# PIERIS PHARMACEUTICALS

*CORPORATE PRESENTATION*
*MAY 2021*

# 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 data from patients enrolled to date will be sufficient to inform the recommended phase 2 dose for the Company's planned proof of concept study of cinrebafusp alfa in gastric cancer; the expected timing and potential outcomes of the reporting by the Company of key clinical data from its programs, references to novel technologies and methods and our business and product development plans, including the advancement of our proprietary and co-development programs into and through the clinic and the expected timing for reporting data, making IND filings or achieving other milestones related to our programs, including PRS-060/AZD1402, cinrebafusp alfa, PRS-344, and PRS-352 and the expected timing of the initiation of the next stage of cinrebafusp alfa's development in gastric cancer. Actual results could differ from those projected in any forward-looking statements due to numerous factors. Such factors include, among others, our ability to raise the additional funding we will need to continue to pursue our business and product development plans; the inherent uncertainties associated with developing new products or technologies and operating as a development stage company; our ability to develop, complete clinical trials for, obtain approvals for and commercialize any of our product candidates, including our ability to recruit and enroll patients in our studies; competition in the industry in which we operate; delays or disruptions due to COVID-19; and market conditions. These forward-looking statements are made as of the date of this 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, 2020 and the Company's Quarterly Reports on Form 10-Q.

# Executive Summary

## Superior Medicines via Efficient Biology

- Protein therapeutics that exploit biology validated by mAbs; engineered for focused activity at disease locus
- Improved activity, reduced side effects, increased convenience

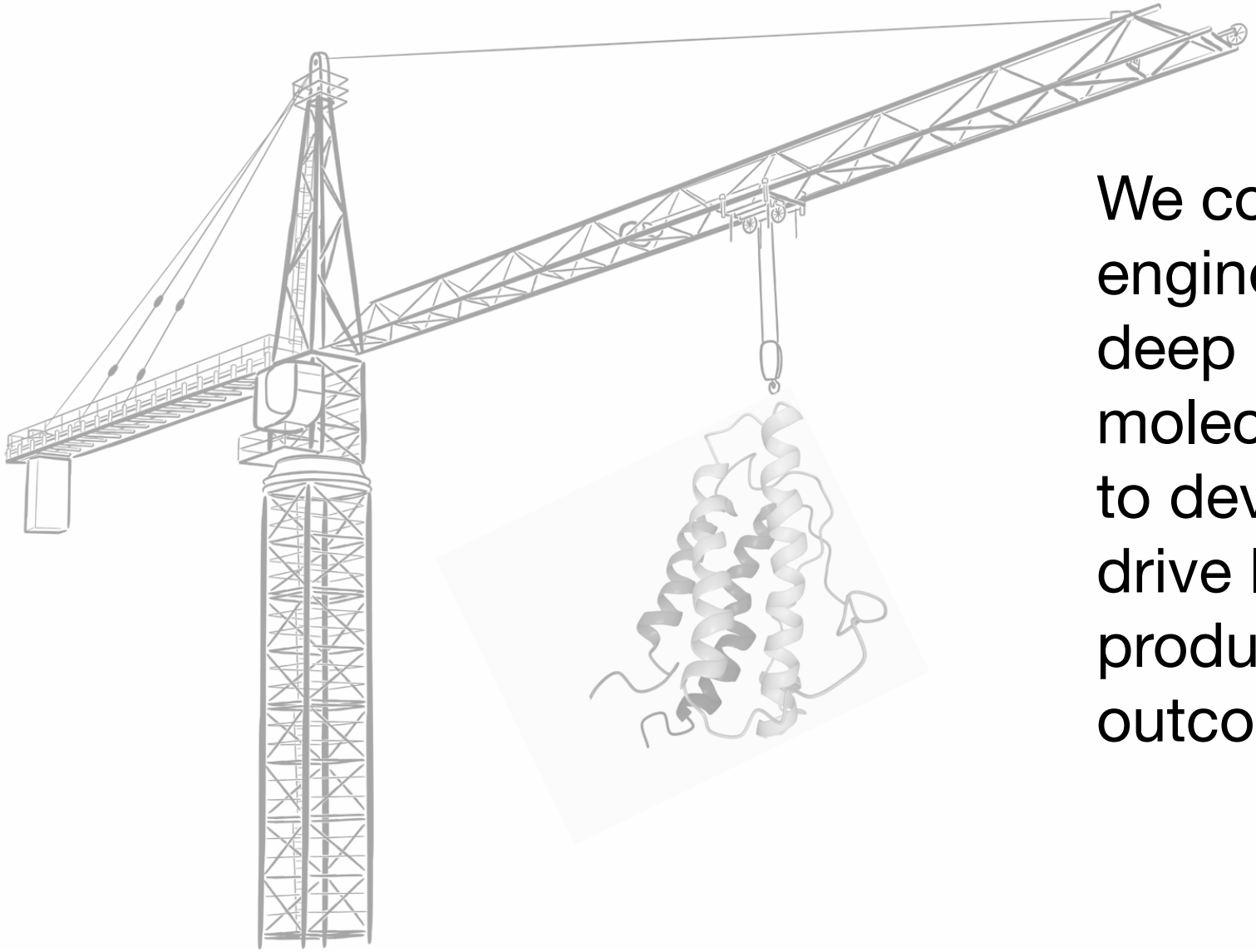
## Two Focus Areas

- Oral inhaled antagonists for respiratory disease
- Locally activated immuno-oncology bispecifics
- 2 POC readouts in ‘22; 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

# Our Platform



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

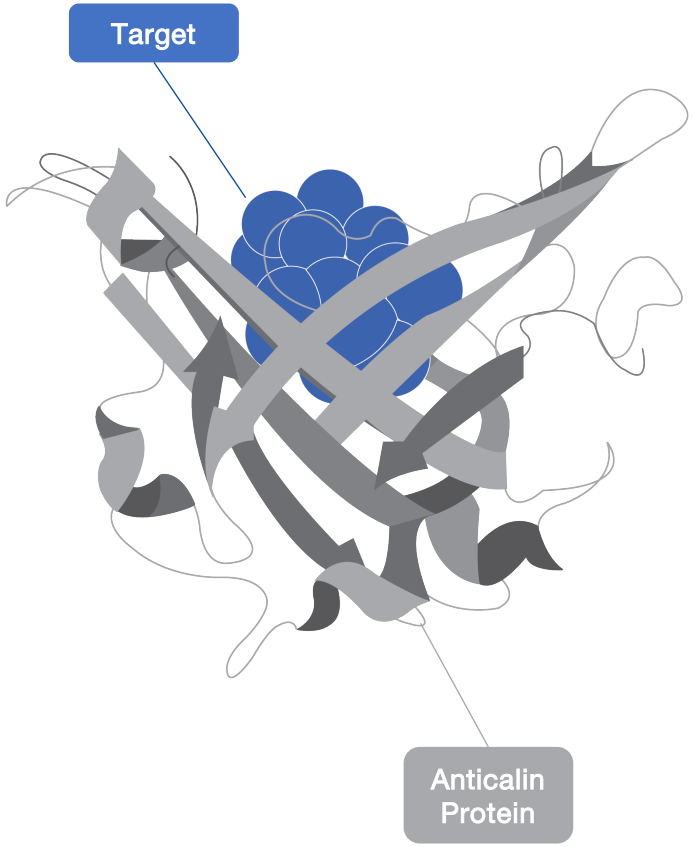
# Anticalin® Proteins as Therapeutic Modalities

## 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



# Our Pipeline

| RESPIRATORY | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| CANDIDATE | TARGETS | INDICATION | PARTNER | OUR COMMERCIAL RIGHTS | DISCOVERY | PRECLINICAL | PHASE I | PHASE II |
| PRS-060/AZD1402 | IL4-Rα | Asthma | AstraZeneca | Worldwide Profit-Share Option | | | | |
| Proprietary Programs | n.d. | n.d. | n/a | Worldwide | | | | |
| AstraZeneca Programs* | n.d. | n.d. | AstraZeneca | Worldwide Profit-Share Options | | | | |
| Genentech Programs+ | n.d. | n.d. | Genentech A Member of the Roche Group | Royalties | | | | |
| *4 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 I | PHASE II |
| 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 Seattle Genetics, 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 | | | | | | | | |

# Collaboration Snapshot

**AstraZeneca**

- PRS-060/AZD1402 + 4 additional programs
- Upfront & milestones to date: $70.5M
- $10M equity investment from AstraZeneca
- Eligible to receive up to approximately $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
- 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: PD-L1/4-1BB antibody-Anticalin bispecific, for which Pieris holds full U.S. rights
- Upfront & milestones to date: ~$40M
- Eligible to receive up to approximately $447M 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: 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 asthmatics |
| Commercial Rights | Co-development and U.S. co-commercialization options, including gross margin share |

PRS-060/AZD1402

# PRS-060 Phase 2a Trial

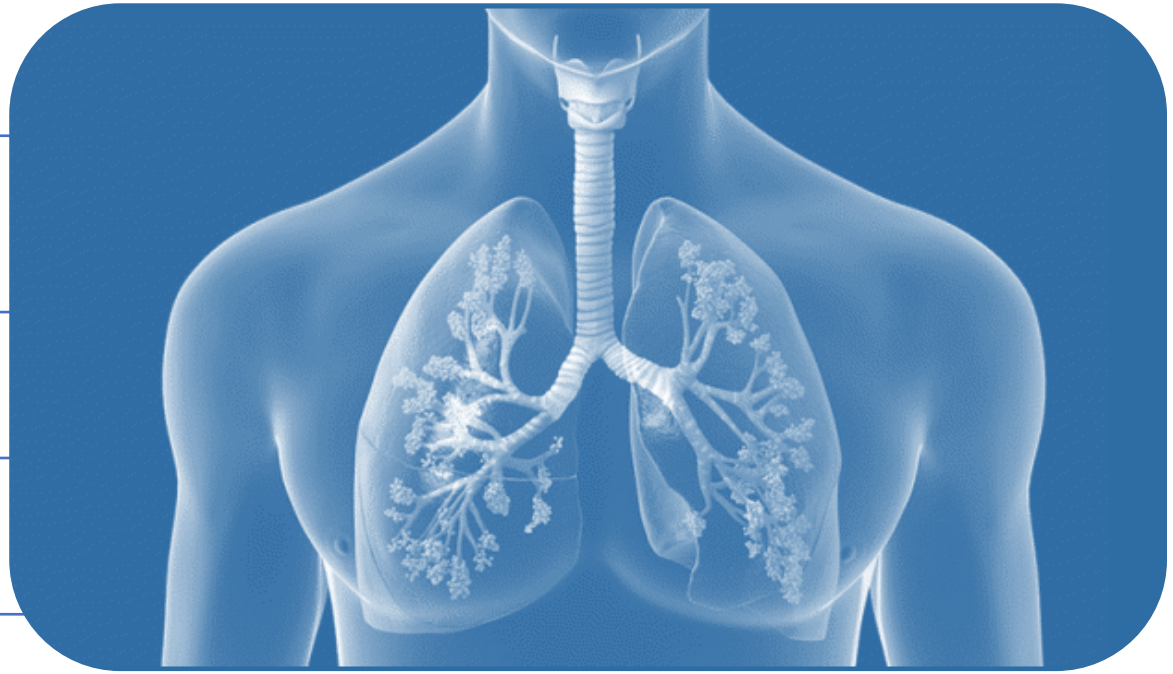
| | |
|---|---|
| Part 1 | **Patient Population:** Moderate controlled asthmatics<br>**Primary Endpoint:** Safety and tolerability<br>**Number of Patients:** ~45 |
| Part 2 | **Patient Population:** Moderate uncontrolled asthmatics with blood eosinophil count of ≥ 150 cells/μL and FeNO ≥ 25 ppb at screening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

