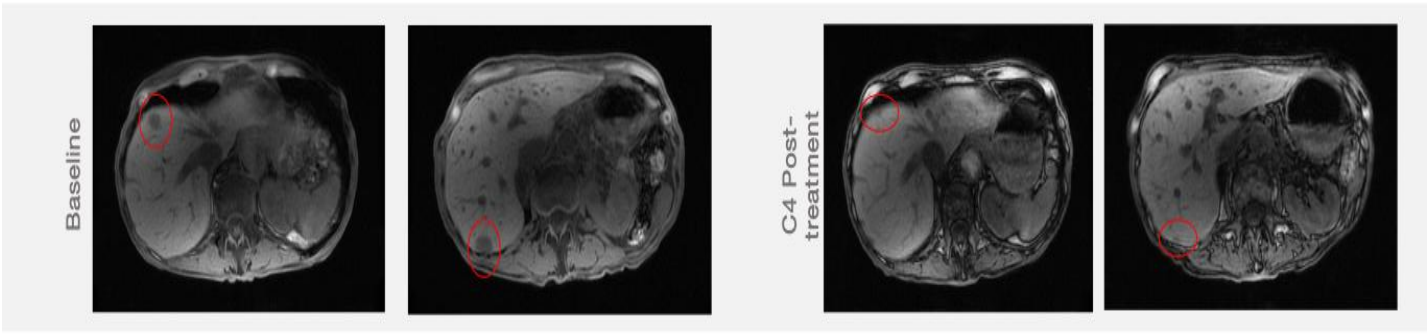
- Cohort 11b | 8 mg/kg every two weeks
- 80-year old woman; initial diagnosis in June 2017
- Stage IV gastric adenocarcinoma
- Metastases to liver, lymph node and adrenal glands
- HER2 IHC 3+; PD-L1 positive (CPS=3)
- NGS: ERBB2 amplification, TP53 mutation, alteration of CDK12 and SF3B1

Oncology Treatment History	Duration	Best Response
Trastuzumab, Pembrolizumab + Capecitabine/oxaliplatin	July 2017 – June 2018	Stable Disease
Nivolumab with IDO1 inhibitor (investigational drug)	Aug 2018 – Jan 2019	Stable Disease

Lesions	Lesion Site	Lesion Size (mm)				
		Baseline	C2 Post-treatment	C3 Post-treatment	C4 Post-treatment	C6 Post-treatment
Target 1	Liver	14	12	10	9	8
Target 2	Liver	20	16	10	8	9
Target 3	Pancreas	19	16	14	14	14
% Change from Baseline			-17%	-36%	-42%	-42%
Non-target 1	Lung	Present	Present	Present	Present	Present
Non-target 2	Stomach	Present	Present	Present	Present	Absent
Non-target 3	Stomach	Present	Present	Present	Present	Absent

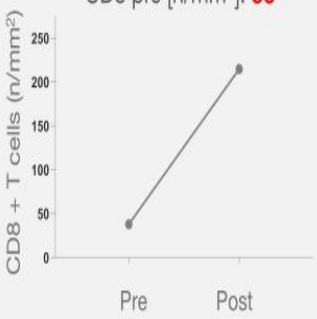
Data cut-off: 24-Jan-20

CD8+ T Cell Numbers in the Tumor and Circulating s4-1BB Increase Post-Treatment in Responding Gastric Cancer Patient

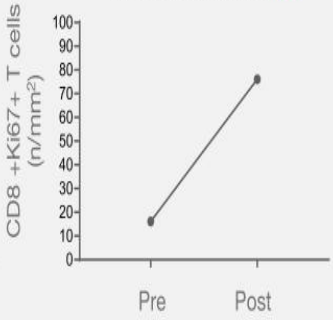


Tumor

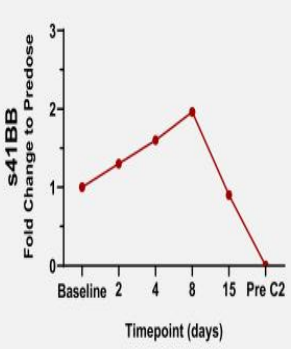
CD8 fold change: **5.7**
CD8 pre [n/mm²]: **38**

