

PIERIS PHARMACEUTICALS



CORPORATE PRESENTATION
January 2022

SUPERIOR MEDICINES THROUGH EFFICIENT BIOLOGY



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, 2020 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

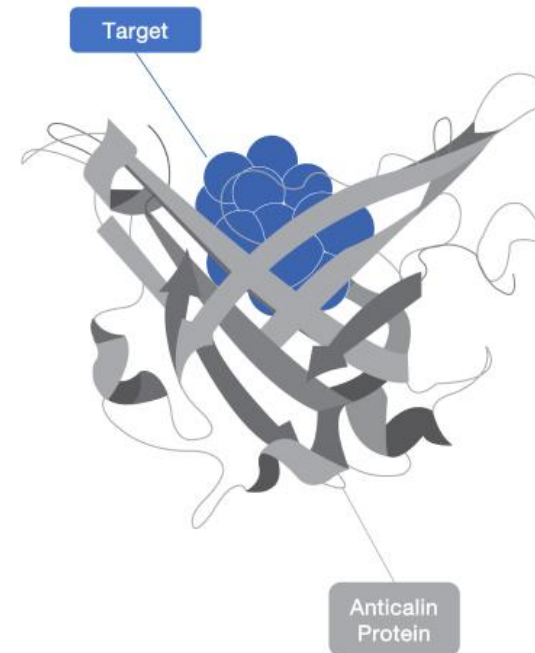
Anticalin® Proteins as Therapeutic Modalities

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

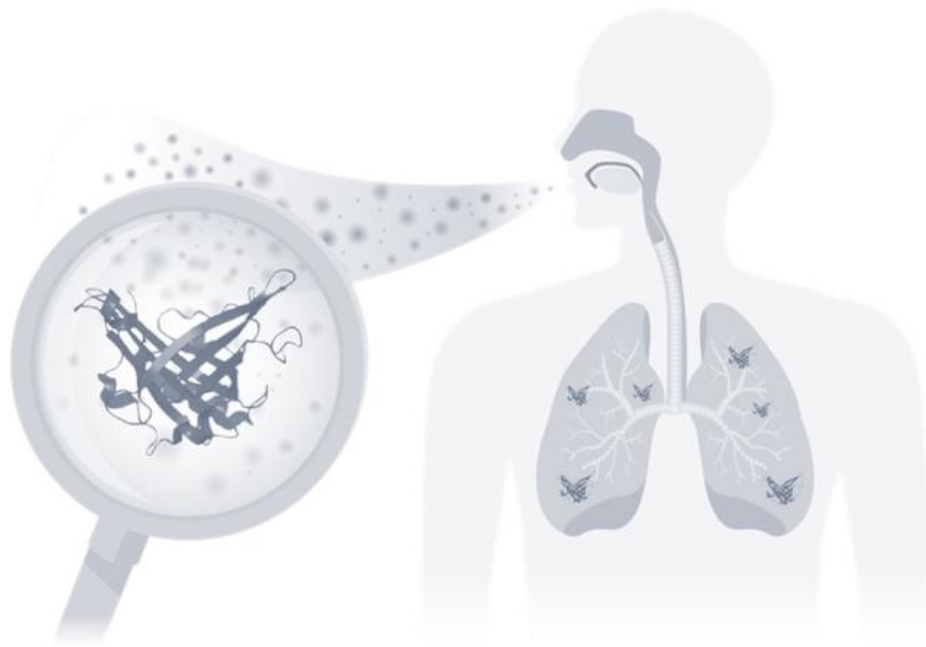
Translational Science Expertise to Deploy Platform in Meaningful Way

- 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

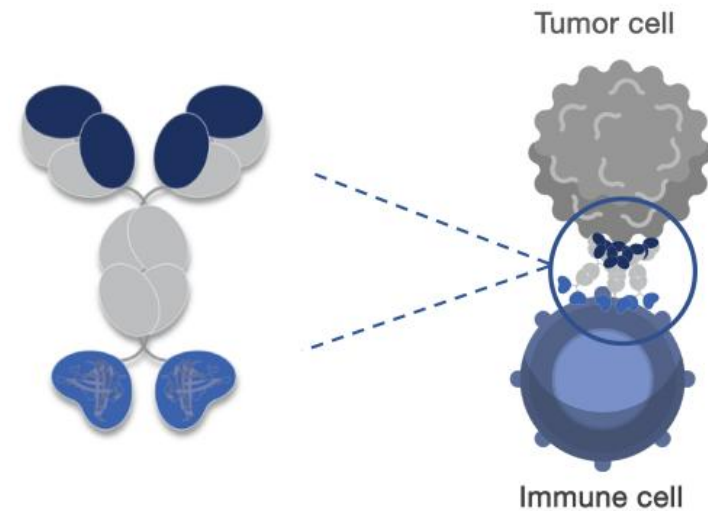


Two-fold Focus of Anticalin Platform Deployment

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-R α	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 <small>A Member of the Roche Group</small>	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 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



- 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 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



- 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



- 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



- 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-4R α Antagonist

Candidate	PRS-060/AZD1402
Function/MoA	Inhibiting IL4-R α (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)	<input checked="" type="checkbox"/> Part 1a: Low + Med Dose <input type="checkbox"/> Part 1b: High 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)	<input type="checkbox"/> Part 2a: Low + Med Dose <input type="checkbox"/> Part 2b: High Dose	Participant Population: Moderate uncontrolled asthmatics on ICS/LABA with blood EO count of ≥ 150 cells/ μ L 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



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

U.S.

19.0M

asthma patients over 12 years of age in the U.S.

7.8M

with moderate-to-severe asthma (41%)

3.1M

uncontrolled (40%)



1.9M high EOs (60%)



1.2M low EOs (40%)

EU

47.8M

asthma patients over 12 years of age in the EU

21.5M

with moderate-to-severe asthma (45%)

8.6M

uncontrolled (40%)

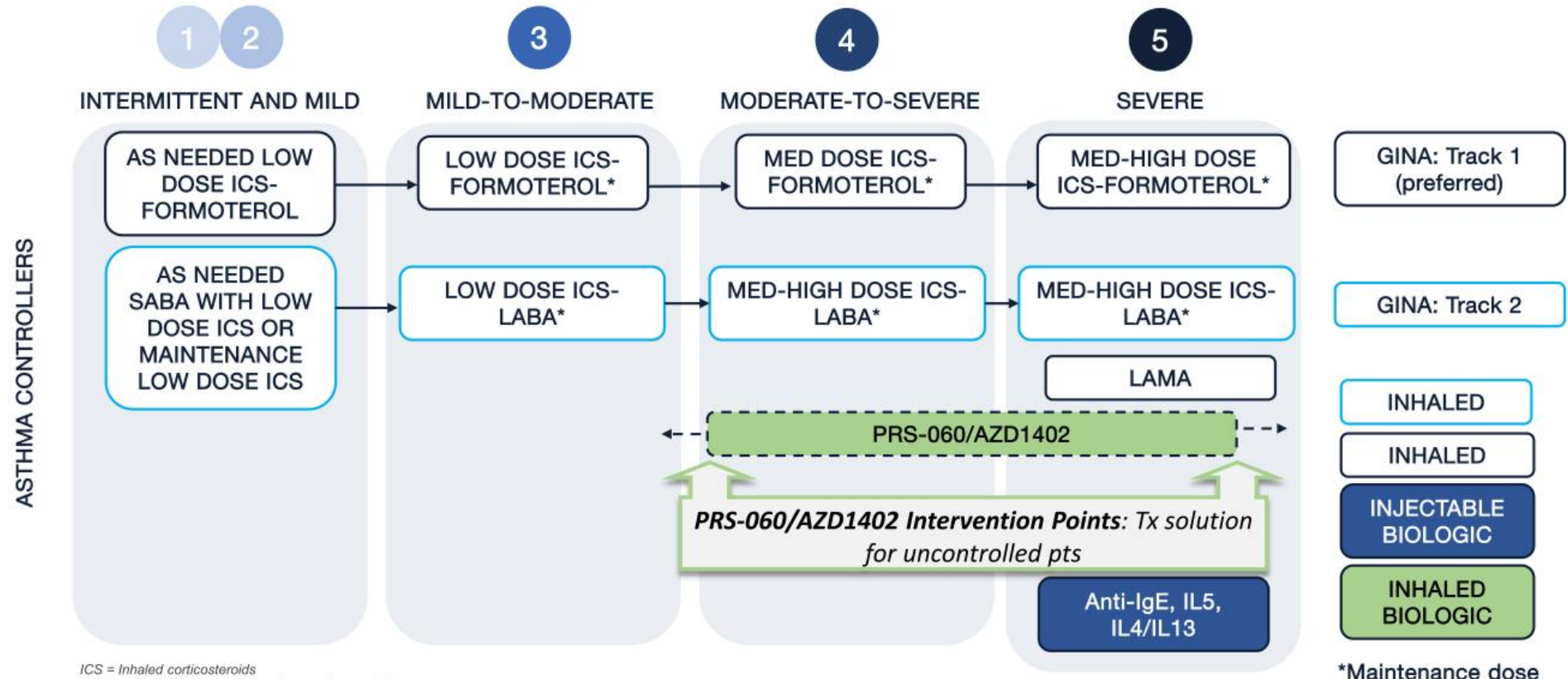


5.2M high EOs (60%)