Enrollment initiated 1Q 2021

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 & the Advantages of Anticalin-based Bispecifics

## 4-1BB

**High-value Target**

- Drives meaningful clinical benefit through proliferative, killing and durability impact on tumor-specific T cells
- Improves metabolic fitness for increased survival of T cells

**Historical Challenges**

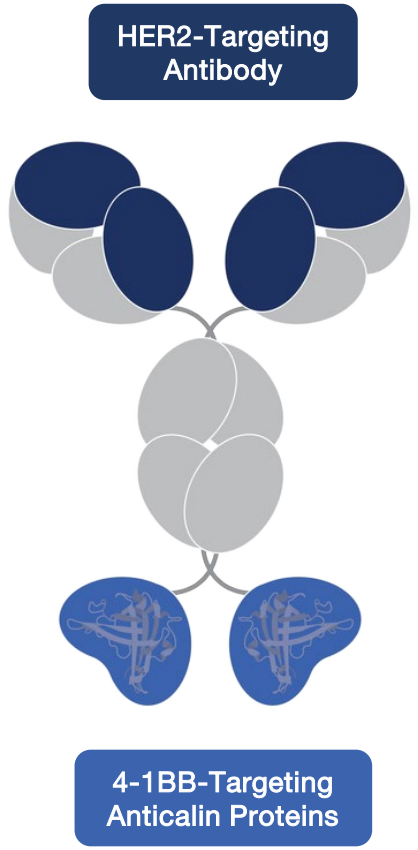
- Despite activity, inefficient mAb approaches have led to systemic 4-1BB activation, resulting in hepatic toxicity

**Our Solution**

- Designed to efficiently activate 4-1BB on tumor-specific T cells, avoiding undesirable activation in the liver
- Initial clinical data are supportive of this approach
- Multiple 4-1BB-based follow-on programs

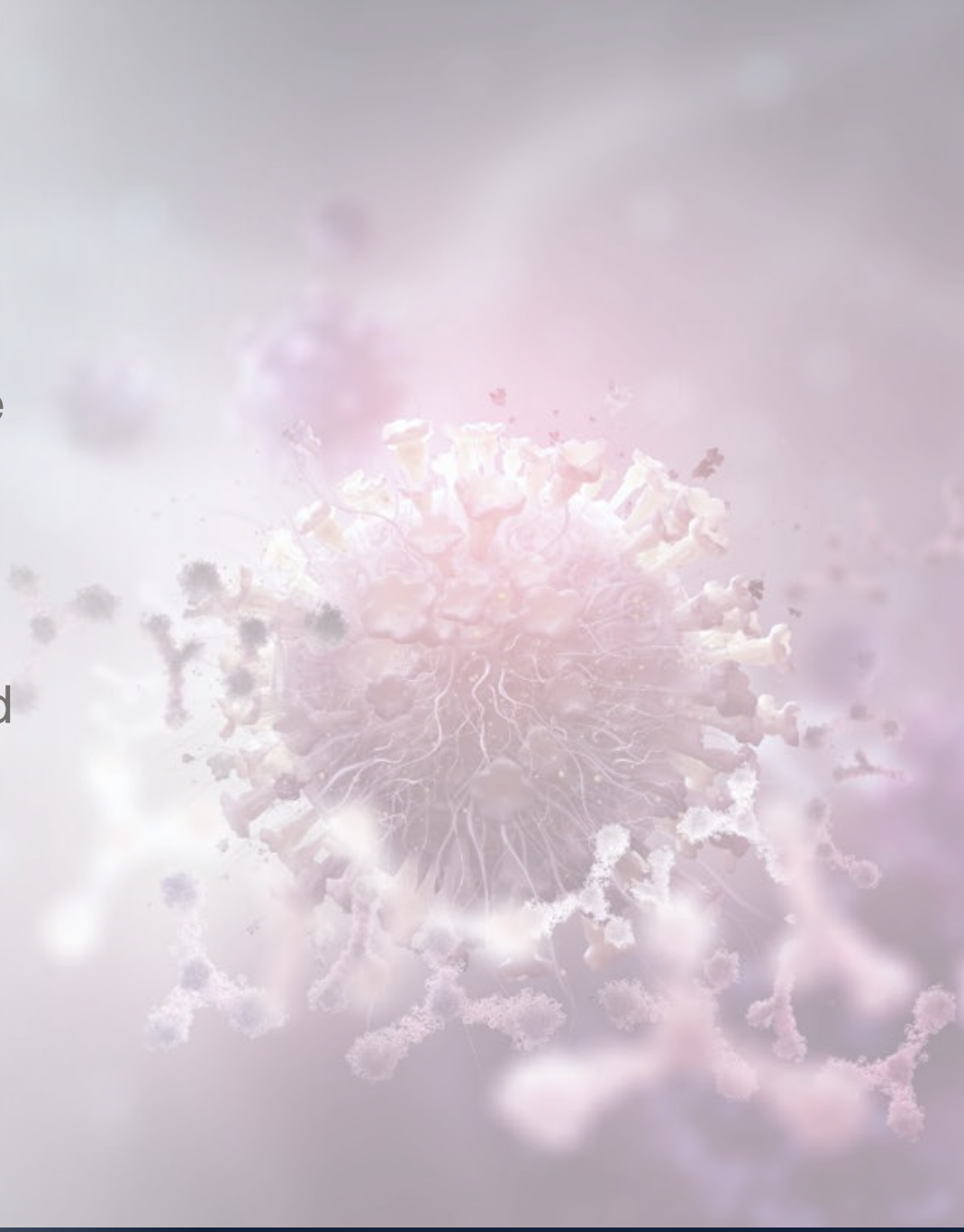
# Cinrebafusp Alfa (PRS-343): Proprietary Lead IO Asset

| | |
|---|---|
| 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 Phase I 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
- Moving into phase 2 in HER2-high and HER2-low gastric cancer
- 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

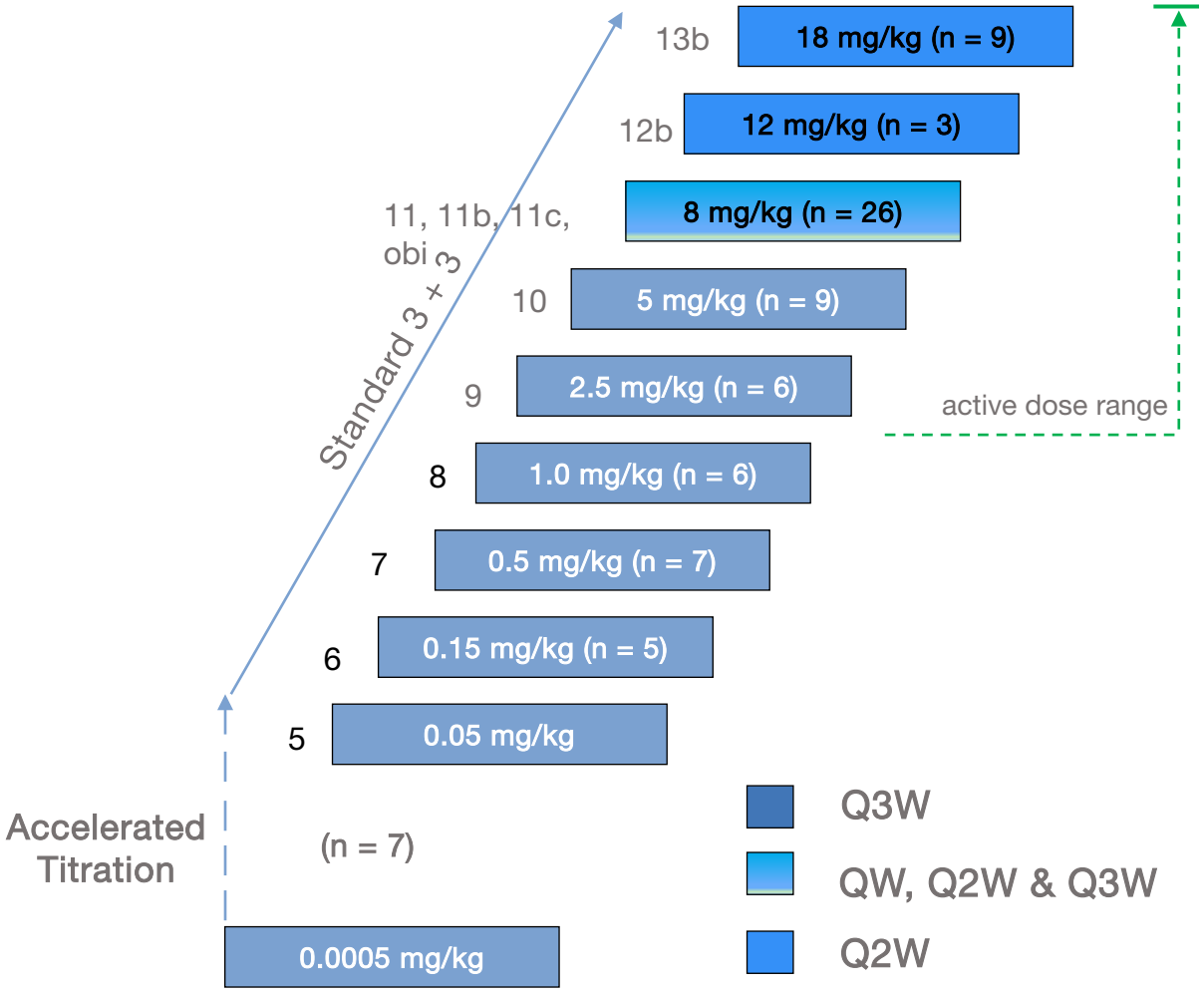
**Secondary:** Characterize PK/PD & Immunogenicity
Preliminary anti-tumor activity