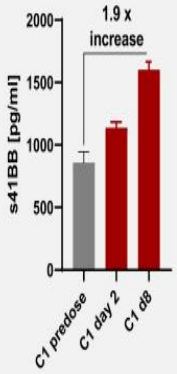


CD8Ki67 fold change: **5.8**
CD8 pre [n/mm²]: **16**



Serum





CD8⁺ T cell Numbers

CD8⁺ T cell Proliferation

Soluble 4-1BB

Case Study #2: Rectal Cancer Patient with Confirmed Complete Response

Patient Profile, Treatment History and RECIST

Patient Profile

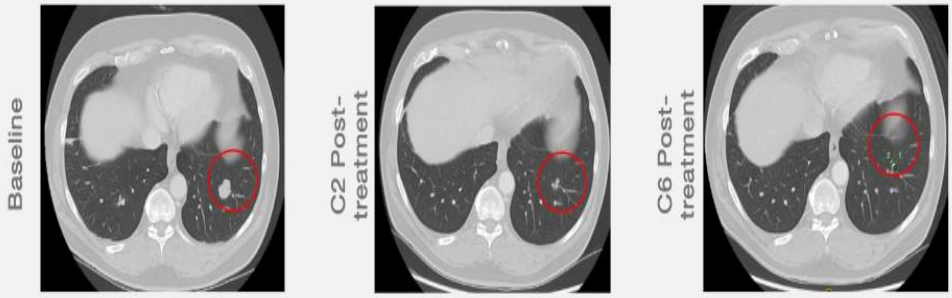
- Cohort 13b | 18 mg/kg Q2W
- 59-year-old male; initial diagnosis March 2017
- Stage 4 rectal adenocarcinoma cancer; metastasized to heart and lung
- FoundationOne Her2 amplification; in-house testing IHC 3+
- MSS, TMB low (2 mt/Mb)

Oncology Treatment History	Duration
Capecitabine + XRT	Apr-May 2017
Neoadjuvant Folfox	May-Sep 2017
Resection	Dec 2017
Folfiri/Avastin	Mar-Jul 2018
5FU/Avastin maintenance	Aug 2018-May 2019
Irinotecan/Avastin	May-Nov 2019
SBRT	Nov 2019

Lesions	Lesion Site	Lesion Size (mm)			
		Baseline	C2 Post-treatment	C4 Post-treatment	C6 Post-treatment
Target 1	Lung	22	13	0	0
% Change from Baseline			-41%	-100%	-100%
Non-target 1	-	Present	Present	Absent	Absent

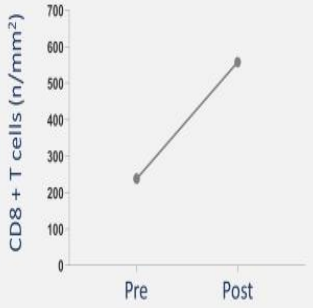
Data cut-off: 27-Jul-20

CD8+ T Cell Numbers in the Tumor and Circulating s4-1BB Increase Post-Treatment in CR Rectal Cancer Patient

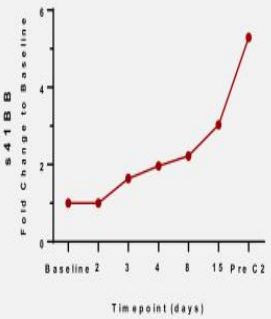


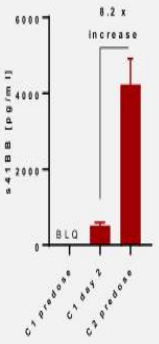
Tumor

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



Serum





Cinrebafusp Alfa – Combination with Atezolizumab

Treatment-Related Adverse Events (Combination Trial)
All Subjects

Occurred in > 1 Patient	Combination with Atezolizumab	
	n = 148 (%)	% Grade 3
Infusion Related Reaction	38 (26%)	3 (2%)
Fatigue	12 (8%)	
Nausea	8 (5%)	
Vomiting	38 (26%)	
Abdominal pain	2 (1%)	
Anemia	4 (3%)	2 (1%)
Anorexia	2 (1%)	
Arthalgia	2 (1%)	
Diarrhea	5 (3%)	1 (1%)
Dry mouth	3 (2%)	
Fever	3 (2%)	
Lightheadedness	2 (1%)	
Lymphocyte count decreased	3 (2%)	1 (1%)
Neutrophil count decreased	3 (2%)	1 (1%)
Peripheral sensory neuropathy	2 (1%)	
Pruritis	4 (3%)	

Two TRAEs above Grade 3: Grade 4 AST increase, Grade 3 transaminitis, and eventually Grade 5 hepatic failure in cohort 7 (8mg/kg + 1200mg atezolizumab); Grade 4 hemolytic anemia (unrelated to cinrebafusp alfa, related to atezolizumab) in cohort 7.