3.4M low EOs (40%)

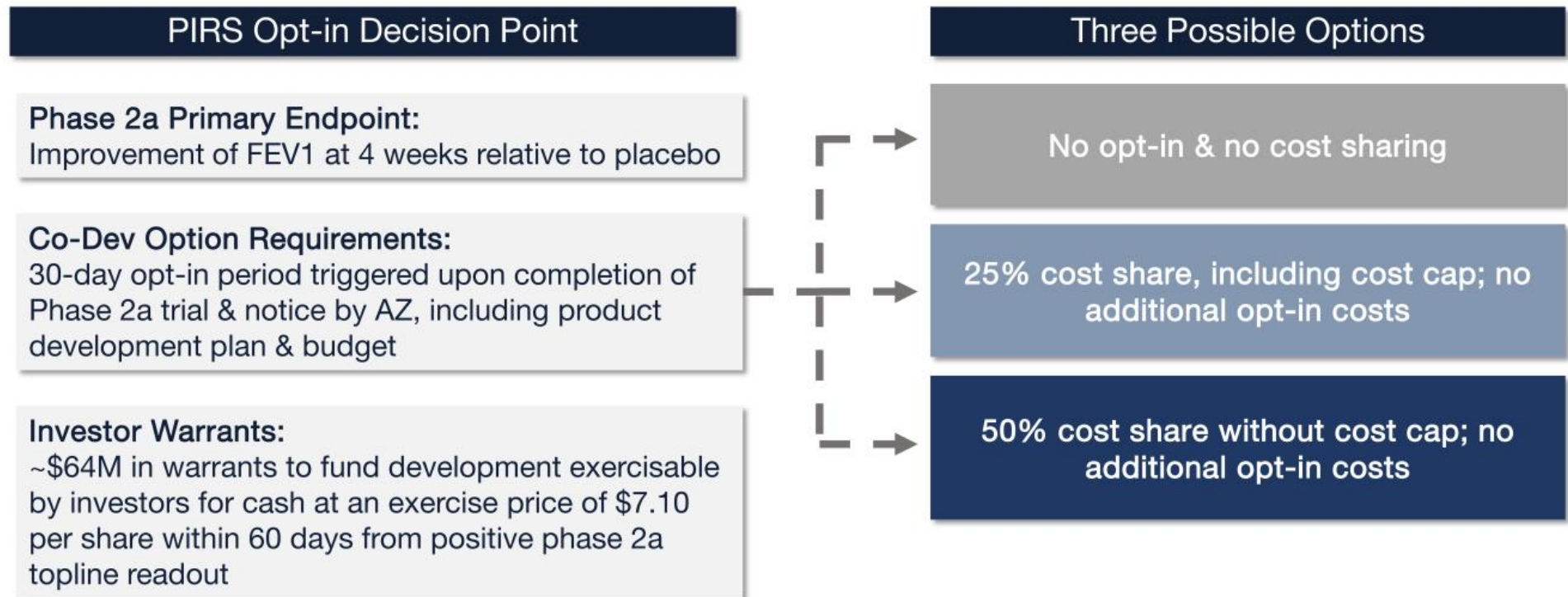
Potential Large Market Opportunity in Moderate-to-Severe Asthma not Addressed by ICS/LABA before Injectable Biologics



ICS = Inhaled corticosteroids
SABA = Short-acting β_2 adrenergic receptor agonists
LABA = Long-acting β_2 adrenergic receptor agonists
LAMA = Long-acting muscarinic antagonists

Global Initiative for Asthma (GINA) Steps (2021)

Co-Development Options for PRS-060/AZD1402



PRS-220: Inhaled CTGF Antagonist

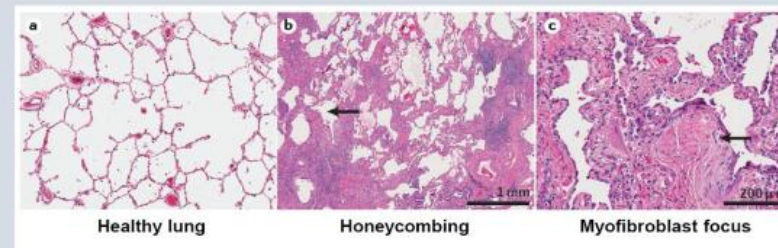
Candidate	PRS-220
Function/MoA	Inhibiting CTGF/CCN2
Indications	IPF and PASC-PF*
Development	Entering phase 1 in healthy subjects this year
Commercial Rights	Fully proprietary



*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 diagnosis²

>\$3B

current market in sales

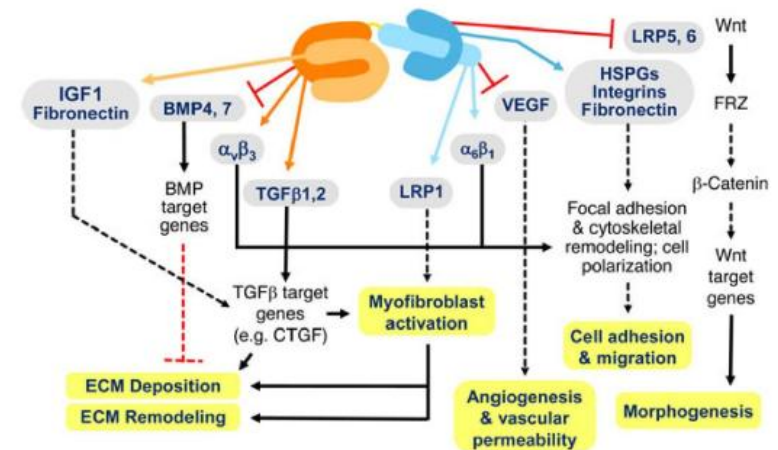
Currently approved treatments provide modest benefit, in addition to having side effects that require management

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

PASC-PF

Post-acute sequelae of SARS-CoV-2 infection (PASC) pulmonary fibrosis (PASC-PF), also known as post-COVID-19 syndrome pulmonary fibrosis, affects patients who have recovered from acute COVID-19

Prevalence

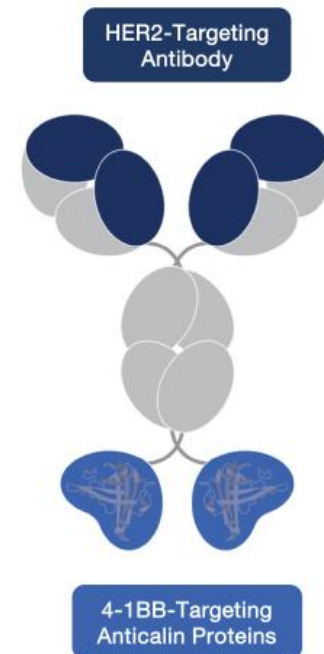
About a third of patients hospitalized with severe COVID-19 have persistent interstitial lung abnormalities lasting up to six months after infection

CTGF

Blocking CTGF with an inhaled Anticalin protein may reduce the extent and persistence of fibrotic interstitial lung disease in patients after moderate and severe COVID-19

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

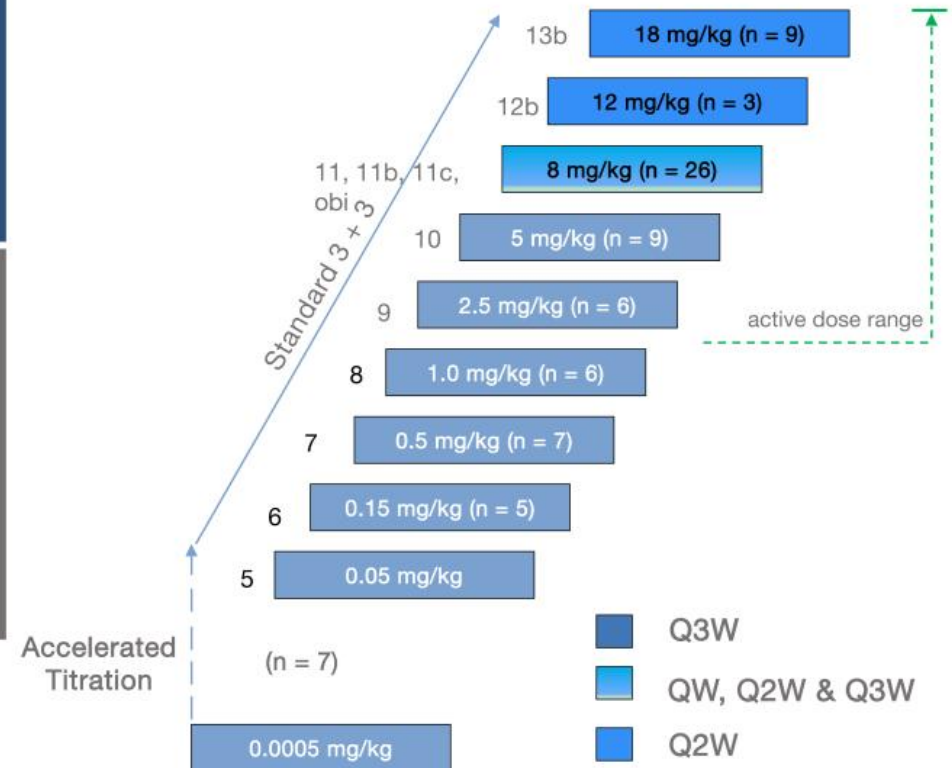
Secondary: Characterize PK/PD & immunogenicity
Preliminary anti-tumor activity

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.

