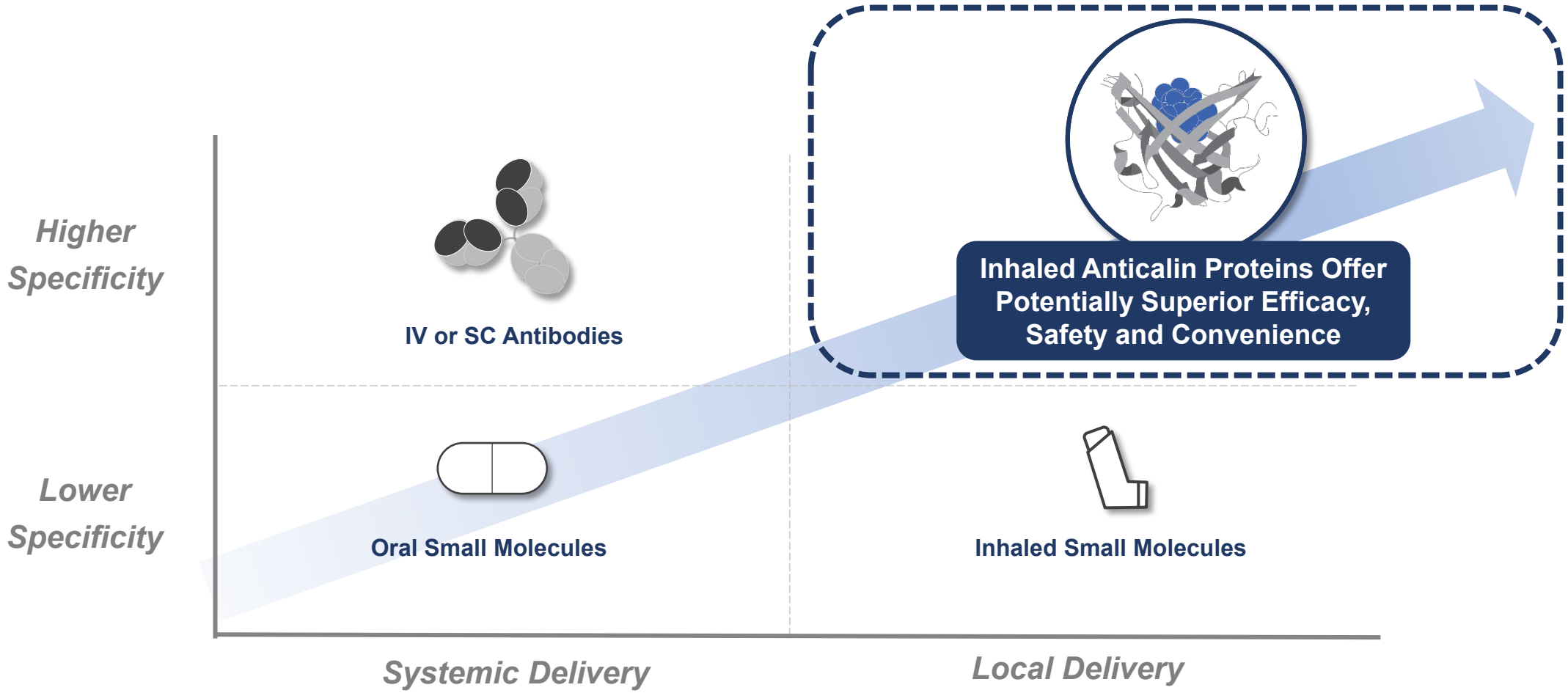
PIERIS PHARMACEUTICALS

CORPORATE PRESENTATION
June 2023

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, our expected cash runway, our product candidates' clinical and therapeutic potential in their intended indications; the receipt of royalty and/or milestone payments provided for in our collaboration agreements; 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, achieving other milestones related to our programs, including elarekibep, PRS-220, PRS-400, PRS-344/S095012, PRS-346/SGN-BB228 and PRS-342/BOS-342, or reporting on partnering or other strategic opportunities for cinrebafusp alfa; our continued progress in the areas of co-stim bispecifics and inhaled therapeutics; the therapeutic potential and safety profile of our Anticalin platform; the unmet need and potential addressable market for our product candidates, the potential advantages of our product candidates over those of existing therapeutics and/or those of our competitors, and the advancement of and funding for our developmental programs generally. 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, including through partnering transactions, 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, including in collaboration with other parties; 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; the fact that data and results from preclinical and clinical studies may not necessarily be indicative of future results; 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 or geo-political issues, including the conflict in Ukraine; 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 (SEC) available at www.sec.gov, including without limitation the Company's most recent Annual Report on Form 10-K, the Company’s subsequent Quarterly Reports on Form 10-Q and the Company's other filings from time to time with the SEC.