Data cut-off: 27-Jul-20

Summary of Responses of Cinrebafusp Alfa in Combination with Atezolizumab

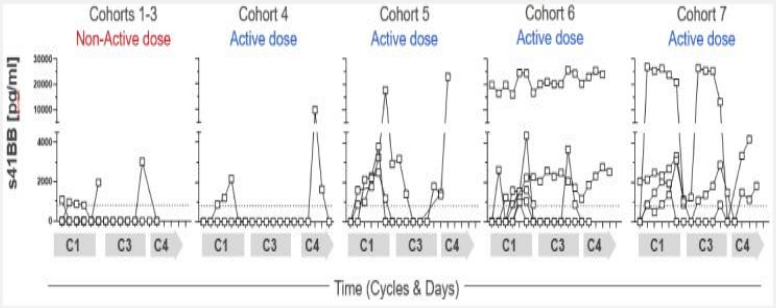
Cohort	7	6	5	4	Total
Best Response	8mg/kg, Q3W	5mg/kg, Q3W	2.5mg/kg, Q3W	1mg/kg, Q3W	
Evaluable Patients	8	8	8	3	27
PR	1	2	-	1	4
SD	4	1	1	0	6
ORR	13%	25%	0%	33%	15%
DCR	63%	38%	13%	33%	37%

Data cut-off: 27-Jul-20

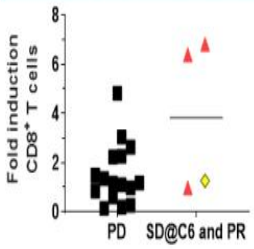
Soluble 4-1BB Increases in Active Dose Cohorts & Clinical Benefit is Associated with Tumoral Immune Cell Activation