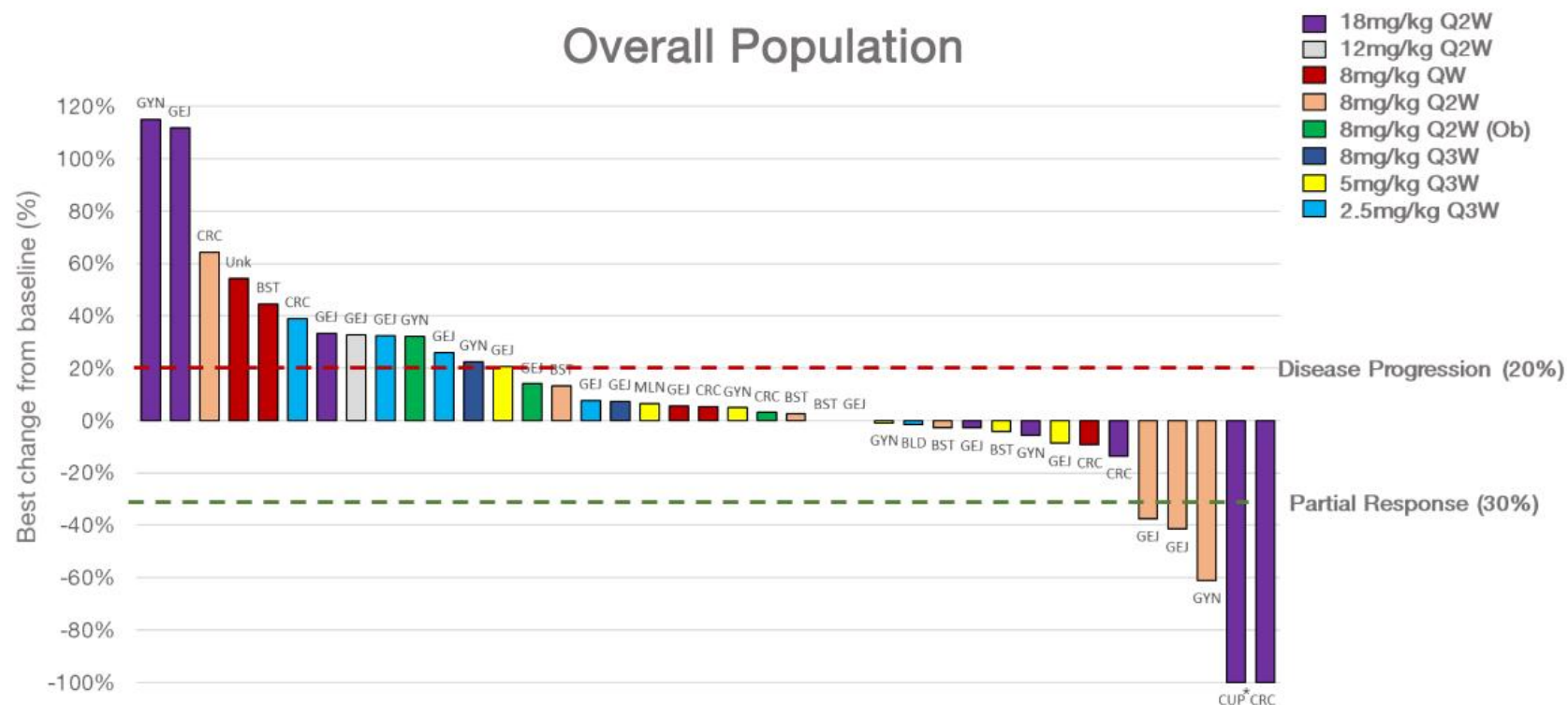
Data cut-off: 25-Feb-21

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

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

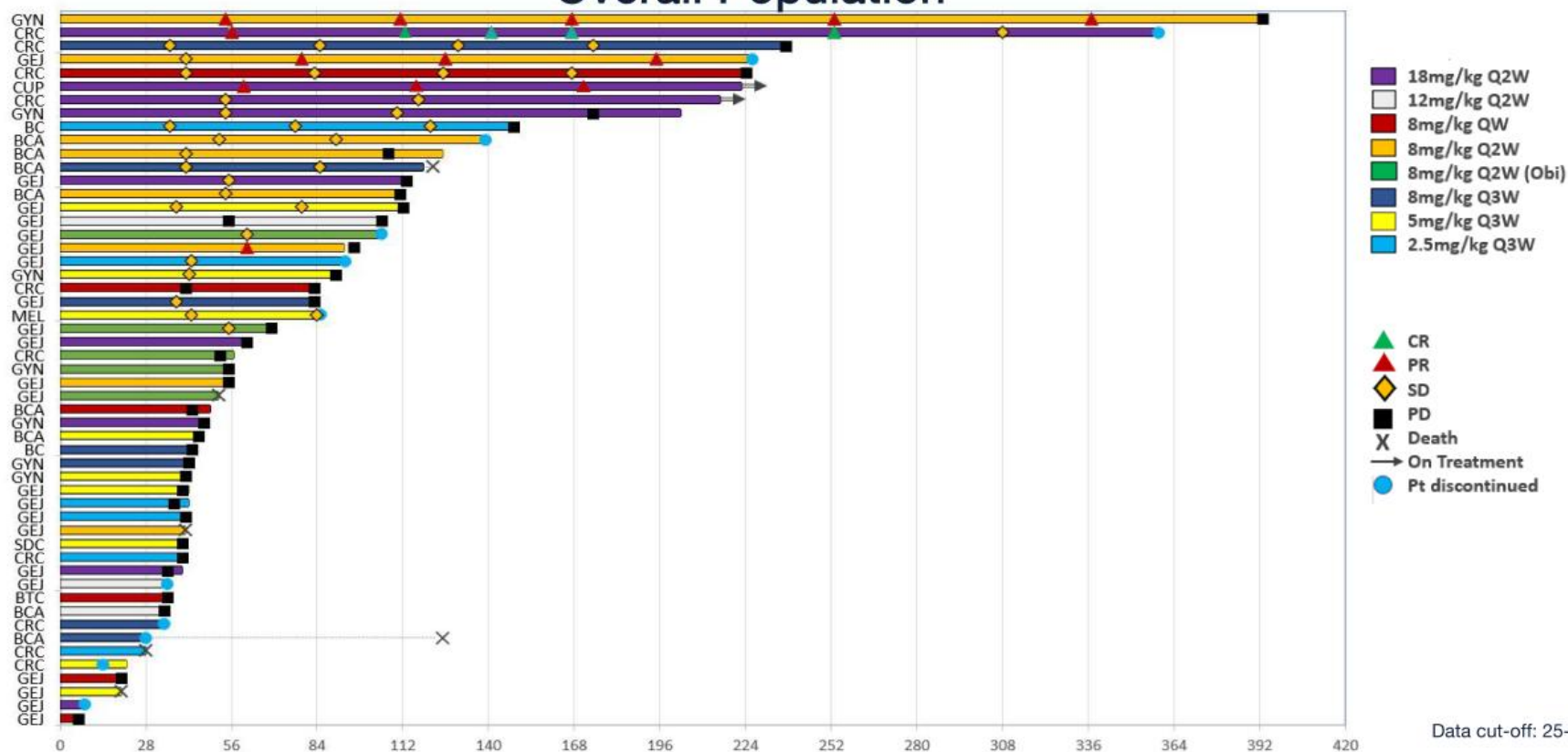


Data cut-off: 25-Feb-21

*Manual update for CUP patient from Medidata 9-Apr-21

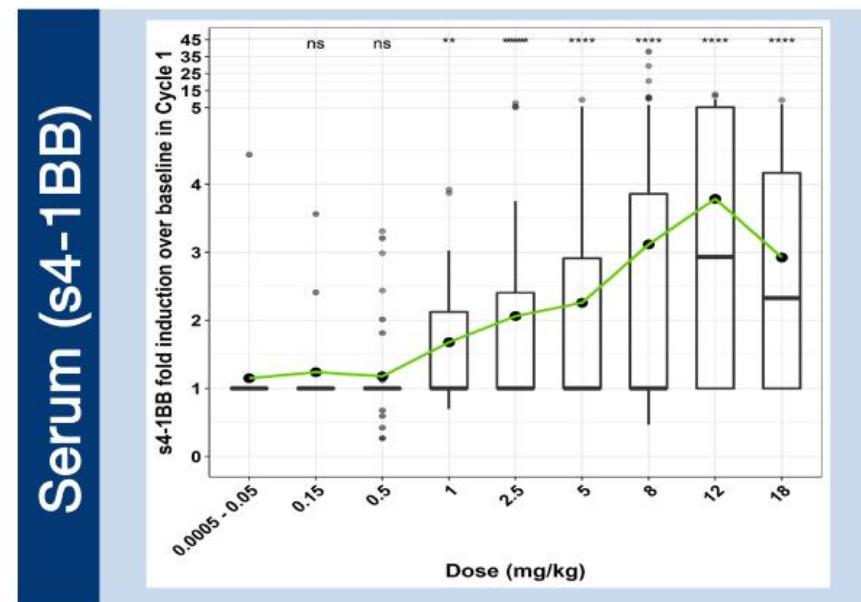
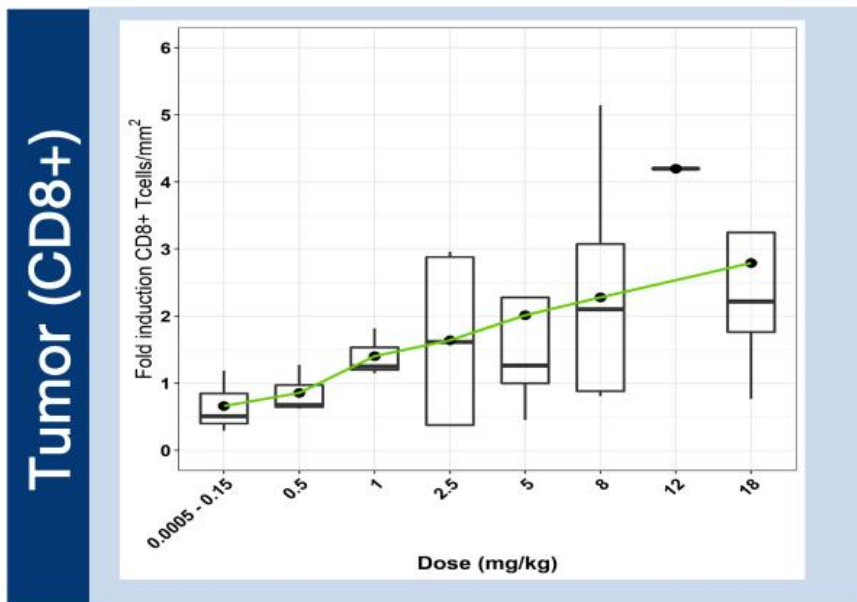
Durable Responses with Cinrebafusp Alfa Among Heavily Pre-treated Population

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



↓ Biopsy
Pre-dose