Inhaled Administration of Biologics Would Address Many Limitations of Currently Approved Respiratory Therapeutics



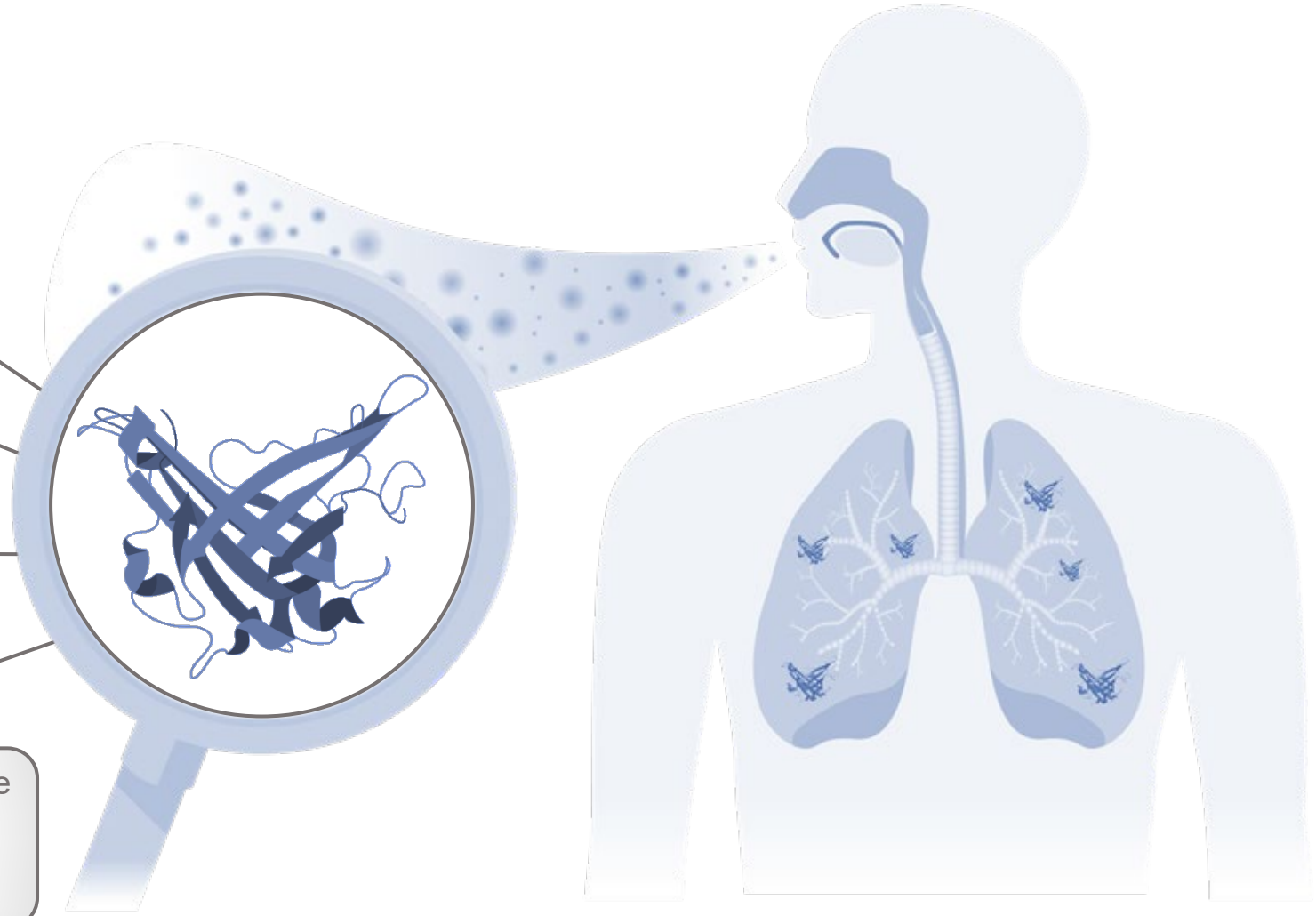
Anticalin Proteins are Well Suited for Inhaled Administration

Scaffold derived from ***human lipocalins*** (extracellular binding proteins endogenous to the lung)