## 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 Baseline Characteristics (N = 78)

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

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

Data cut-off: 25-Feb-21

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

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

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

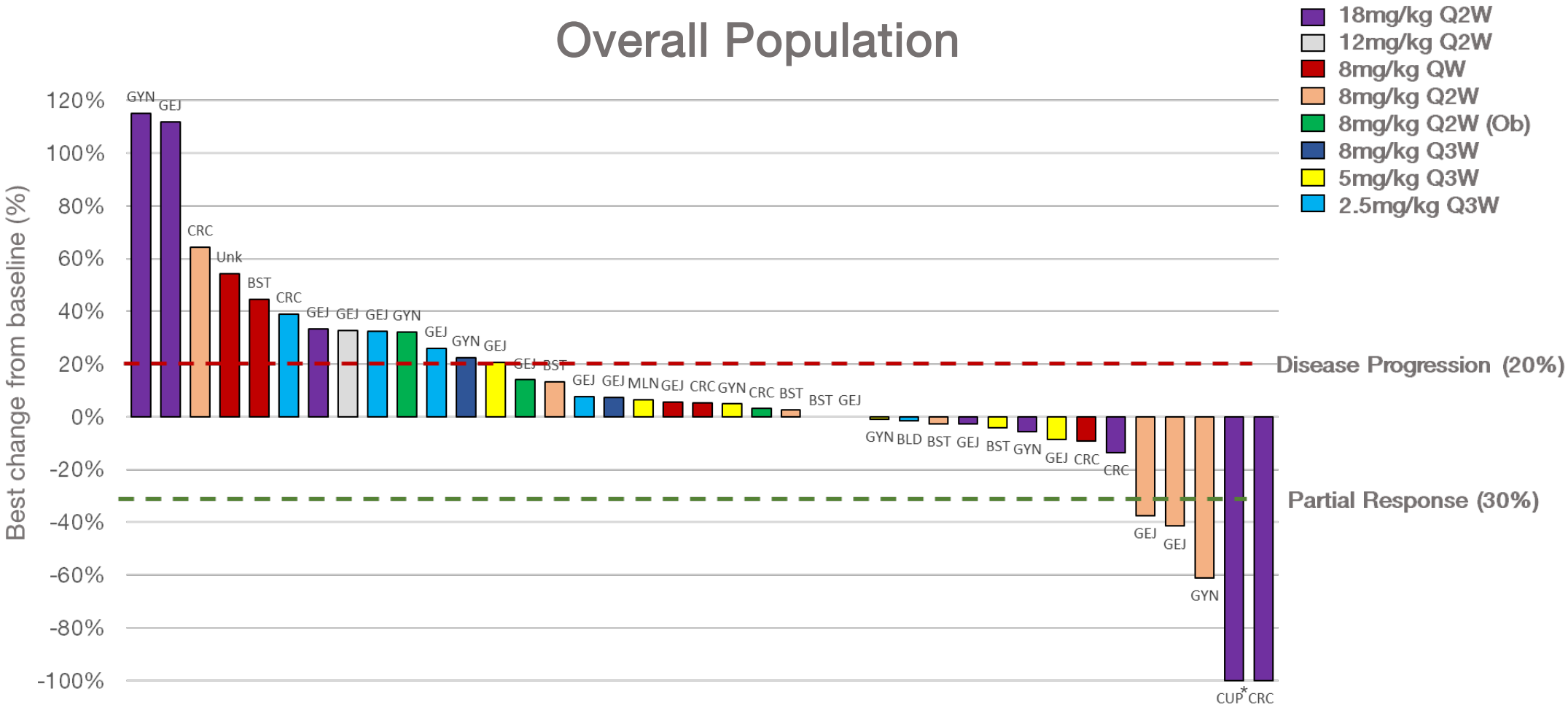
Data cut-off: 25-Feb-21

# 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% |

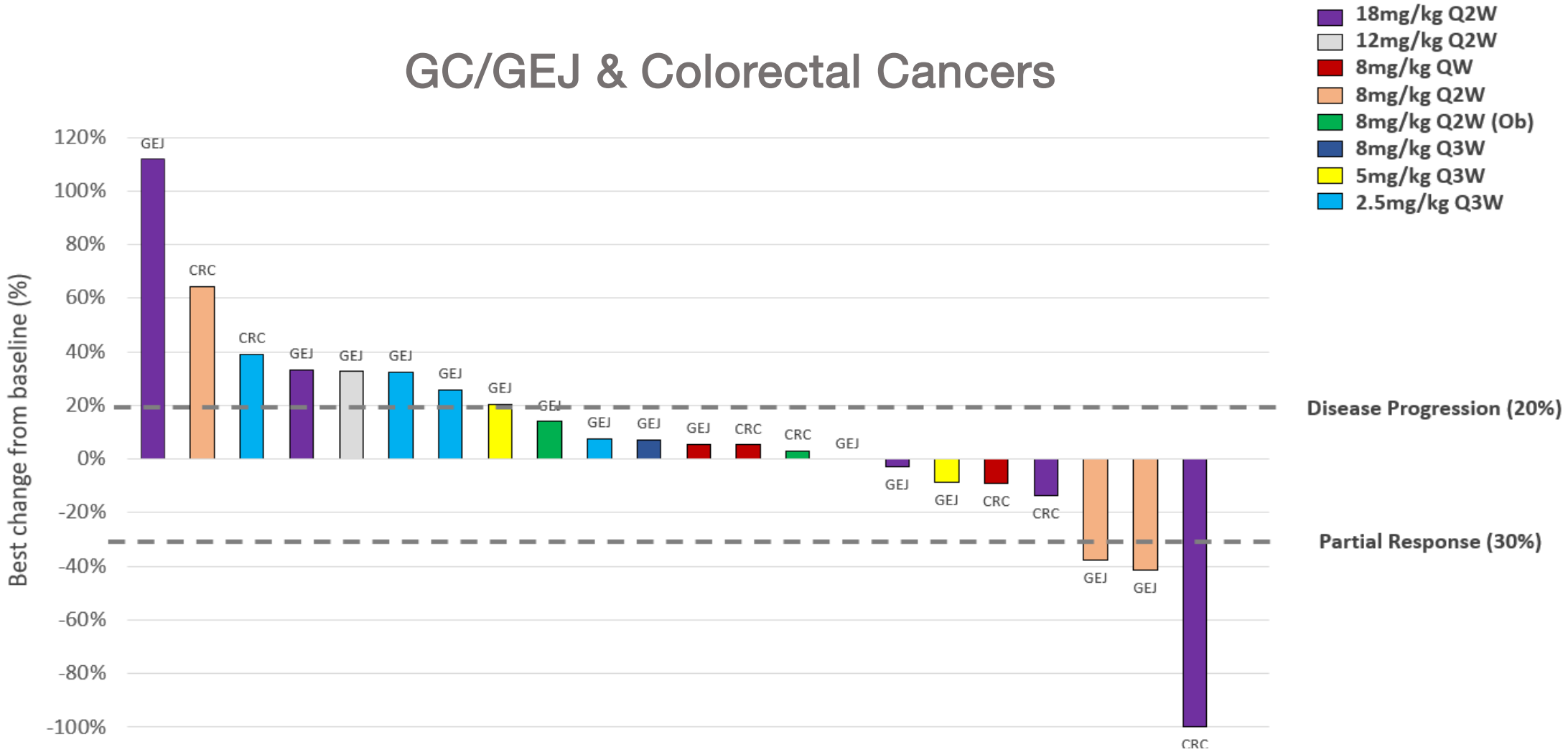
Data cut-off: 25-Feb-21

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




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

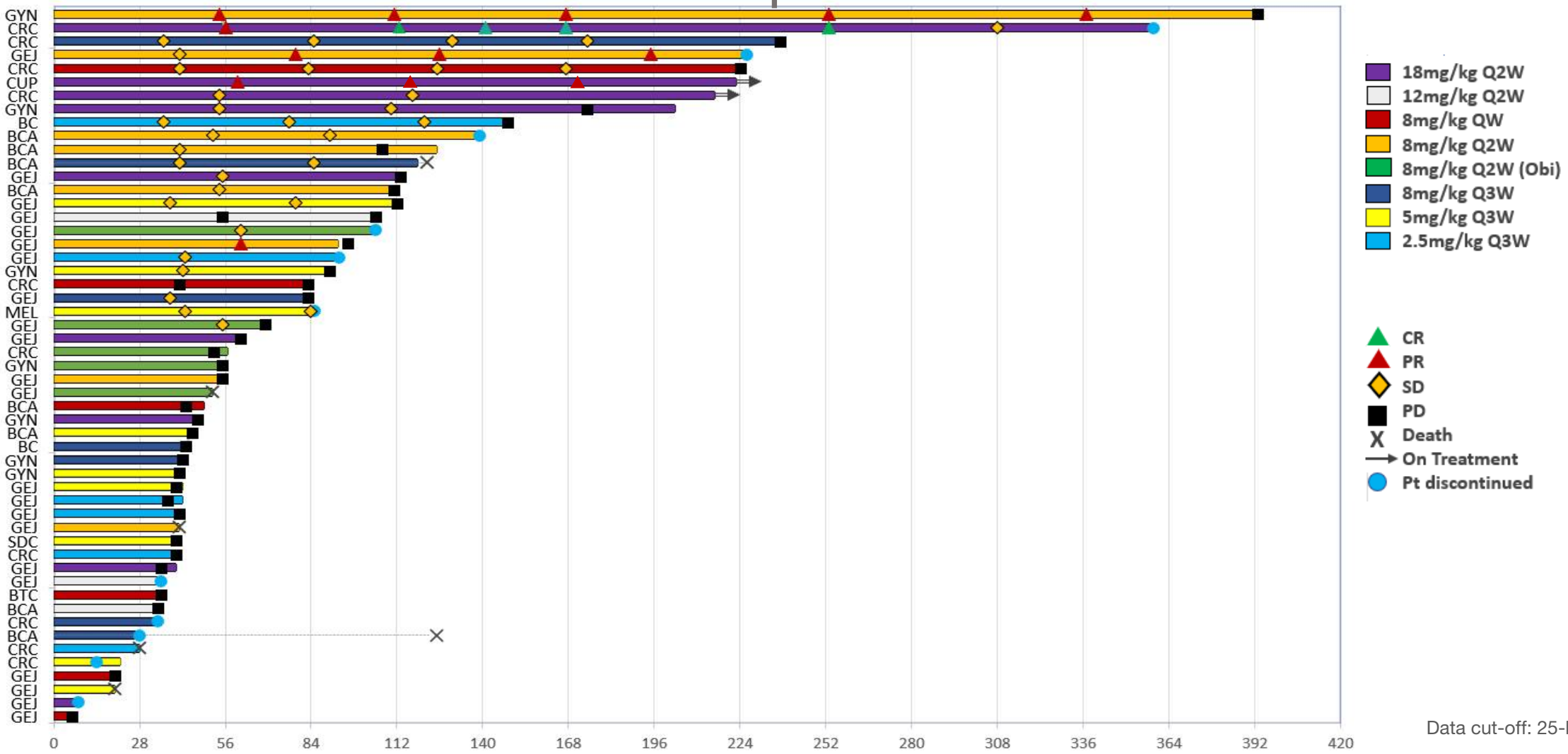
# Cinrebafusp Alfa Phase 1 Monotherapy Efficacy Data: Analysis of Patients Treated at Active Doses