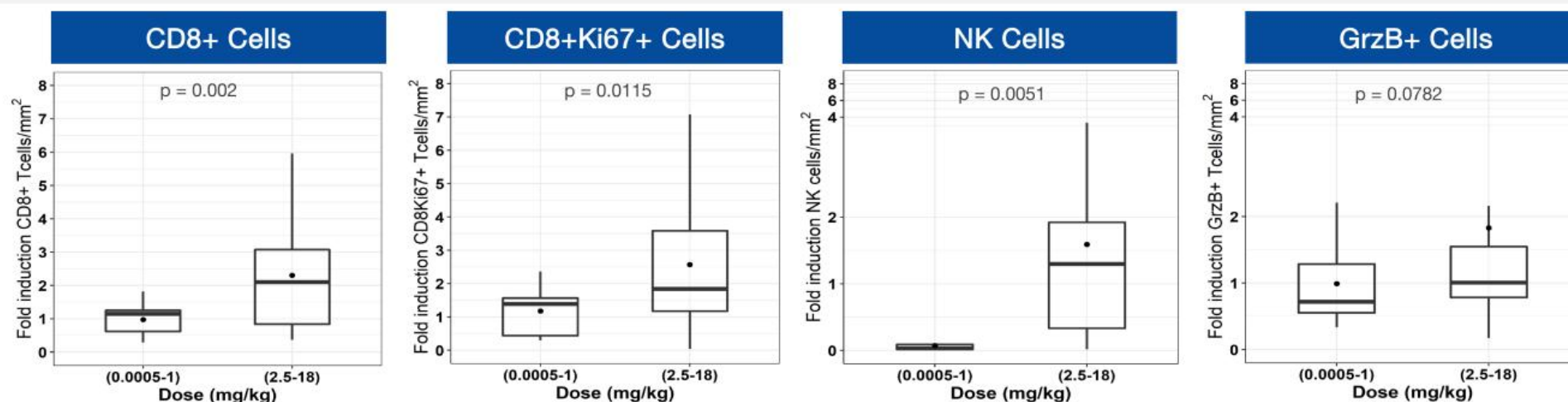
↓
PRS-343
(Cycle 1 Day 1)

↓
PRS-343
(Cycle 2 Day 1)

↓ Biopsy
Post-dose
(Cycle 2 Days 2-8)

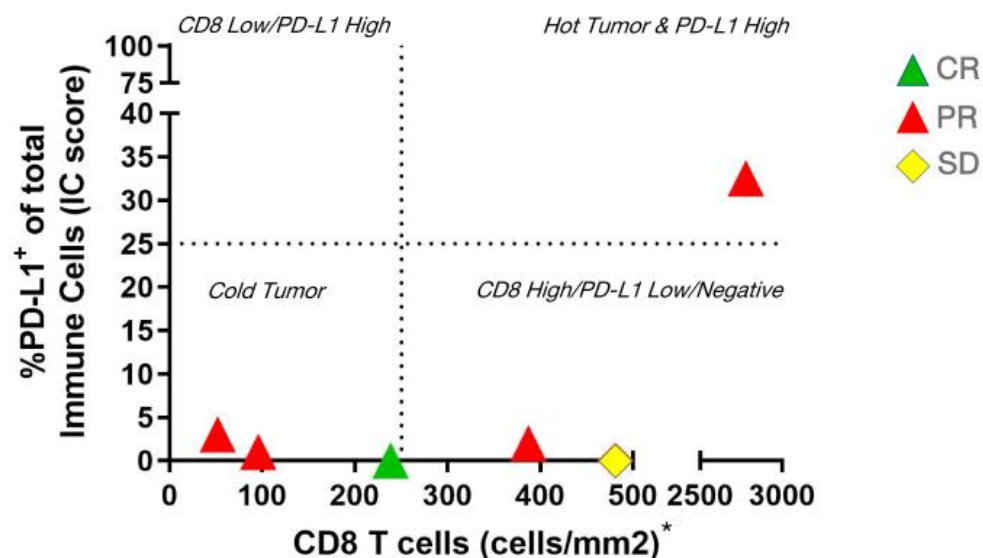


Based on preclinical and clinical data, serum concentration of $> 20 \mu\text{g/ml}$ defines active dose range beginning at 2.5 mg/kg (Cohort 9)



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

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



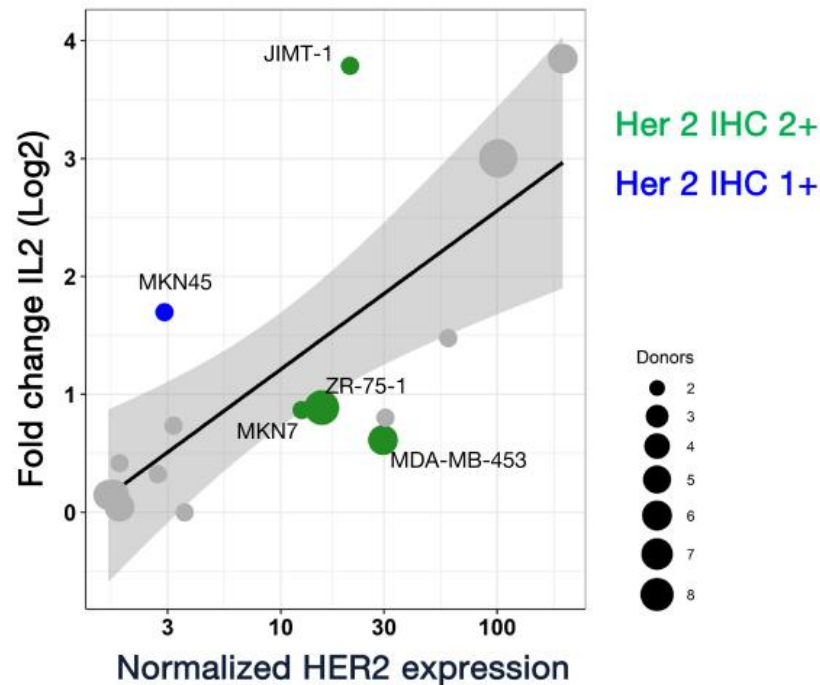
* Threshold informed by (Tumeh et al., 2014 and Blando et al., 2019)