Very ***low predicted immunogenicity*** risk

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 regimes***



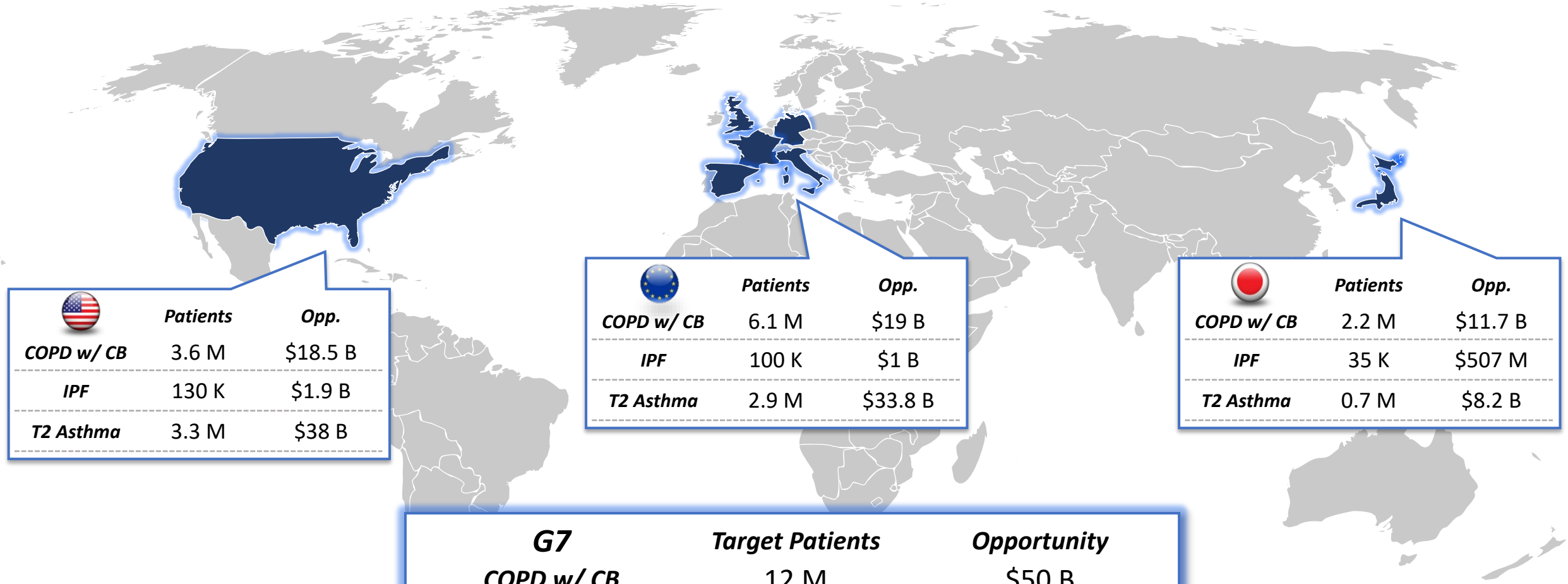
Pieris Has a Diversified Inhaled Respiratory Pipeline

Program	Target	Indication	Discovery	Preclinical	Phase 1	Phase 2	Partner
Elarekibep* (PRS-060/AZD1402)	IL4Rα	Asthma	Phase 2a fully sponsored by AZ; co-dev option				AstraZeneca
PRS-220	CTGF	IPF#	>50% grant-funded‡				*Proprietary*
PRS-400	Jagged-1	COPD-CB◊					*Proprietary*
AstraZeneca*	n.d.	n.d.					AstraZeneca

** Pieris has separate co-development options on both programs and U.S. co-commercialization options on elarekibep*
 # Idiopathic pulmonary fibrosis ("IPF") and other forms of fibrotic lung diseases
‡ ~$17 million grant from the Bavarian government expected to cover more than half of phase 1 development costs
◊COPD-CB - chronic obstructive pulmonary disease with chronic bronchitis

Clinical-stage pipeline with potential to transform the treatment paradigm of respiratory diseases

Pieris' Respiratory Portfolio Targets Large Opportunity Indications in Both Primary and Specialty Markets