Data cut-off: 25-Feb-21

# Durable Responses with Cinrebafusp Alfa Among Heavily Pre-treated Population

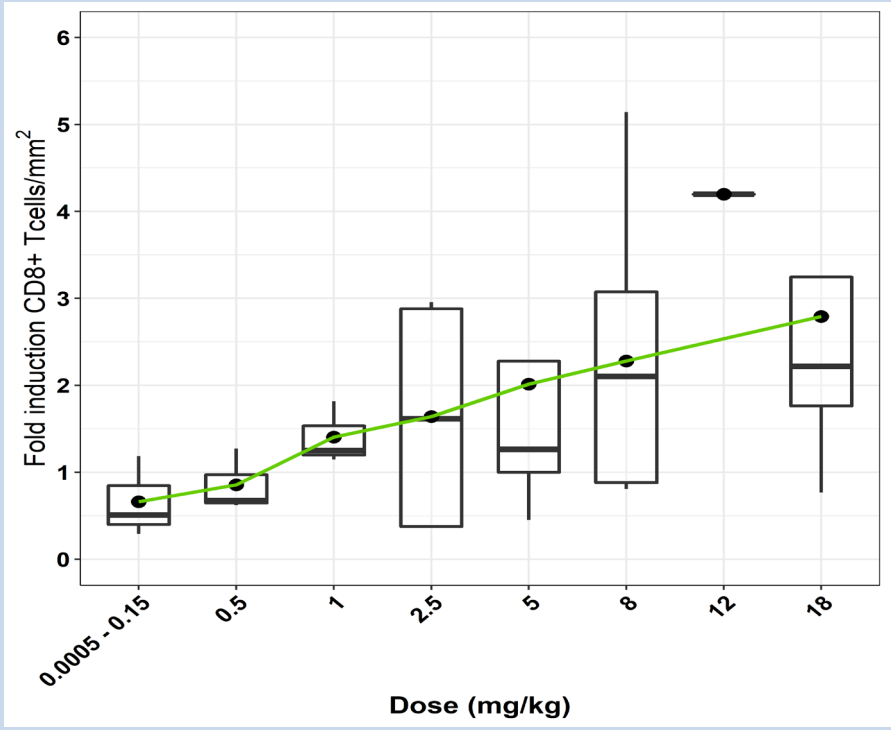
## Overall Population



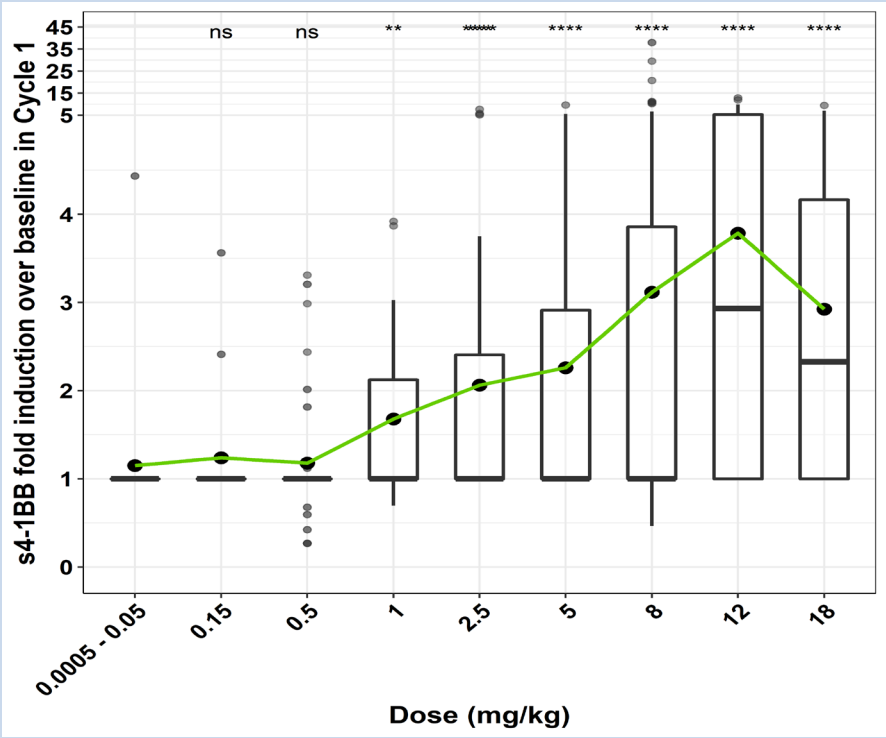

Data cut-off: 25-Feb-21

# Cinrebafusp Alfa Shows Dose-dependent Activity Across Key Pharmacodynamic Parameters

## Tumor (CD8+)




## Serum (s4-1BB)




Connects group averages

Median

Mann-Whitney U Test

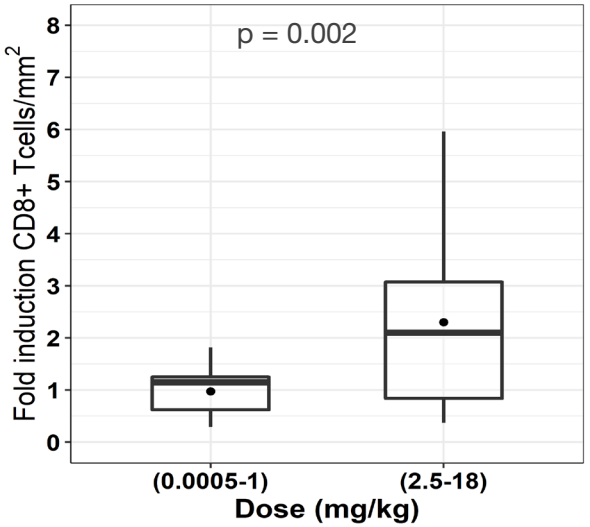
Dose at 8 mg/kg incorporates patients treated at Q1W, Q2W, or Q3W

Data cut-off: 25-Feb-21

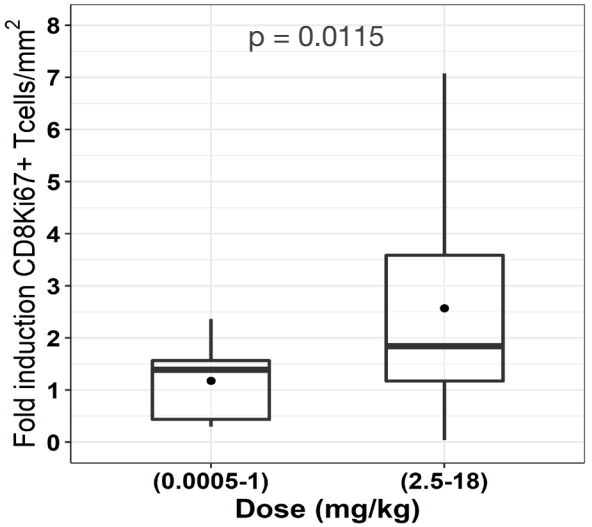
# Cinrebafusp Alfa Activates Adaptive and Innate Immunity in the Tumor