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

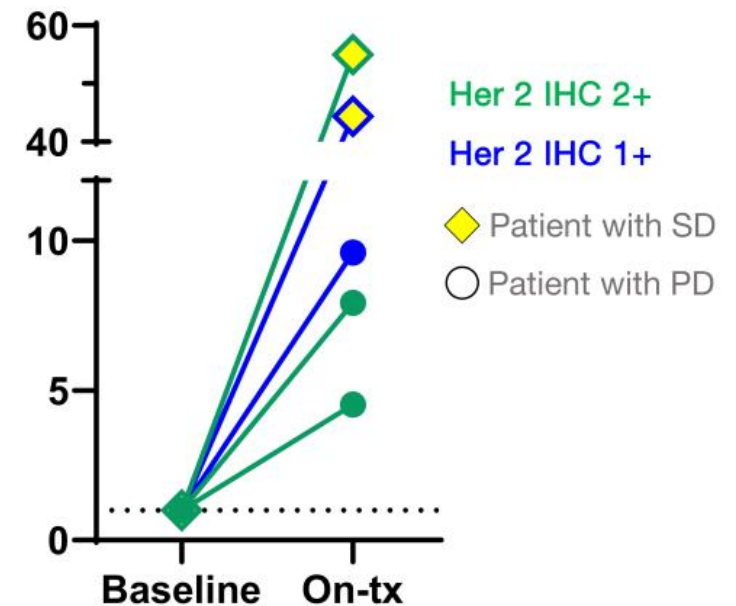
Data cut-off: 25-Feb-21

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 lines¹



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



Data cut-off: 25-Feb-21

¹Hinner et al., Clin Can Res 2019

Cinrebafusp Alfa Clinical Development Plan

Phase 2 Details

Gastric Cancer 2L	ARM A	Cinrebafusp Alfa + Ramucirumab + Paclitaxel
		HER2-High (IHC3+ or IHC2+/ISH+)

Gastric Cancer 2L+	ARM B	Cinrebafusp Alfa + Tucatinib
		HER2-Low (IHC2+/ISH- or IHC1+)

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

Part A

N = ~ 20 pts

Target ORR ≥ 50%

Part B

Go/No-Go Analysis

add. 20 – 40 pts

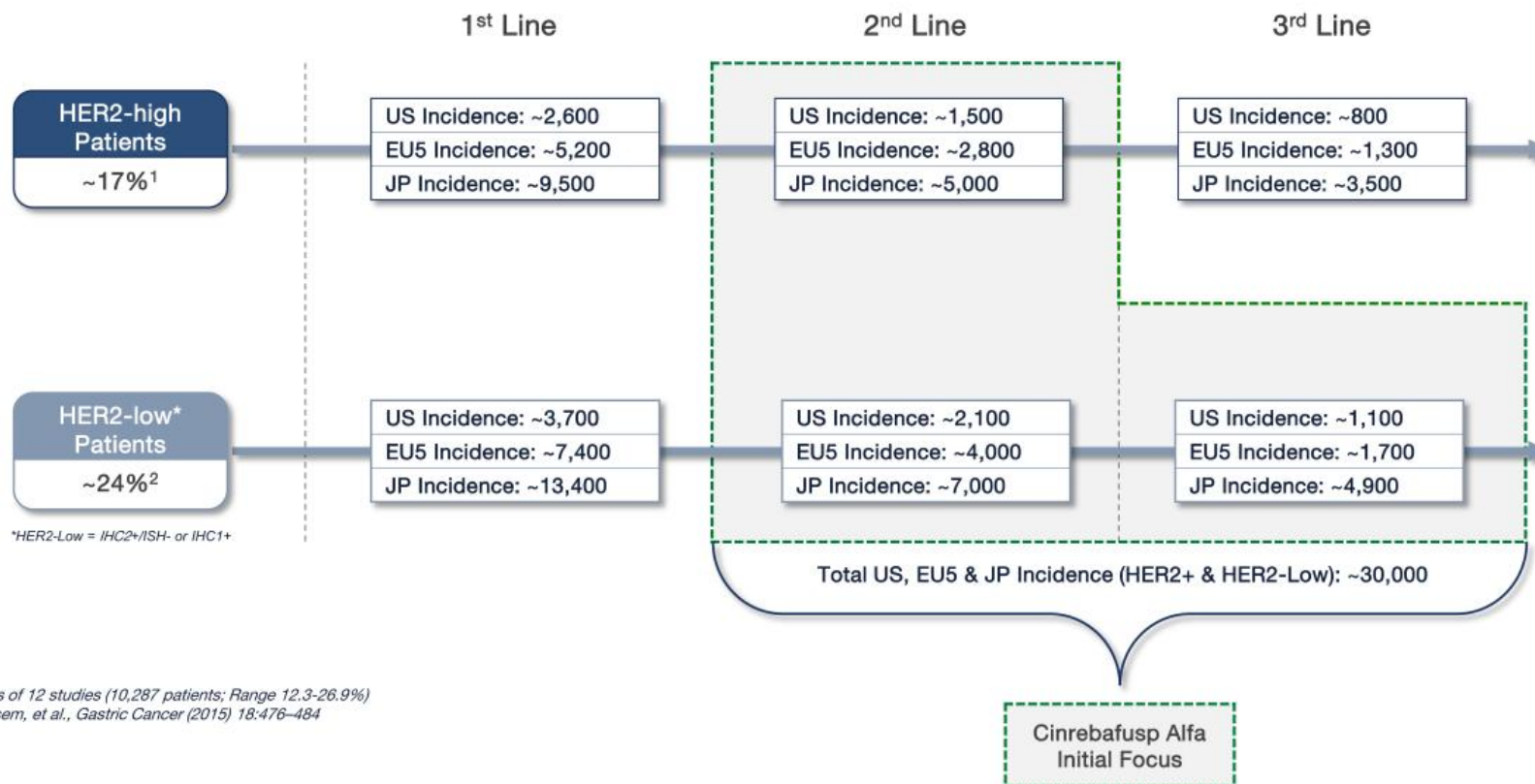
N = ~ 20 pts

Target ORR ≥ 40%

add. 20 – 40 pts

High bar to progress to Part B based on ORR,
durability, and safety

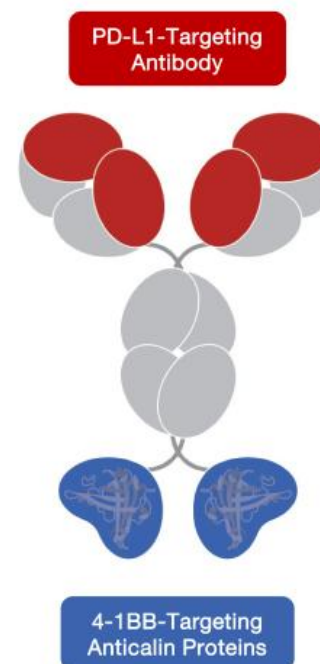
Cinrebafusp Alfa Opportunity in HER2-High & HER2-Low Gastric Cancer