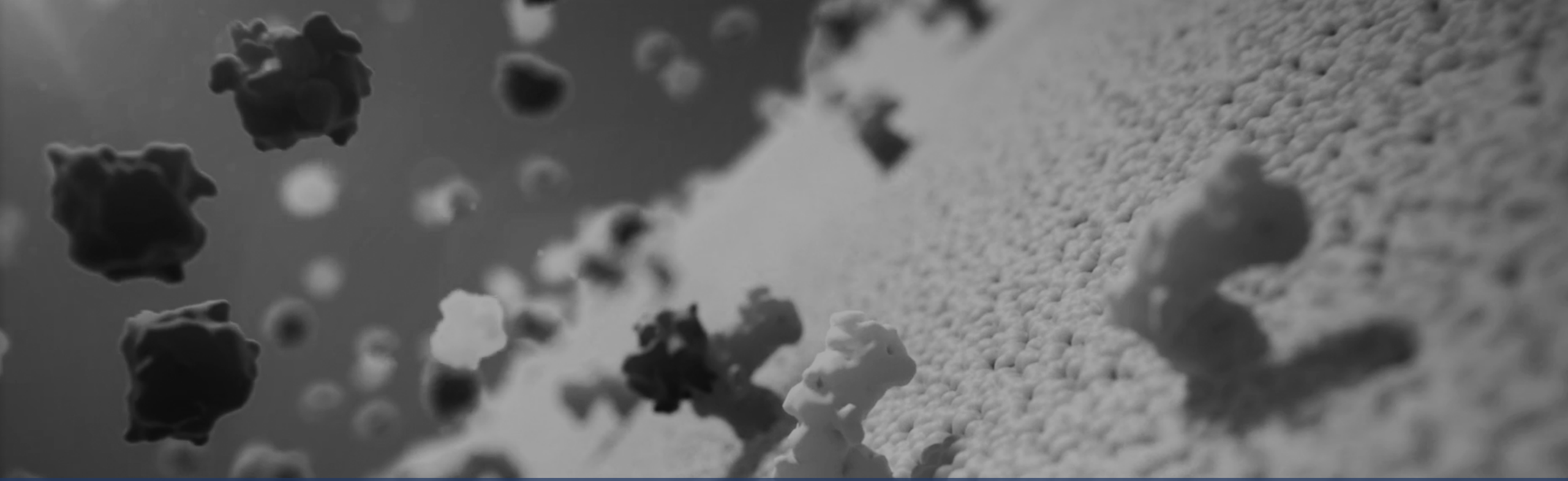
	Patients	Opp.
COPD w/ CB	3.6 M	$18.5 B
IPF	130 K	$1.9 B
T2 Asthma	3.3 M	$38 B

	Patients	Opp.
COPD w/ CB	6.1 M	$19 B
IPF	100 K	$1 B
T2 Asthma	2.9 M	$33.8 B

	Patients	Opp.
COPD w/ CB	2.2 M	$11.7 B
IPF	35 K	$507 M
T2 Asthma	0.7 M	$8.2 B

G7	Target Patients	Opportunity
COPD w/ CB	12 M	$50 B
IPF	265 K	$3.5 B
T2 Asthma	6.9 M	$80 B

Commercial opportunity represents total patients and average biologic price per Artisan analysis. No market share assumptions are factored into opportunity calculations

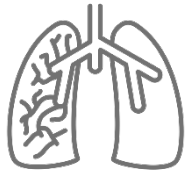


Elarekibep (PRS-060/AZD1402)
Inhaled IL4Ra Antagonist

IL-4Ra is a Well Validated Target in T2 Asthma and COPD

Despite their high impact in patients, injectable mAbs have penetrated just a small percentage of the immense, addressable patient population

IL4Ra is…

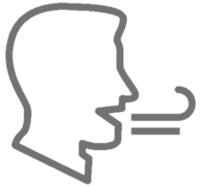


…a local driver of disease

IL-4 & IL-13 signaling of IL4Ra causes mucus hypersecretion, airway smooth muscle contraction, and epithelial inflammation