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

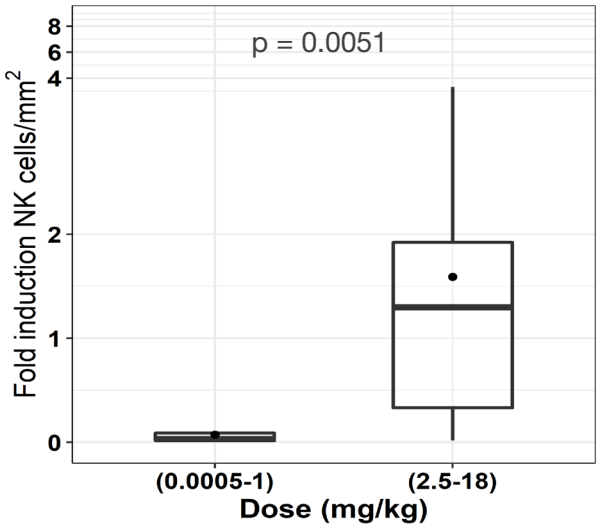
## CD8+ Cells



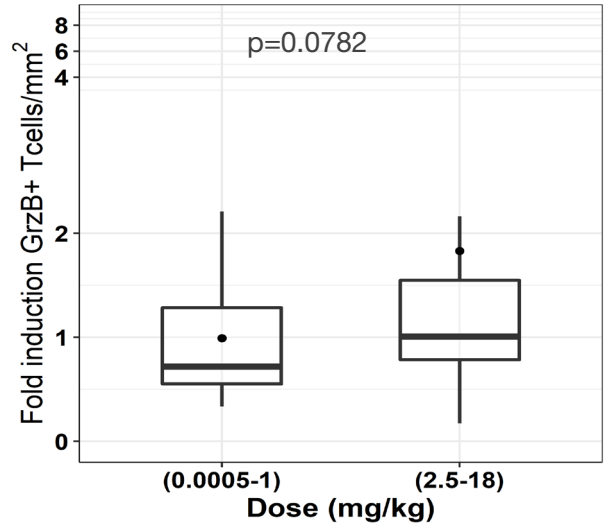

## CD8+Ki67+ Cells




## NK Cells




## GrzB+ Cells



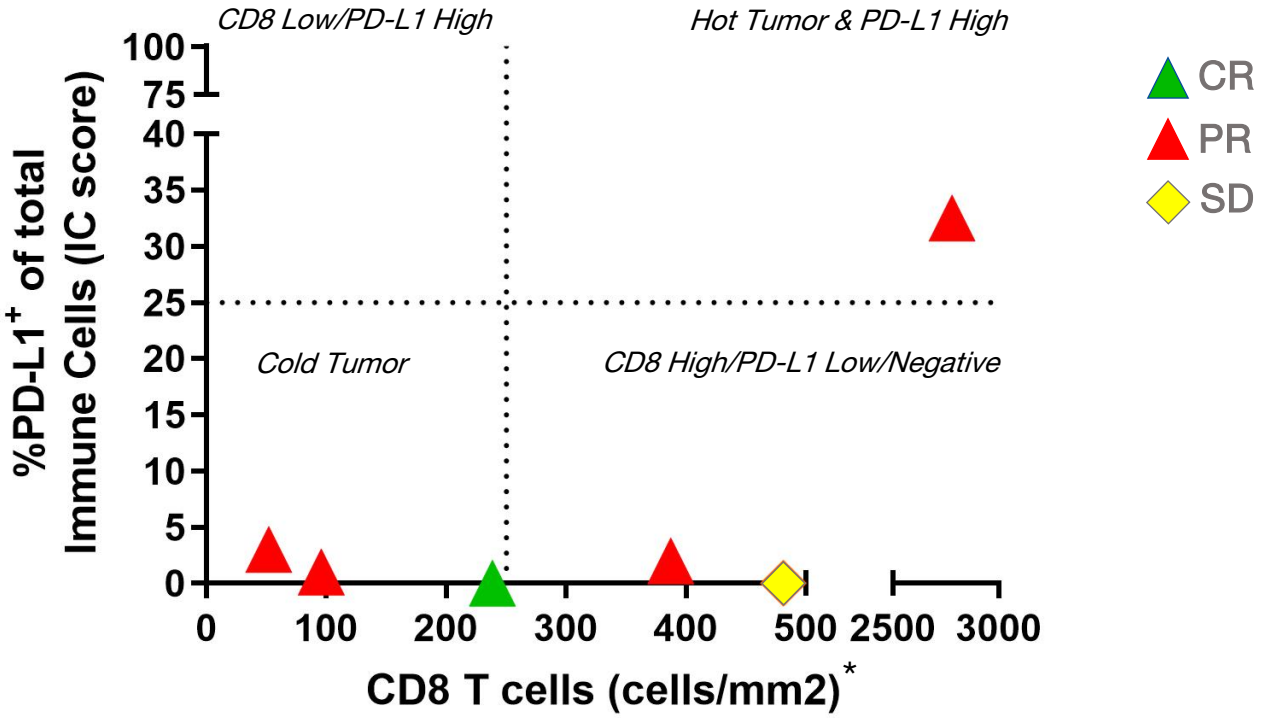

● Denotes group averages
— Median

Unpaired One-Tailed Welch`s

Data cut-off: 25-Feb-21

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

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



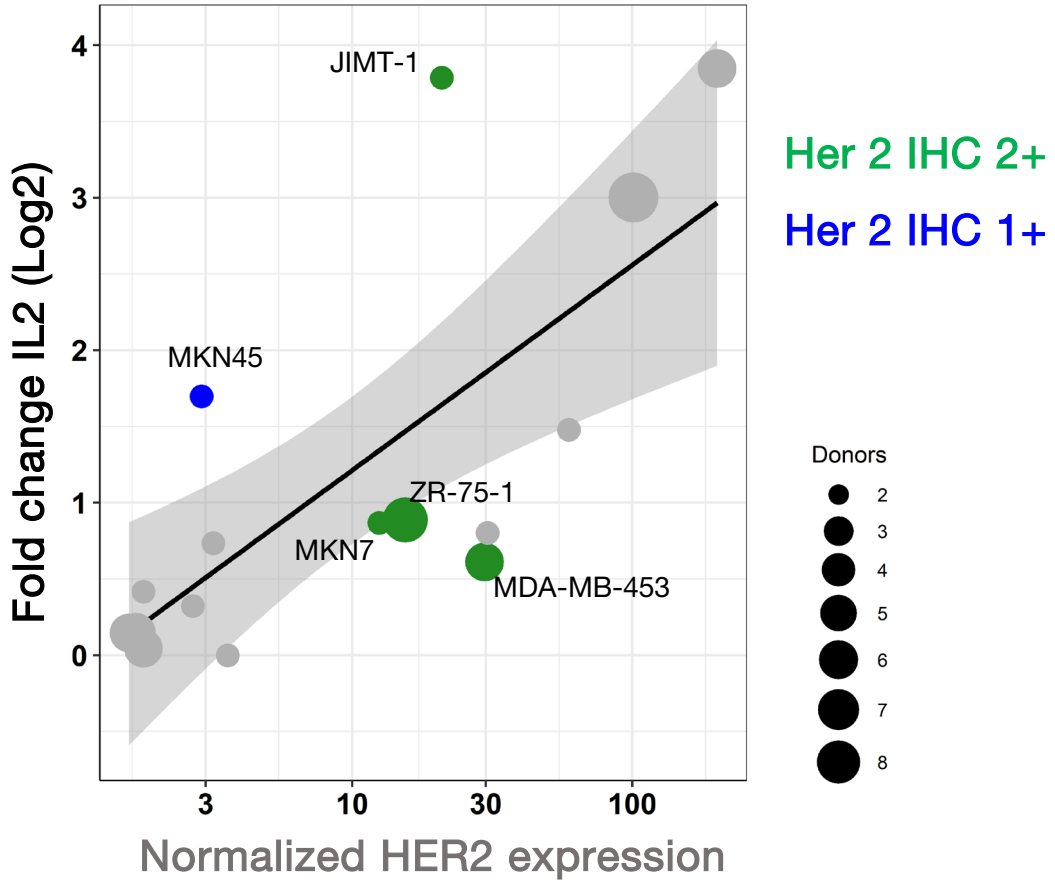

* Threshold informed by (Tumeh et al., 2014 and Blando et al., 2019)

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

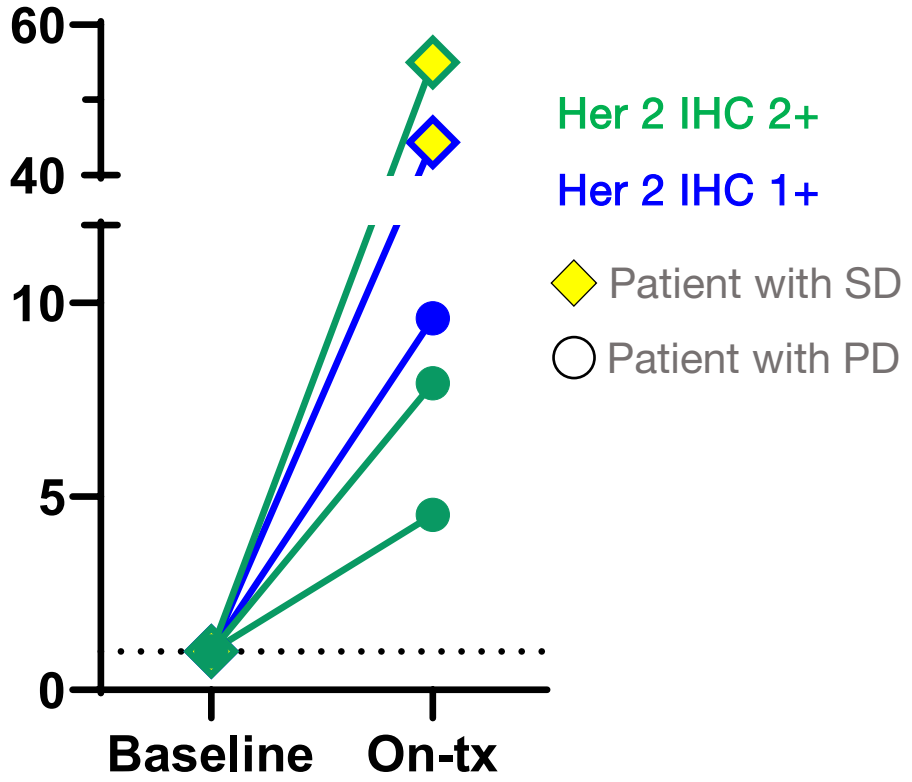
Data cut-off: 25-Feb-21

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

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




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




Data cut-off: 25-Feb-21

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

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

## Patient Profile, Treatment History and Treatment Outcome

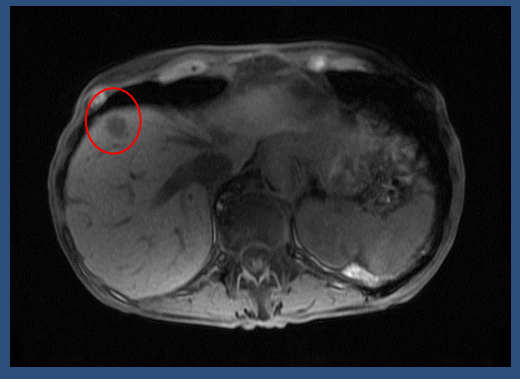
### Gastric Cancer Patient with Partial Response