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

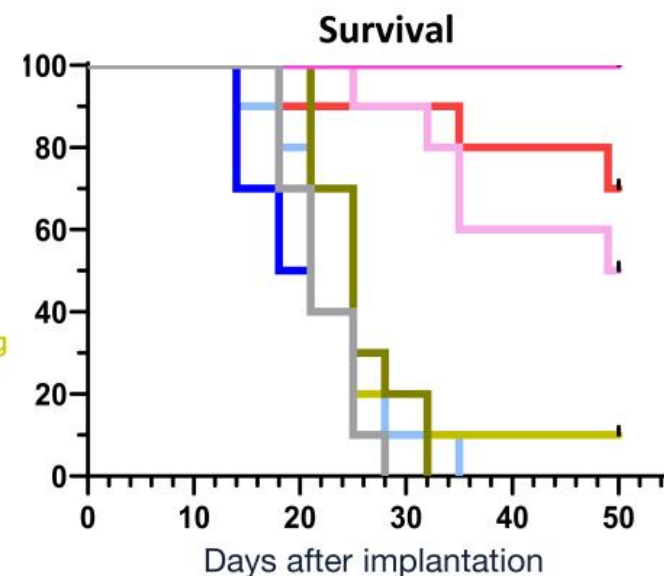
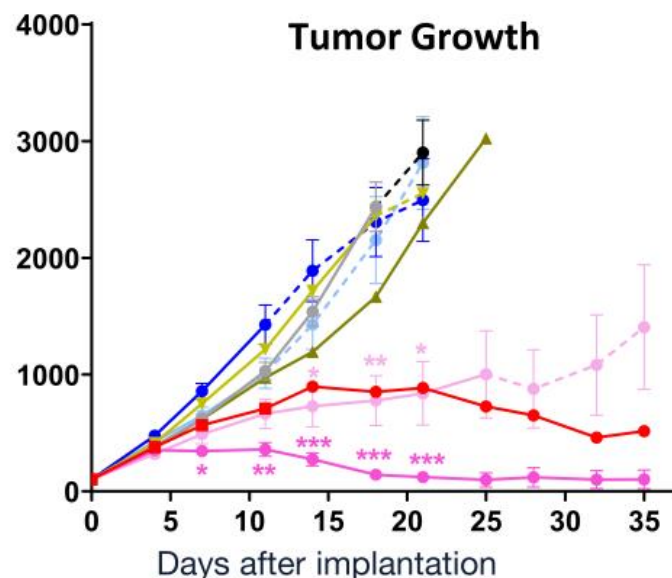
PRS-344/S095012: Meaningfully Building on Localized MoA of Cinrebafusp Alfa

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



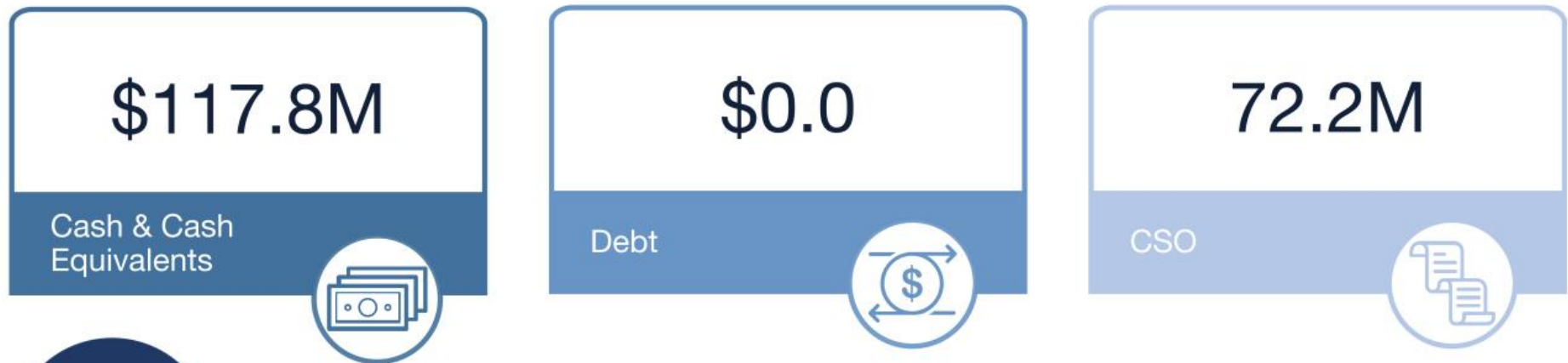
PRS-344 Drives Strong Anti-tumor Activity in Anti-PD-L1 mAb-resistant Mouse Model

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 (Unaudited, 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



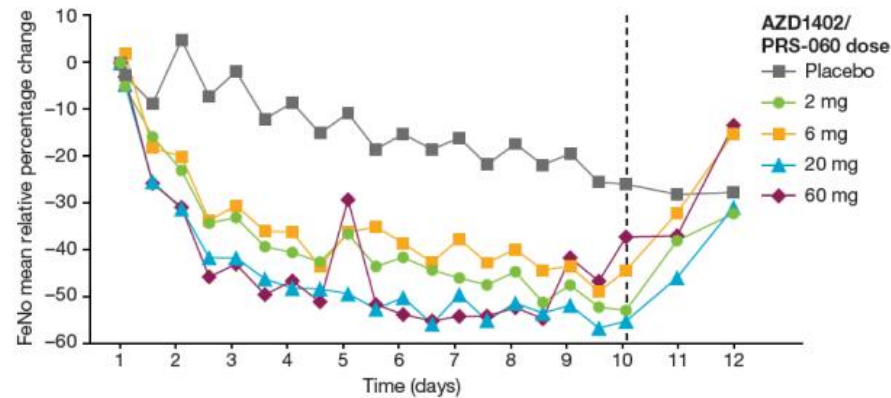
Phase 1b Interim Results: Favorable Safety Profile

- 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

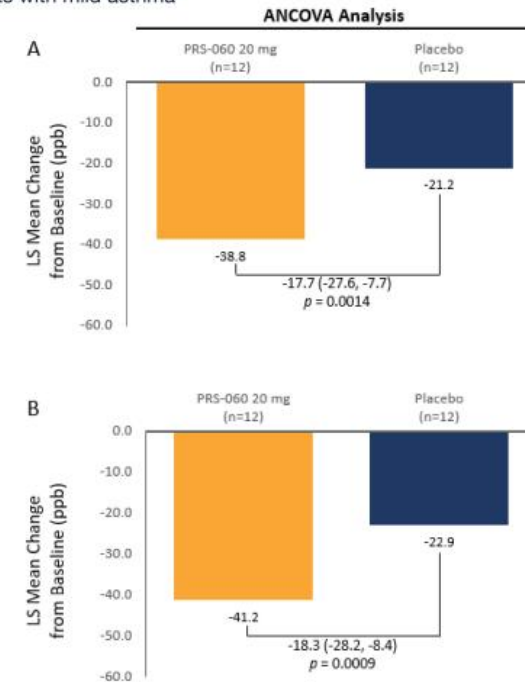
PRS-060 Relative FeNO Reduction (Emax Analysis)



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		

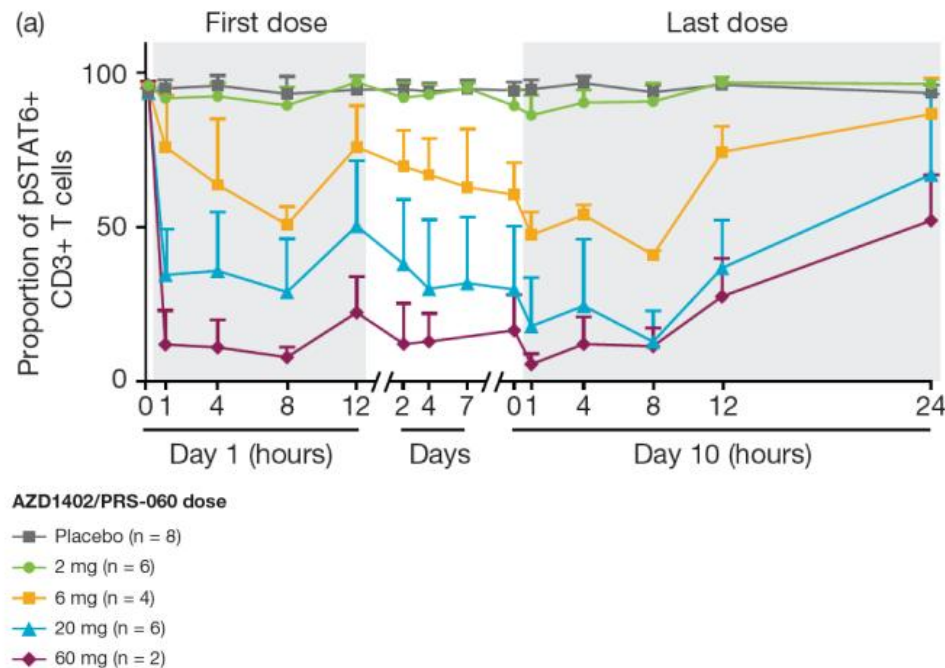
PRS-060 Relative FeNO Reduction (ANCOVA Analysis)

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)