4-1BB target engagement

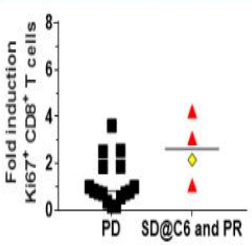
Soluble 4-1BB in serum



CD8⁺ T cell Numbers



CD8⁺ T cell Proliferation



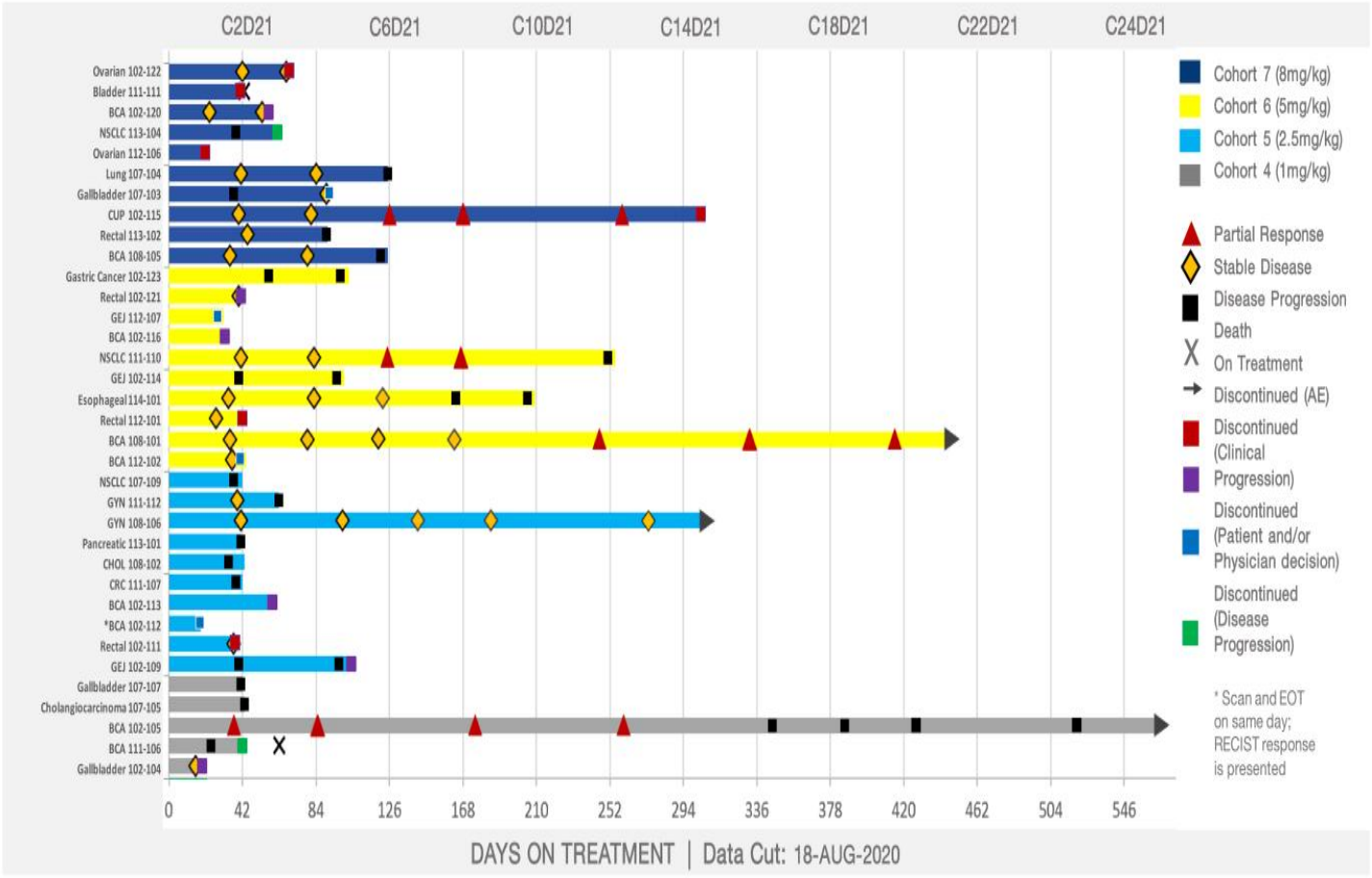
Tumor-localized activity

IHC on tumor tissue

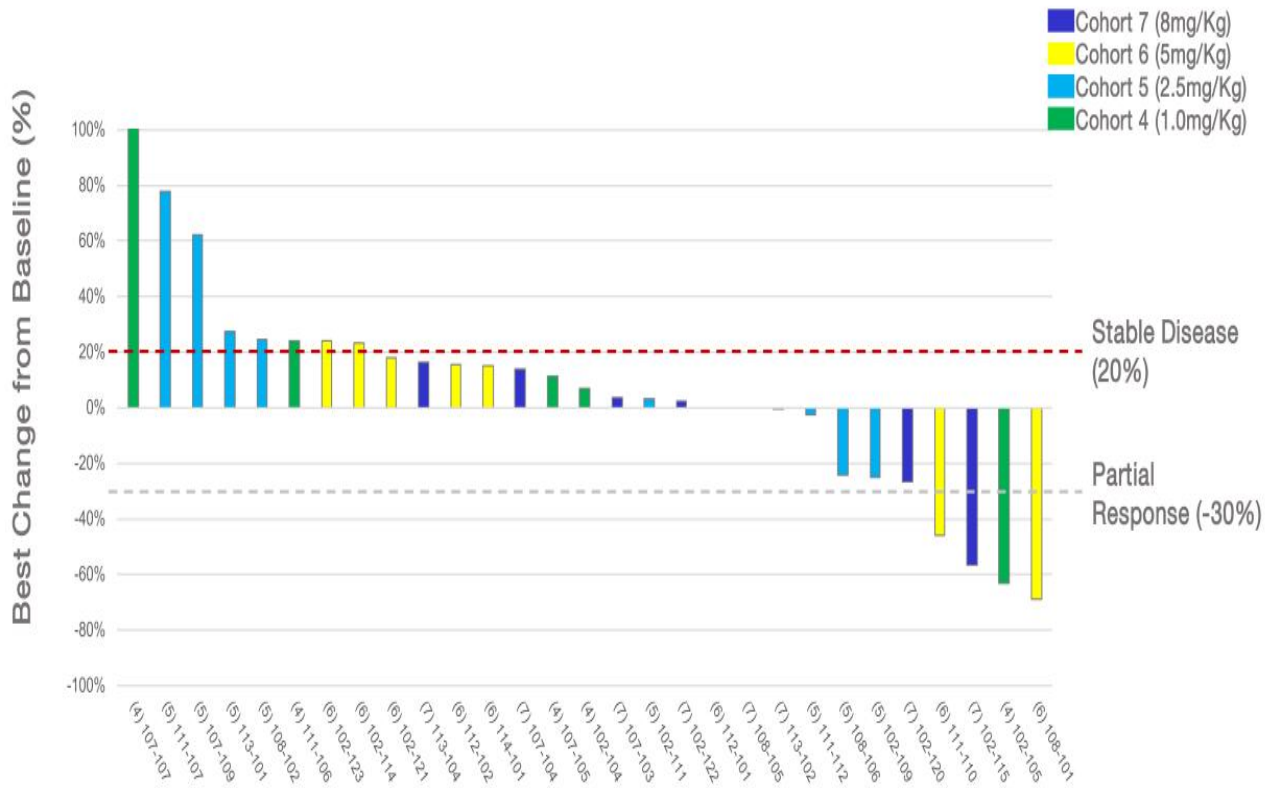
Patients with prolonged clinical benefit show a trend of increased CD8⁺ T cell numbers, proliferation and elevated cytolytic function in tumor biopsies