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

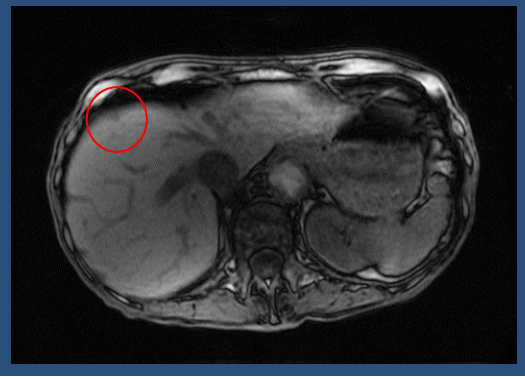
**Prior Treatment includes:**

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

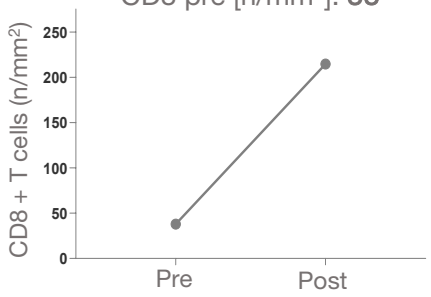
Baseline

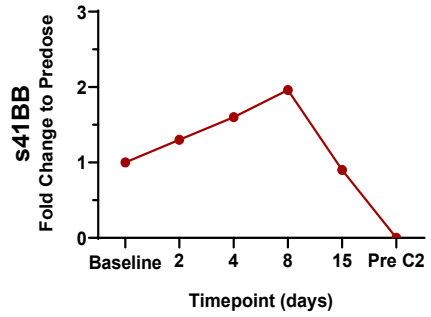


C4 Post-treatment



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



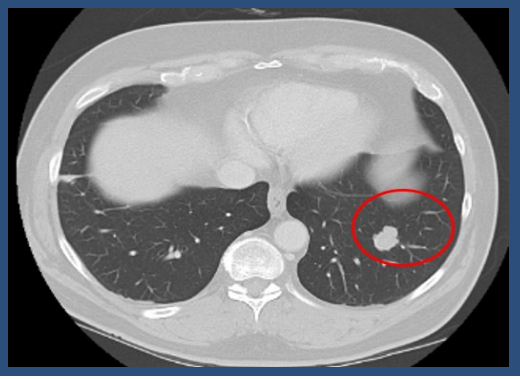

### Rectal Cancer Patient with Complete Response

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

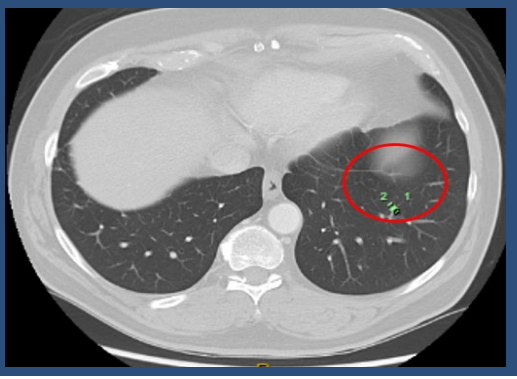
**Prior Treatment includes:**

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

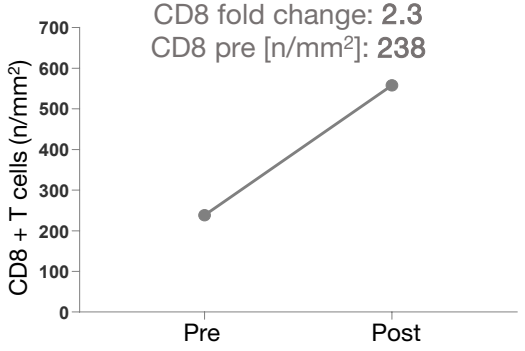
Baseline

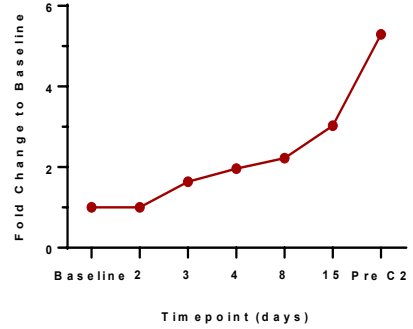


C6 Post-treatment



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



# Case Study: PR in Cancer of Unknown Primary
## Patient Profile, Treatment History and Treatment Outcome

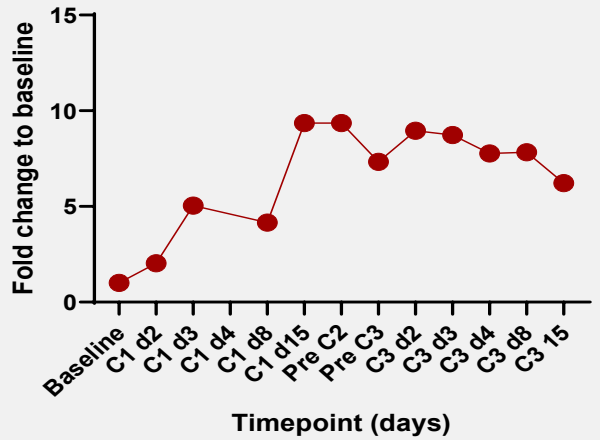
### Patient Profile

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

### Treatment History

Open Radical
Prostatectomy
Radiation
Carboplatin + gemcitabine

s4-1BB Serum




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

Data cut-off: 25-Feb-21

# Case Study: SD in Colorectal Cancer
## Patient Profile, Treatment History and Treatment Outcome

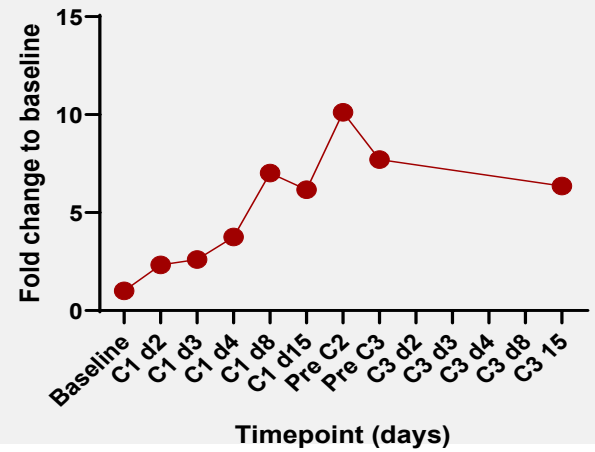
### Patient Profile

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

### Treatment History

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

s4-1BB Serum




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

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

# Cinrebafusp Alfa Clinical Development Plan

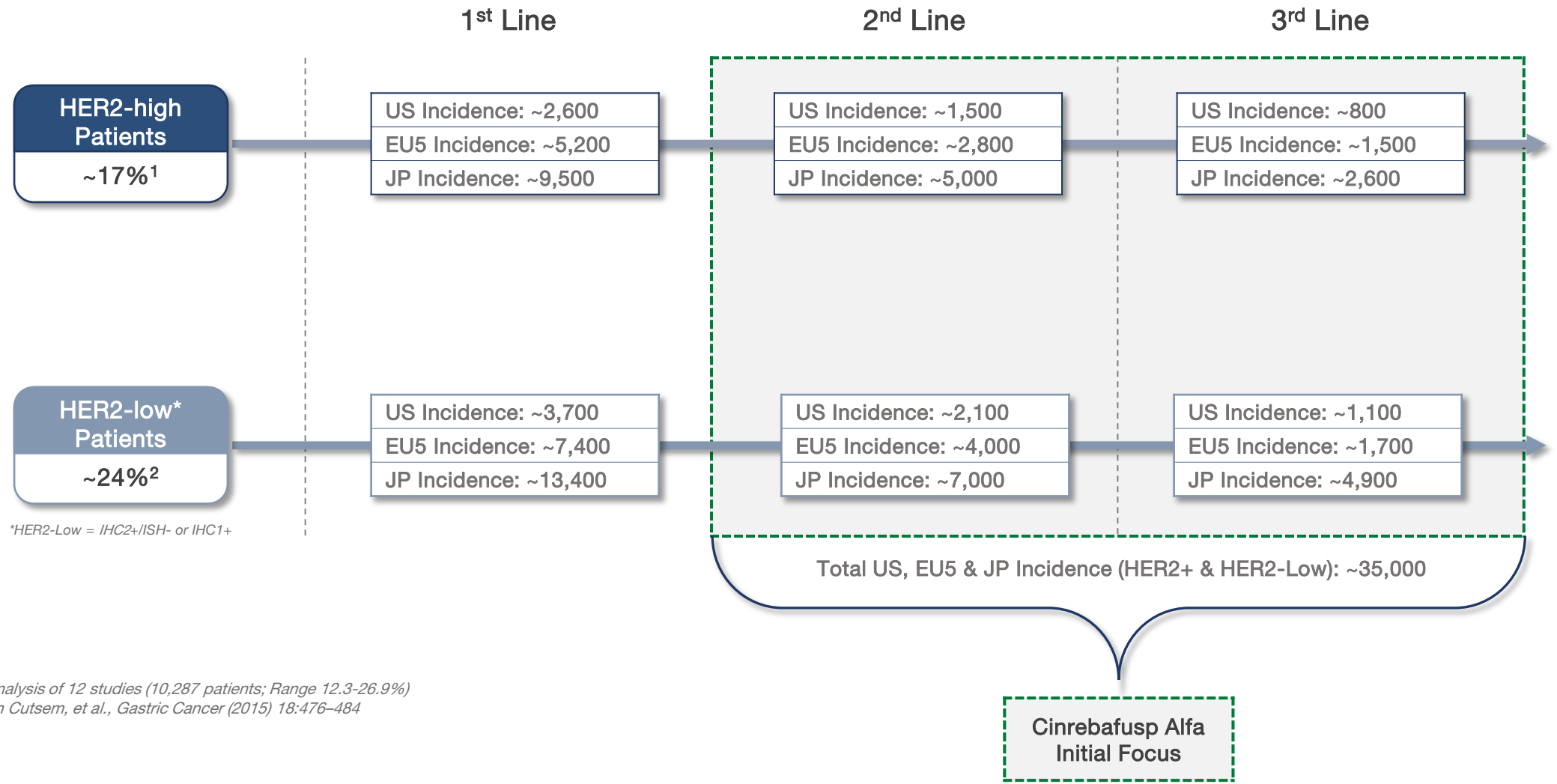
| Phase 2 Details | | | Part A | Part B |
|---|---|---|---|---|
| Gastric Cancer 2L+ | ARM A | Cinrebafusp Alfa + Ramucirumab + Paclitaxel | N = ~ 20 pts | add. 20 – 40 pts |
| HER2-High (IHC3+ or IHC2+/ISH+) | | | | |
| | | | | and |
| Gastric Cancer 2L+ | ARM B | Cinrebafusp Alfa + Tucatinib | N = ~ 20 pts | add. 20 – 40 pts |
| HER2-Low (IHC2+/ISH- or IHC1+) | | | | |

Recommended Phase 2 Dose:
Two-cycle loading dose of 18 mg/kg (Q2W), followed by an 8 mg/kg dose (Q2W) in subsequent cycles

Go/No-Go Analysis

High bar based on ORR, durability, and safety

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




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

# Scientific Rationale for Combining Cinrebafusp Alfa & SoC

**Paclitaxel – Chemotherapy**

- Reduces tumor bulk
- Releases antigen
- Improves T cell : tumor target ratio

**Ramucirumab – Anti-Angiogenic[1-3]**

- Normalizes vascularization
- Alters tumor barrier to T cell penetration
- Reduces Tregs & inhibits TAMs

**Cinrebafusp Alfa – 4-1BB Agonist**

- Increases T cell survival and metabolic fitness in the TME
- Induces T cell memory
- Drives T cell expansion
- Induces anti-tumor cytolytic activity

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

# Scientific Rationale for Combining Cinrebafusp Alfa & Tucatinib

**Tyrosine kinase inhibitors (tucatinib)**

- Upregulates or stabilizes tumor cell surface HER2 expression[2,3,4]
- Increases clustering potential of cinrebafusp alfa on tumor cells to drive enhanced 4-1BB cross-linking

**Cinrebafusp Alfa – Dual MoA**

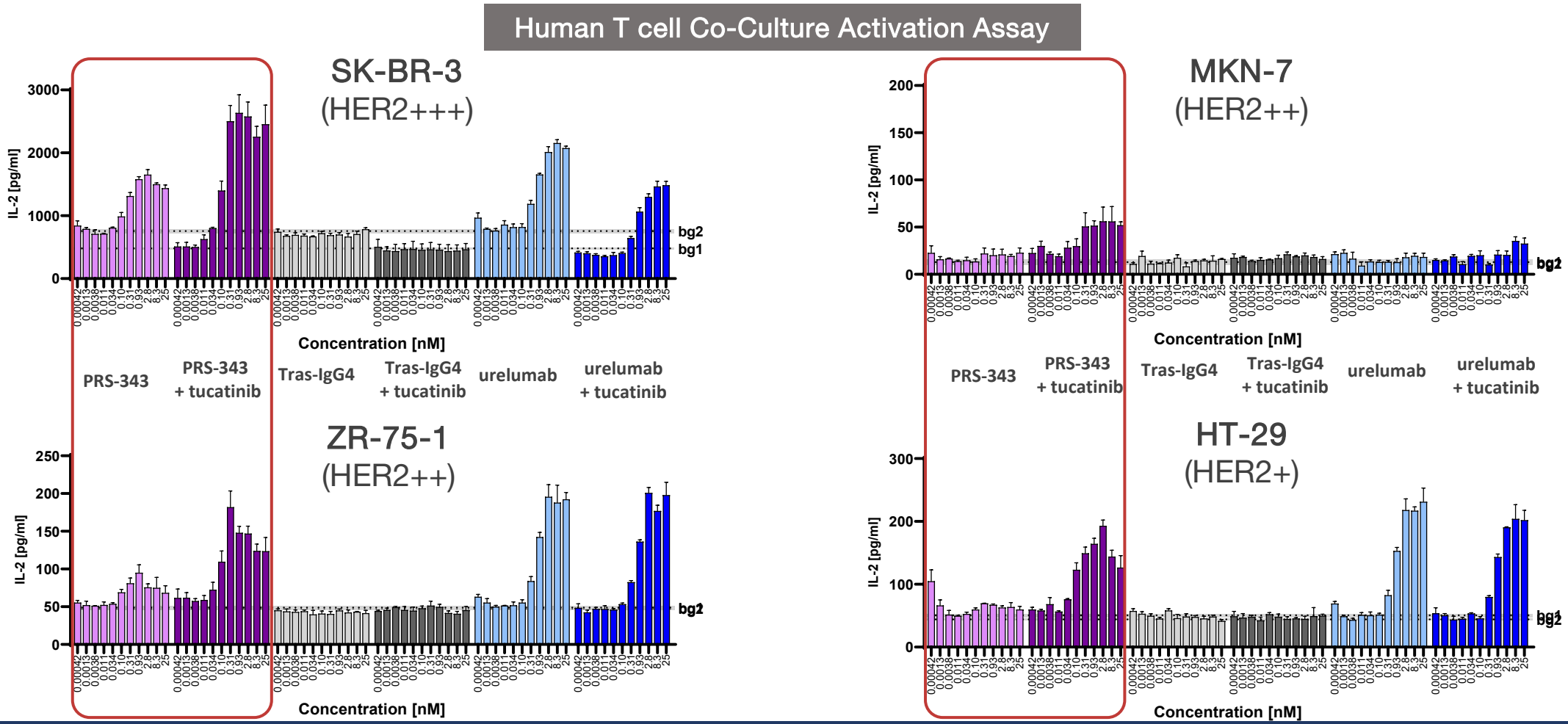
- Inhibits HER2 signaling AND activates tumor-specific T cells in tumor microenvironment

**Complements Both MoAs**

- Enhances inhibition of HER2 signaling by concurrent binding to HER2 on the tumor cell surface and TKI inhibition of the internal kinase signaling domain[1]
- *In vitro*, combination leads to significantly increased T cell activation in the presence of HER2-Low cell lines