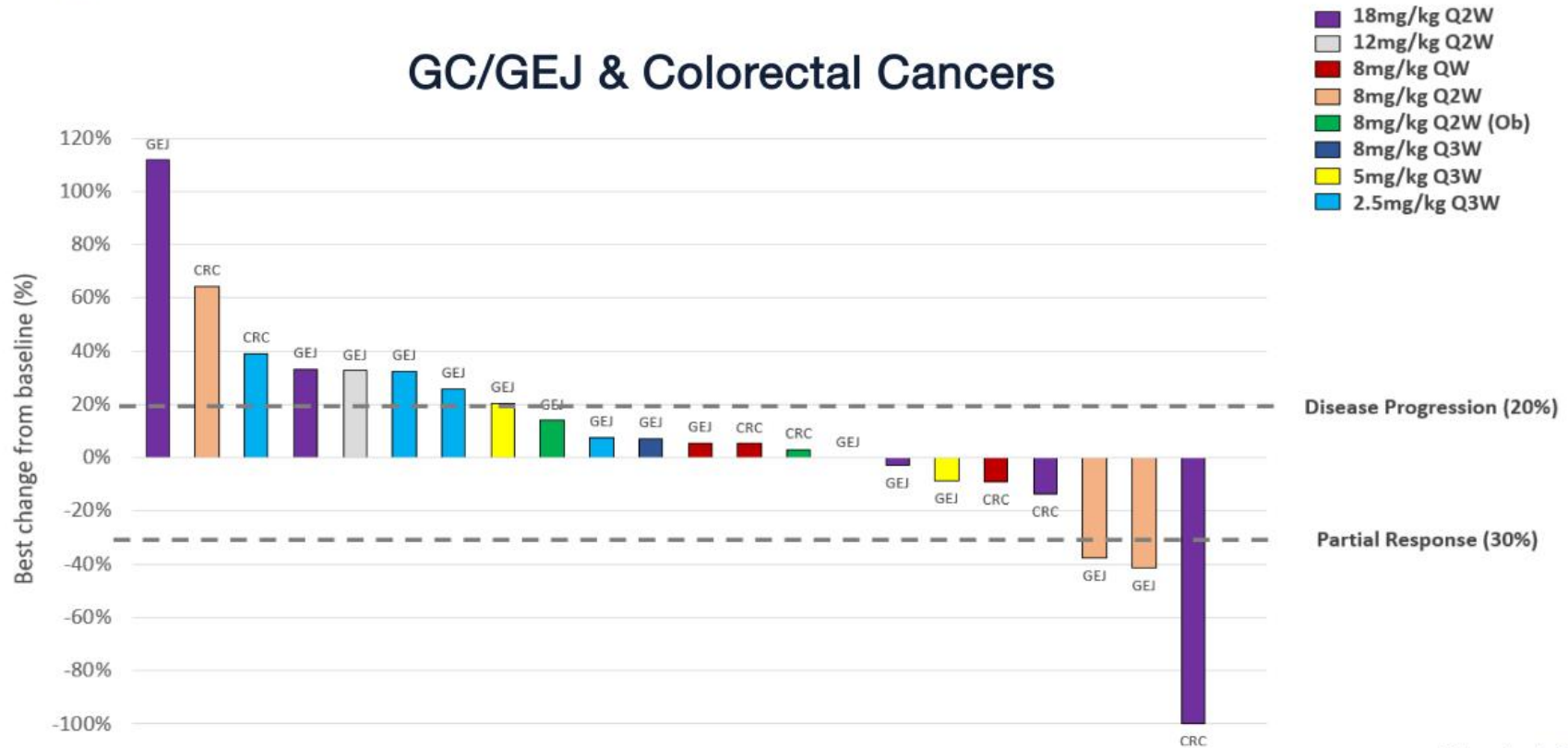
Characteristic	n (%)
Age, Median (range)	63 (24–92)
Gender	
F	46 (59%)
M	32 (41%)
ECOG PS	
0	19 (24%)
1	59 (76%)
Prior Therapy Lines	
1	11 (14%)
2	10 (13%)
3	16 (21%)
4	12 (15%)
5+	29 (37%)
Median # of anti-HER2 Tx	
Breast	6
Gastric	2

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

GC/GEJ & Colorectal Cancers



Data cut-off: 25-Feb-21

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

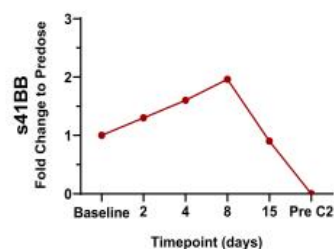
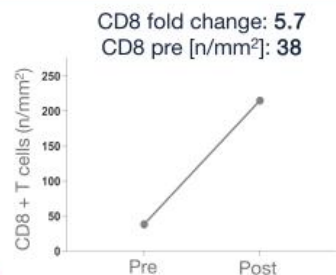
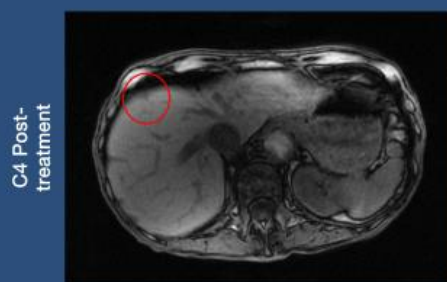
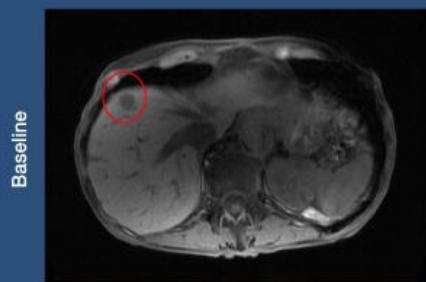
Patient Profile, Treatment History and Treatment Outcome

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)

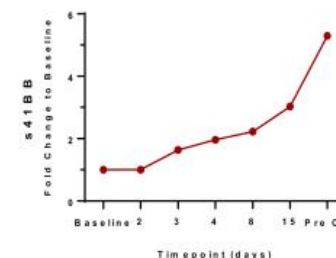
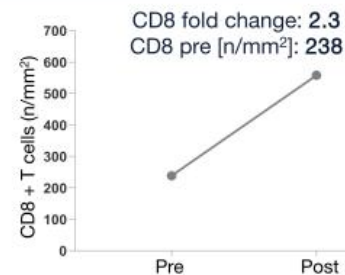


Rectal Cancer Patient with Complete Response

- 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



Case Study: PR in Cancer of Unknown Primary

Patient Profile, Treatment History and Treatment Outcome

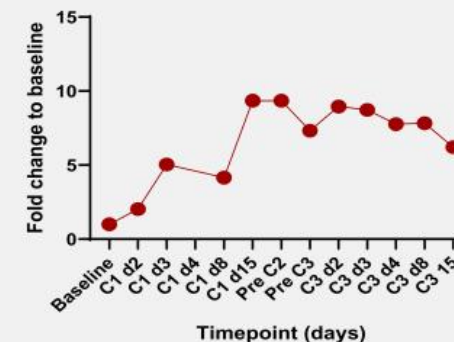
Patient Profile

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	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

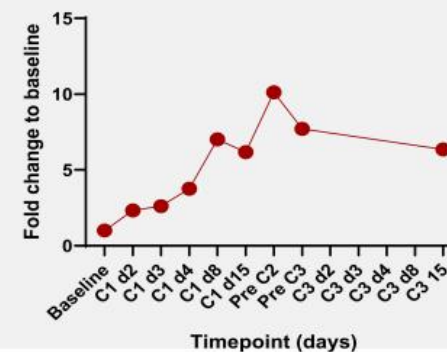
Patient Profile

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	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

Paclitaxel – Chemotherapy

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

Ramucirumab – Anti-Angiogenic¹⁻³

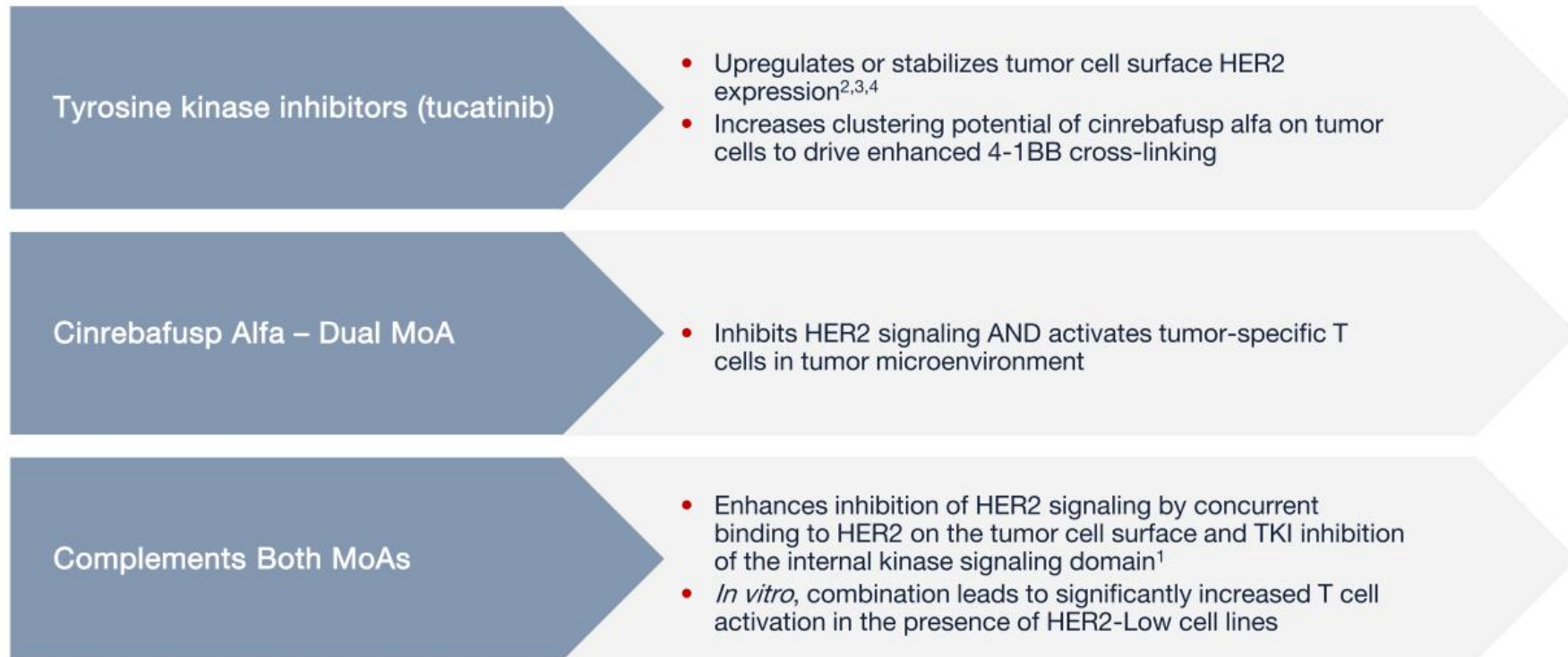
- Normalizes vascularization
- Alters tumor barrier to T cell penetration
- Reduces Tregs & inhibits TAMs