…a clinically validated intervention point

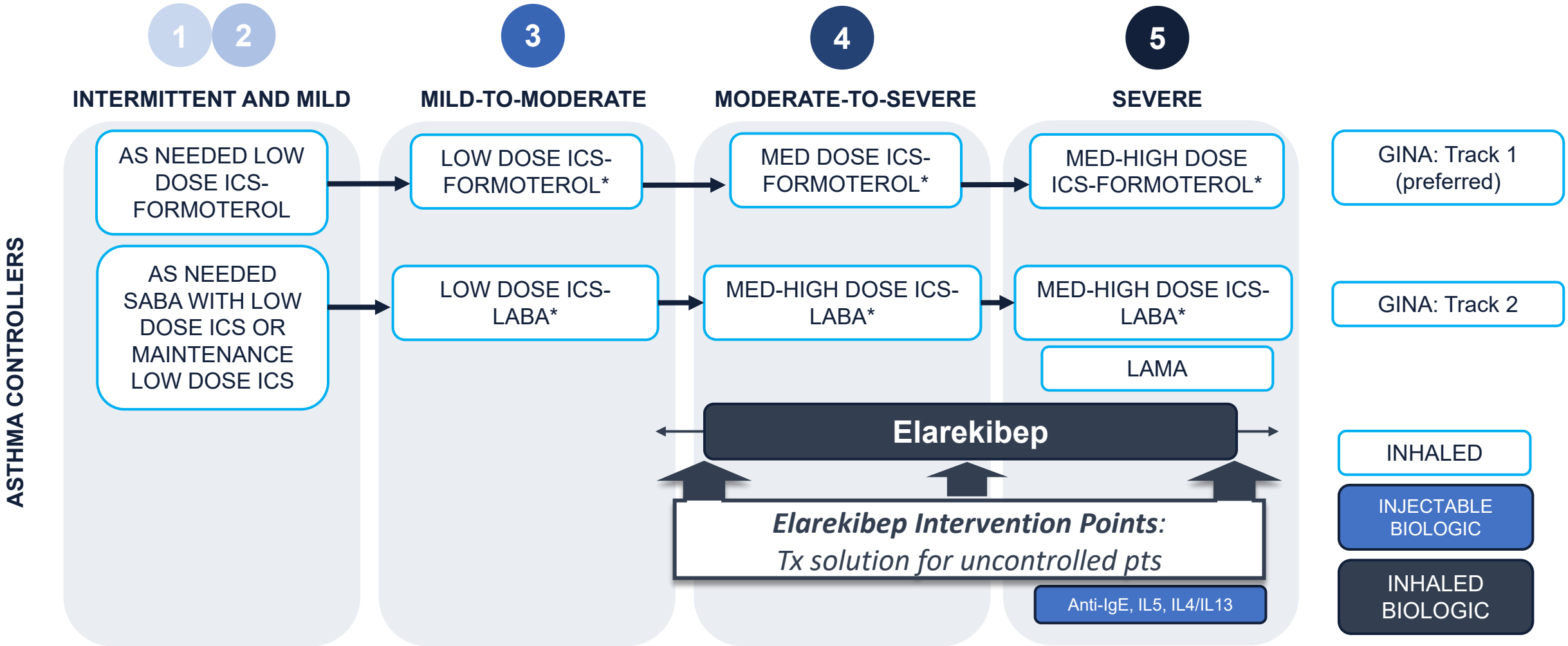
Injectable dupilumab improves symptoms, function and exacerbation control in T2 asthma and COPD



… an attractive opportunity to target locally

An inhaled IL4Ra antagonist offers a more convenient and efficient option than injectable biologics

Elarekibep Could Significantly Expand the Biologic-Eligible Population To Include Those Not Well Controlled by ICS/LABA

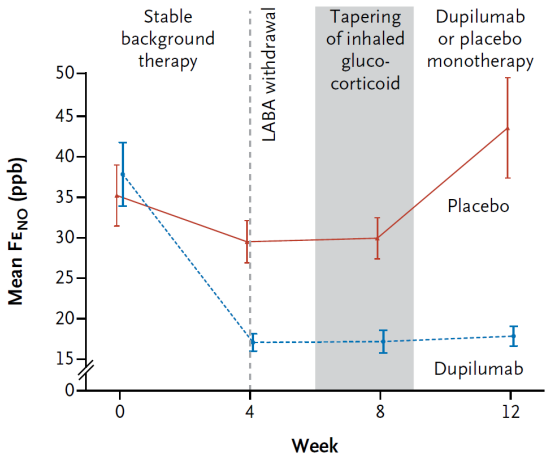


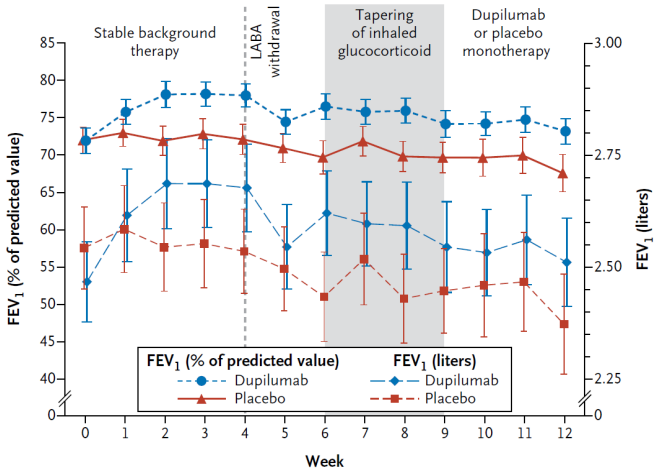
ICS = Inhaled corticosteroids
SABA= Short-acting β2 adrenergic receptor agonists
LABA = Long-acting β2 adrenergic receptor agonists
LAMA = Long-acting muscarinic antagonists