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

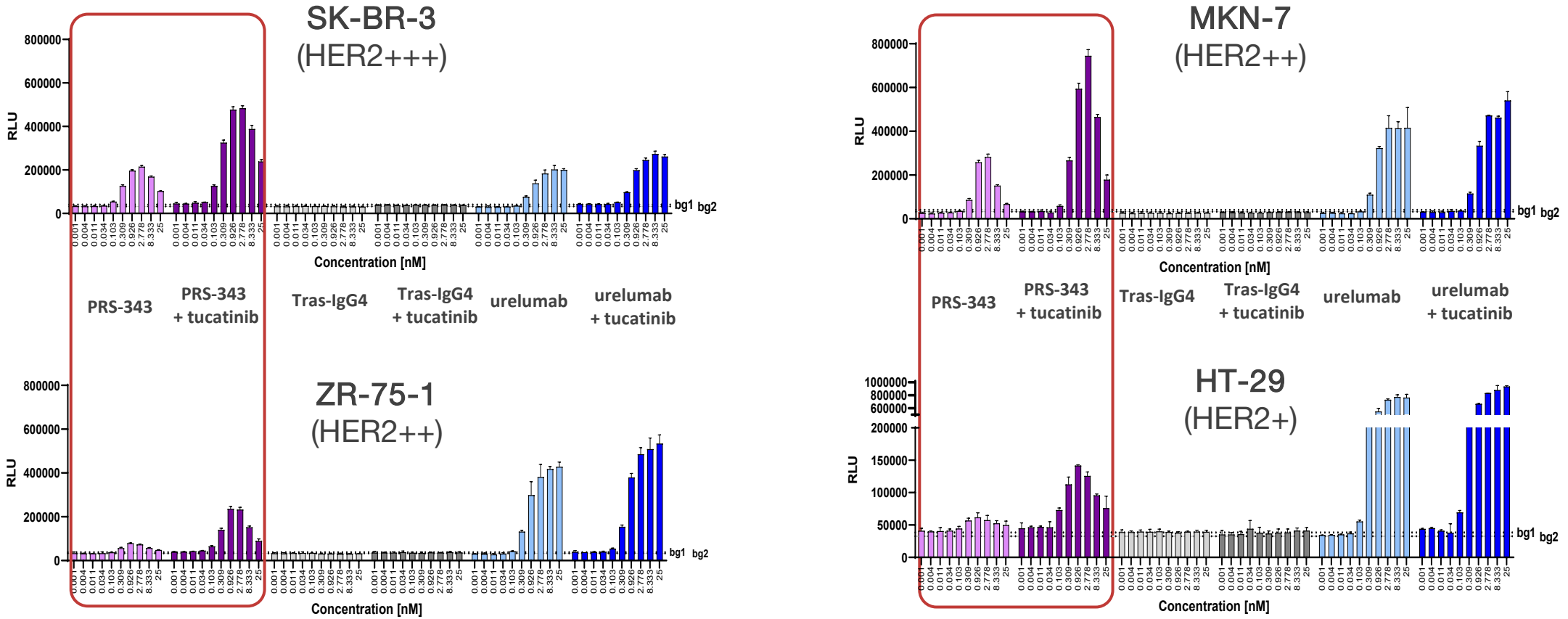
# Cinrebafusp Alfa and Tucatinib Combination Enhances T-cell Activation




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

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

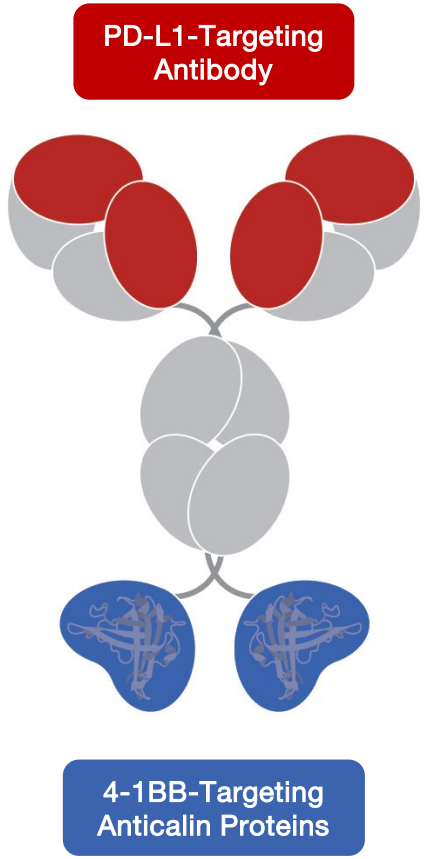
(4-1BB Reporter Cell Assay)




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

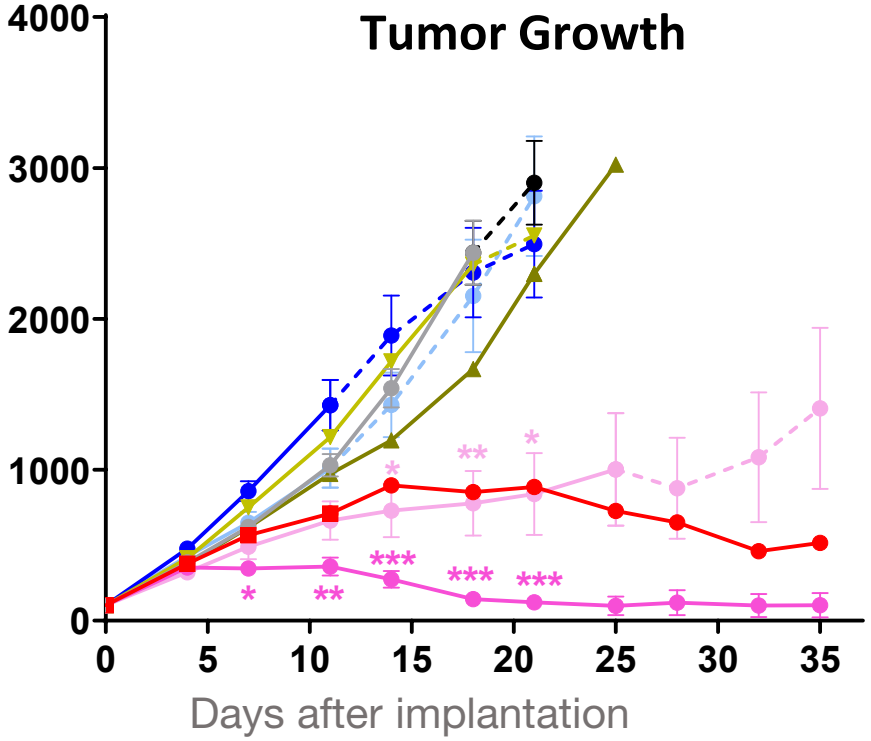
# PRS-344/S095012: Meaningfully Building on Localized MoA of Cinrebafusp Alfa

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

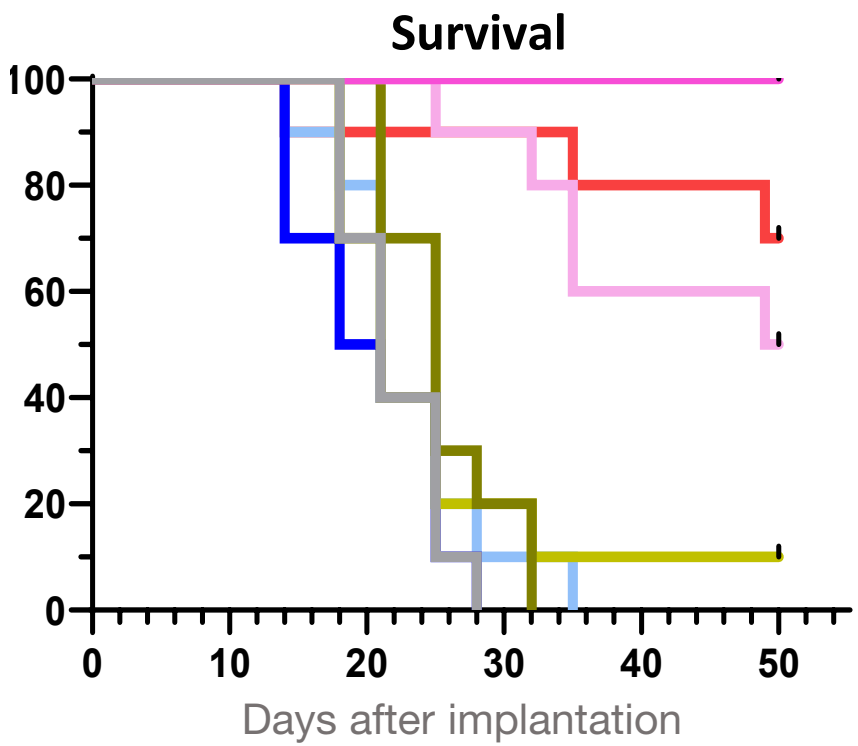


# PRS-344 Drives Strong Anti-tumor Activity in Anti-PD-L1 mAb-resistant Mouse Model

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




Vehicle
Anti-PD-L1 - 7.7 mg/kg
Anti-PD-L1 – 0.77 mg/kg
Urelumab analog – 3 mg/kg
PRS-344/S095012 - 10 mg/kg
PRS-344/S095012 - 1 mg/kg
PRS-344/S095012 - 0.1 mg/kg
PRS-344/S095012 - 0.01 mg/kg




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

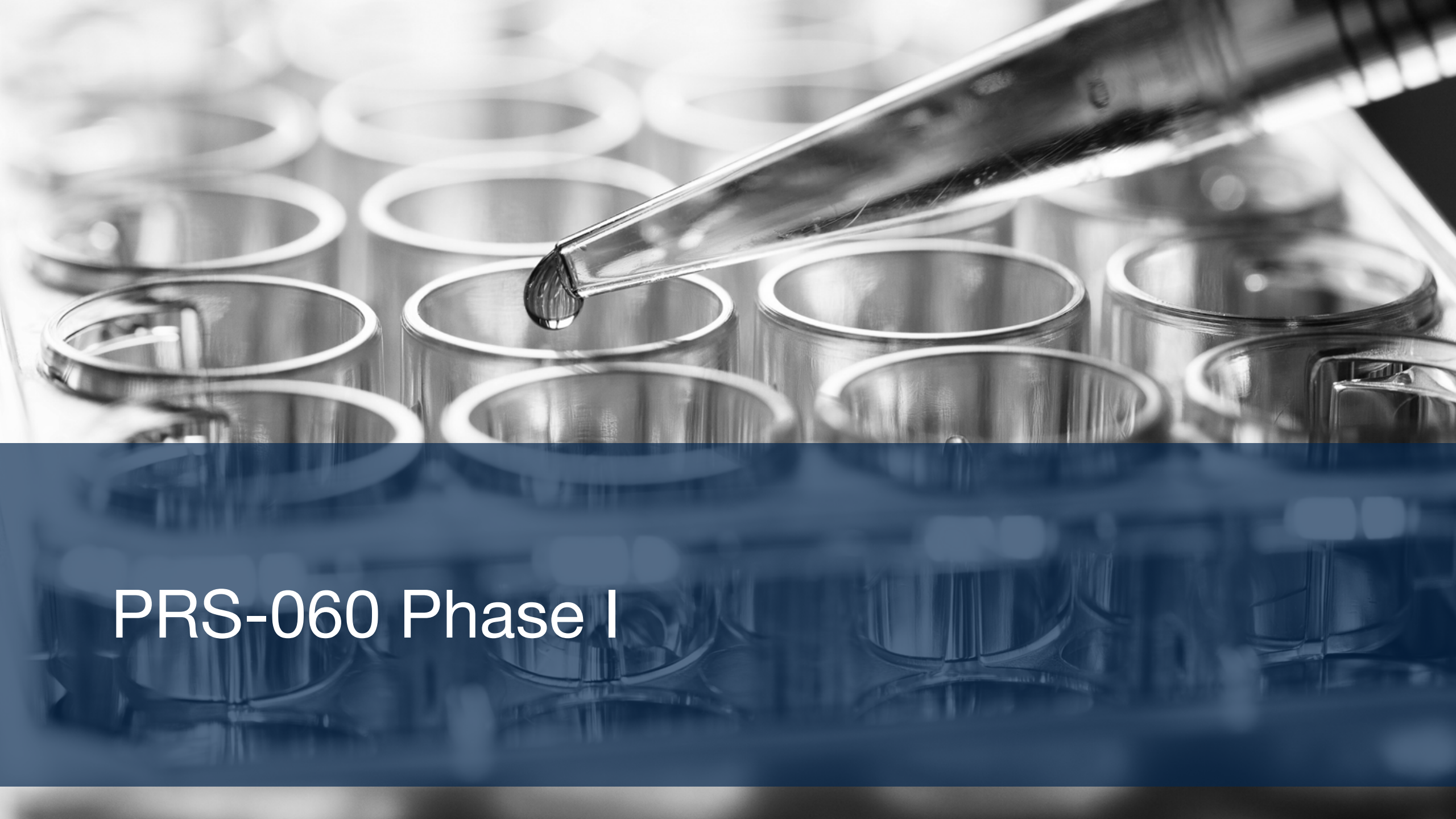
# Financial Overview (As of 3/31/21)

| $66.8M (~$120M proforma*) | $0.0 | 59.7M* |
| --- | --- | --- |
| Cash & Cash Equivalents | Debt | CSO |