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

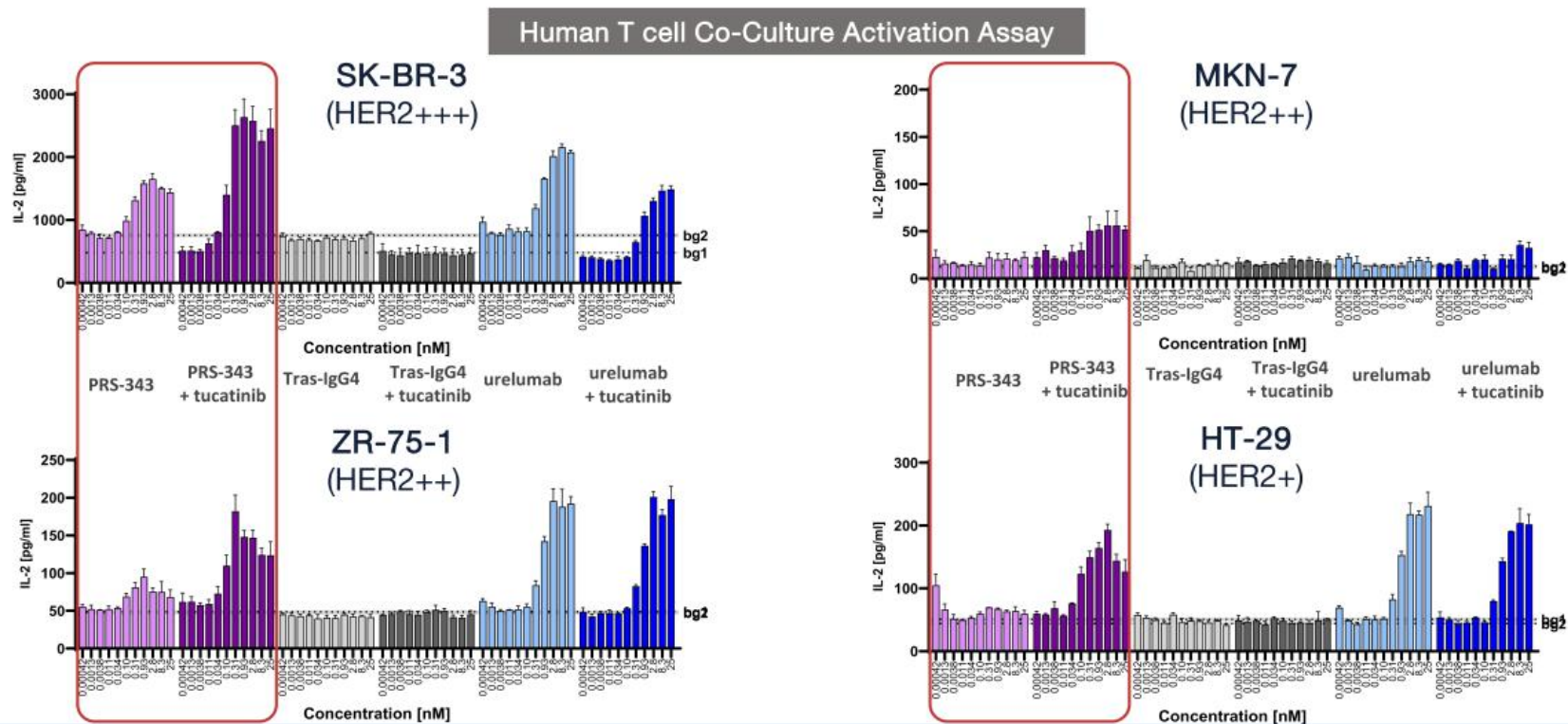
1 - Allen et al., Science Translational Medicine 2017
2 - Juang et al., Front Immunology 2018
3 - Tada et al., Journal for Immunotherapy of Cancer 2018

Scientific Rationale for Combining Cinrebafusp Alfa & Tucatinib



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

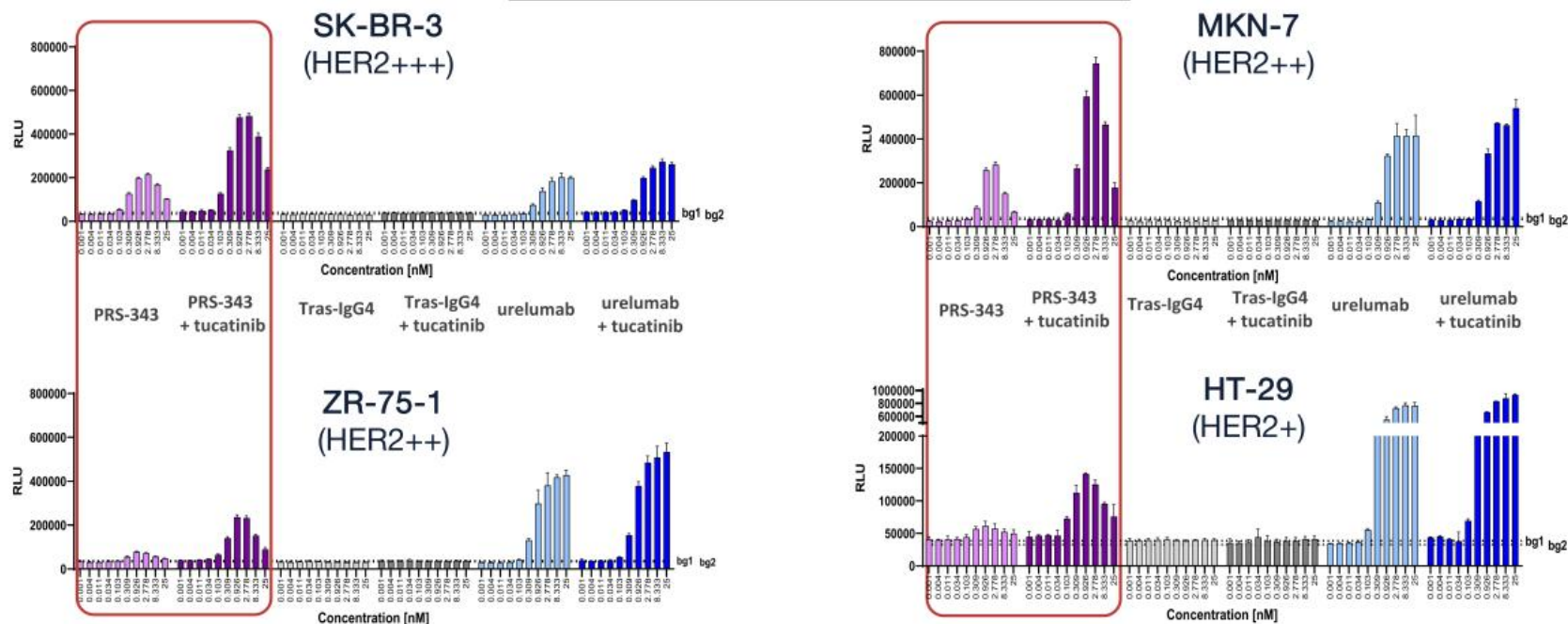
Cinrebafusp Alfa and Tucatinib Combination Enhances T cell Activation



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

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