Substantial increase of s4-1BB is observed in active dose cohorts (4-7), suggesting cinrebafusp alfa-mediated target engagement

Cinrebafusp Alfa + Atezolizumab Duration of Exposure



Best Response in Target Lesions (Combination Study)
Cohorts 4-7



Data cut-off: 27-Jul-20

Case Study: Breast Cancer Patient with Stable Disease (Update)

Patient Profile, Treatment History and RECIST

Patient Profile:

- Cohort 6 | 5 mg/kg Q3W + 1200mg atezolizumab
- 52-year-old male; Initial diagnosis July 2011
- Stage 2 Invasive Ductal Breast Cancer
- FISH HER2/CEP17 ratio 2.4, HER2 copy number 4.8
  In-house testing IHC2+, FISH+
- PD-L1 low in pre-treatment and high in post treatment biopsy

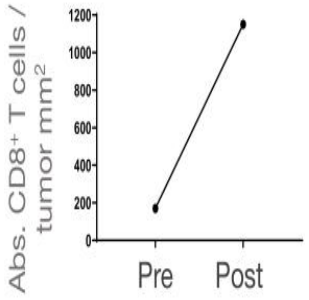
Oncology Treatment History	Duration
Trastuzumab/Docetaxel/ Tamoxifen/Carboplatin	Sep 2011-Jul 2013
Trastuzumab/Pertuzumab/Vinorelbine	Aug 2013-Jan 2016
T-DM1/Fulvestrant	Nov 2017-Mar 2018
Capecitabine/Lapatinib	Mar 2018
Palbociclib/Arimidex	Apr-May 2019

Lesions	Lesion Site	Lesion Size (mm)						
		Baseline	C2 Post-treatment	C4 Post-treatment	C6 Post-treatment	C8 Post-treatment	C12 Post-treatment	C16 Post-treatment
Target 1	right pulmonary ligament lymph node	16	18	15	13	13	6	5
% Change from Baseline			+12.5%	-6%	-19%	-19%	-63%	-69%
Non-target 1-4	-	Present	Present	Present	Present	Present	Present	Present

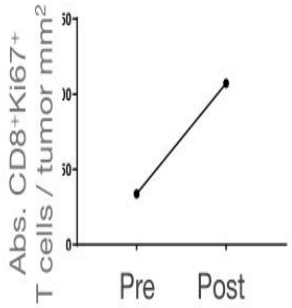
Data cut-off: 27-Jul-20

Tumoral and Circulating s4-1BB Increase Post-Treatment in PR Breast Cancer Patient

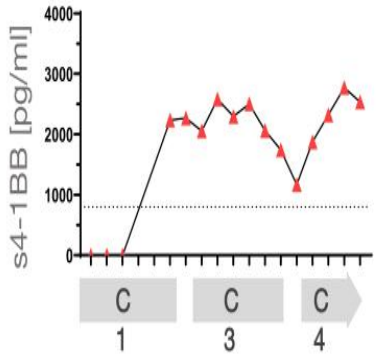
CD8+ T cell Numbers



CD8+ T cell Proliferation



Soluble 4-1BB



CD8+ T cell numbers, proliferation, cytolytic molecules and s4-1BB increase post-treatment, demonstrating 4-1BB arm activity of cinrebafusp alfa

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