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

*Excludes $23M from PRS-060 phase 2a milestone and AstraZeneca equity investments (along with ~3.6M common shares issued), $10 million from Boston Pharmaceuticals and $20 million from Genentech

# 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 |

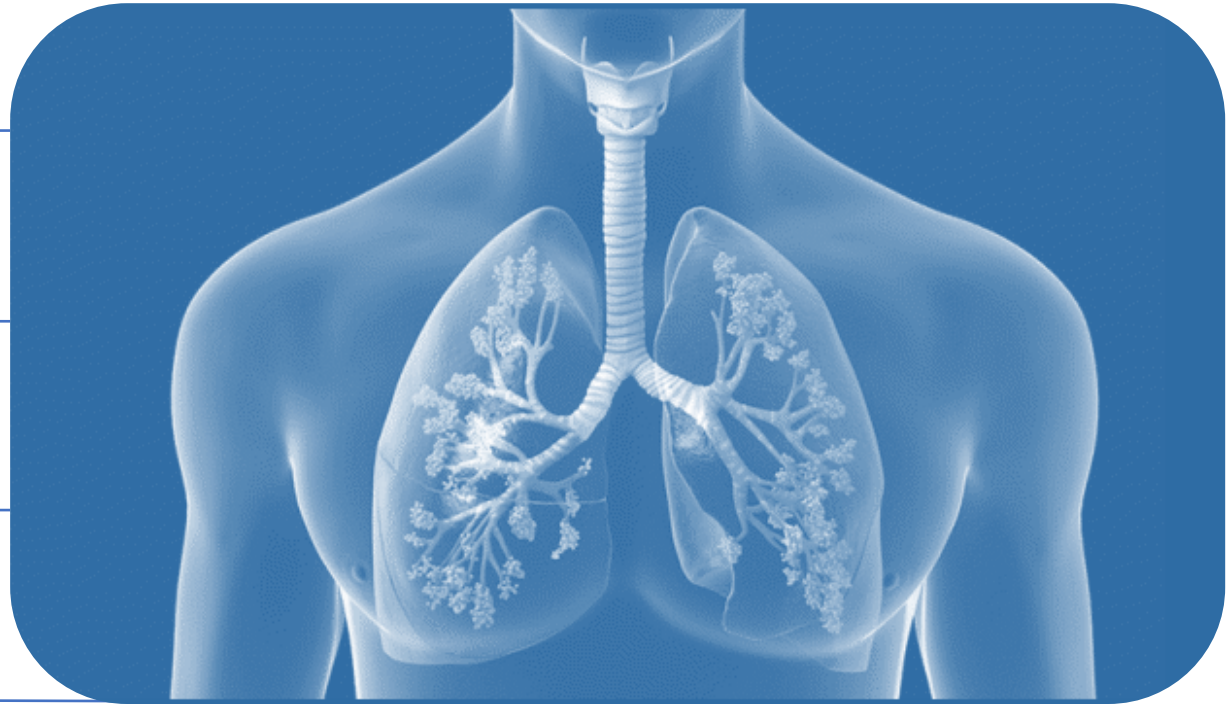
*q.d. on Day 10

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



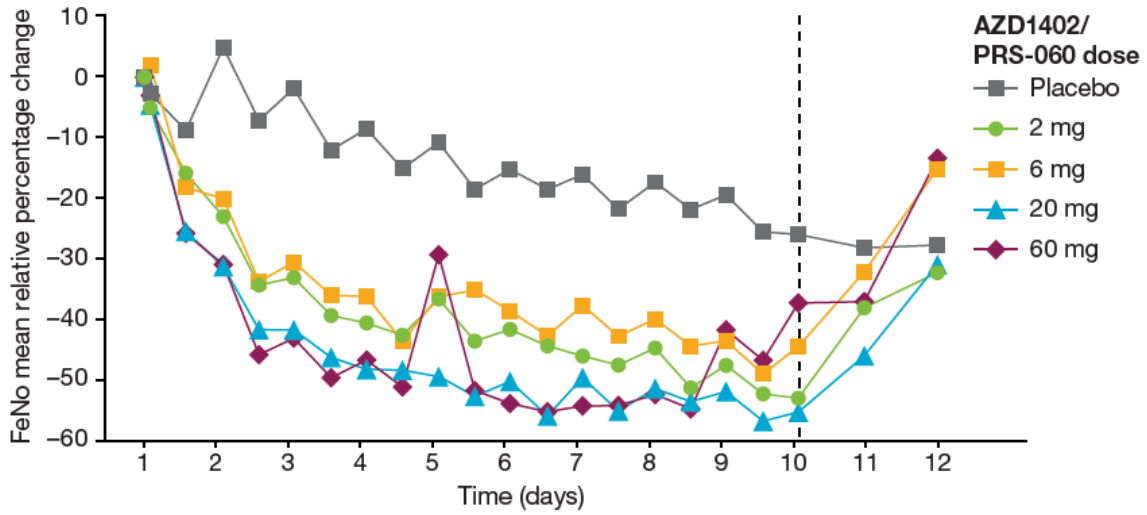
# Phase 1b Interim Results: Favorable Safety Profile

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

| System organ class<br>AE Preferred Terms[b] | Placebo<br>(N = 12)<br>n (%) m | AZD1402/PRS-060[c]<br>(N = 30)<br>n (%) m | Overall<br>(N = 42)<br>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

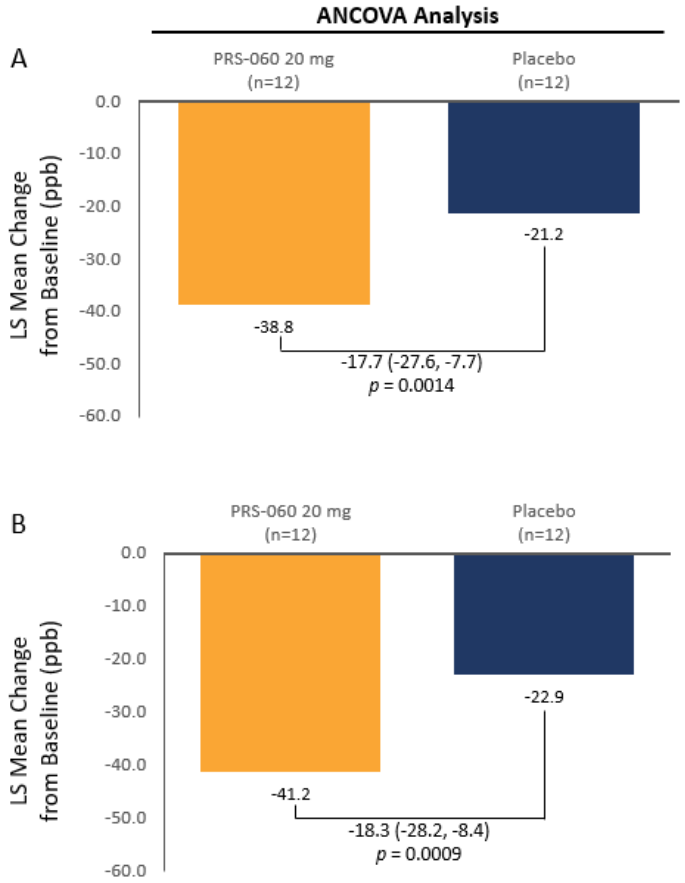
## PRS-060 Relative FeNO Reduction (Emax Analysis)




| 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 | | |

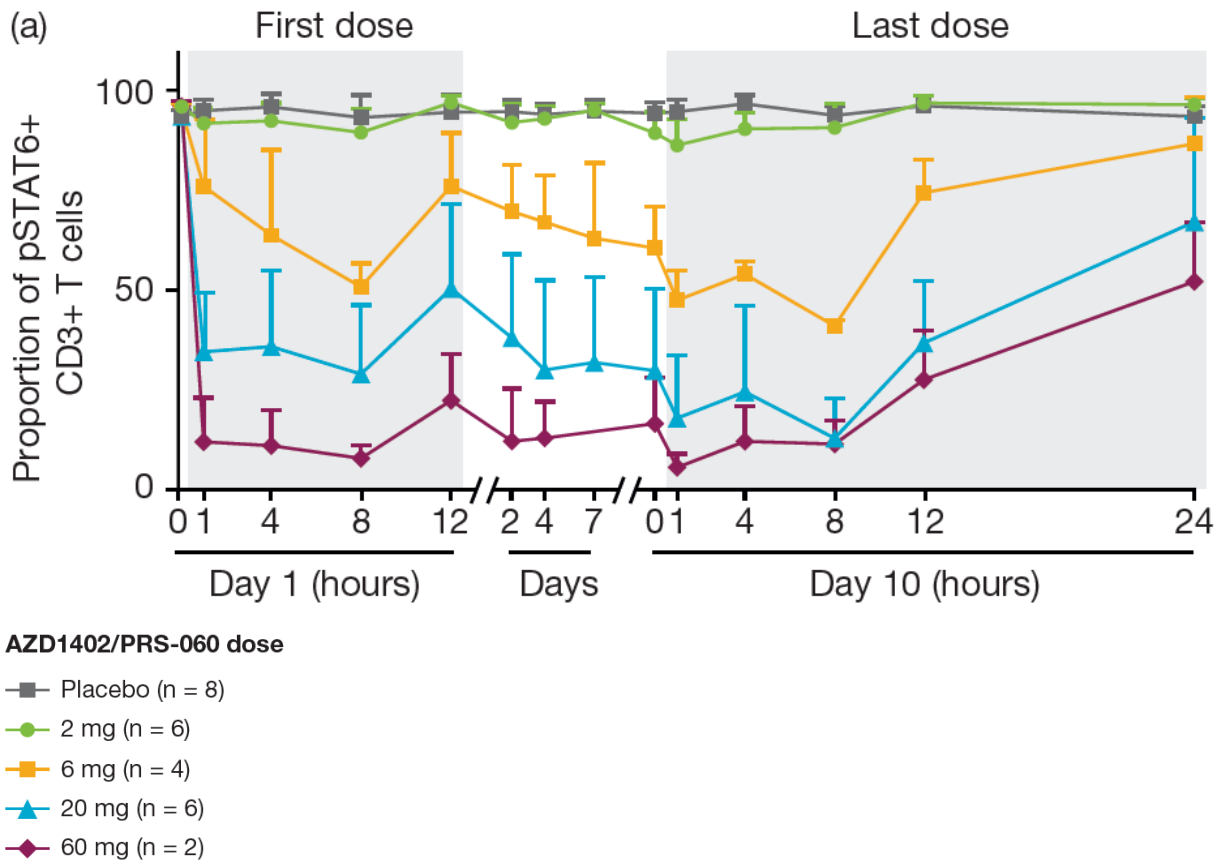
## PRS-060 Relative FeNO Reduction (ANCOVA Analysis)

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

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

# Cinrebafusp Alfa – Biomarkers

# Soluble 4-1BB (s4-1BB): Blood-based Biomarker of 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 is as a negative regulator, keeping 4-1BB-mediated co-stimulation in check

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

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