Global Initiative for Asthma (GINA) Steps (2021)

FeNO Reduction is a Biomarker Predictive of Lung Function Improvement

PoC Studies with dupilumab*

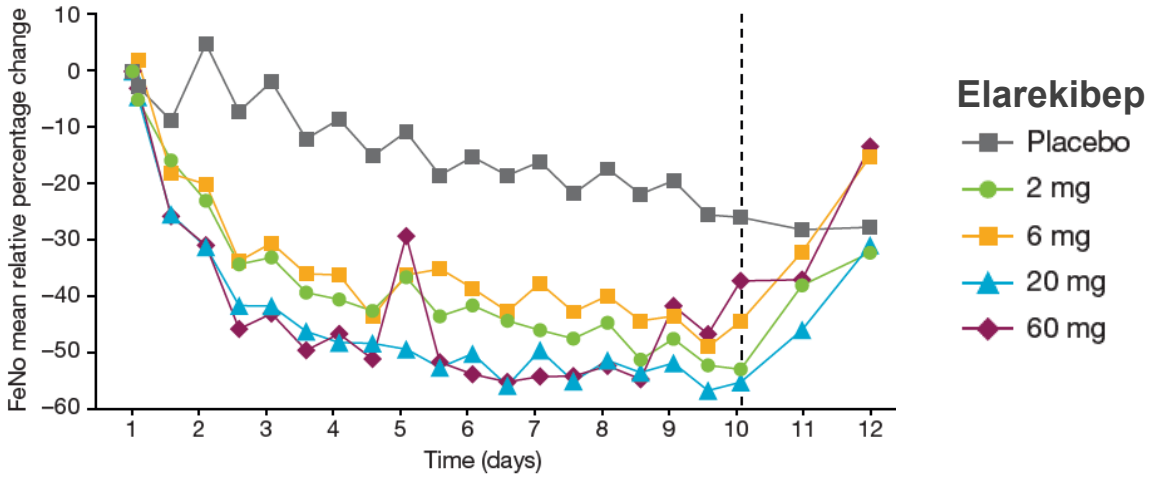




Markedly decreased FeNO at week 4

Significant increase in % of predicted FEV1 and actual FEV1 at weeks 2 & 12

Ph1b Study with elarekibep**



In a Ph1b study in FeNO-elevated, mild asthmatics, elarekibep significantly reduced FeNO over a 10-day period

* Correlation of FeNO with FEV1 at Week 12: r=-0.408 P=0.009, Wenzel N Engl J med 2013

** nebulized doses of elarekibep

Phase 2a Elarekibep Study is Evaluating FEV1 Improvement at Four Weeks in Uncontrolled T2 Asthmatics

Part 1 (Safety)	**Participant Population:** Moderate asthmatics controlled on ICS/LABA **Primary Endpoint:** Safety and tolerability compared to placebo from baseline until follow-up (approximately 56 days) **Doses:** 1 mg, 3 mg, 10 mg
Part 2 (Efficacy)	**Participant Population:** Asthmatics uncontrolled on moderate or high dose ICS/LABA with blood EO count of ≥ 150 cells/μL and FeNO ≥ 25 ppb at screening **Primary Endpoint:** Improvement of FEV1 at four weeks relative to placebo **Dose:** 3 mg (enrolling)

Efficacy readout expected mid-2024

All doses passed safety review

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

Study is sponsored, conducted, and funded by AstraZeneca

Safety Review Included:

- ☑ Incidence of adverse events
- ☑ Changes in laboratory markers
- ☑ Forced expiratory volume in 1 second (FEV1)
- ☑ Pharmacokinetics

Enables doses up to 10 mg dpi to be evaluated in future clinical studies

Co-Development Options for Elarekibep Enable Increased Economic Benefit to Pieris

PIRS Opt-in Decision Point

Phase 2a Primary Endpoint:
Improvement of FEV1 at 4 weeks relative to placebo

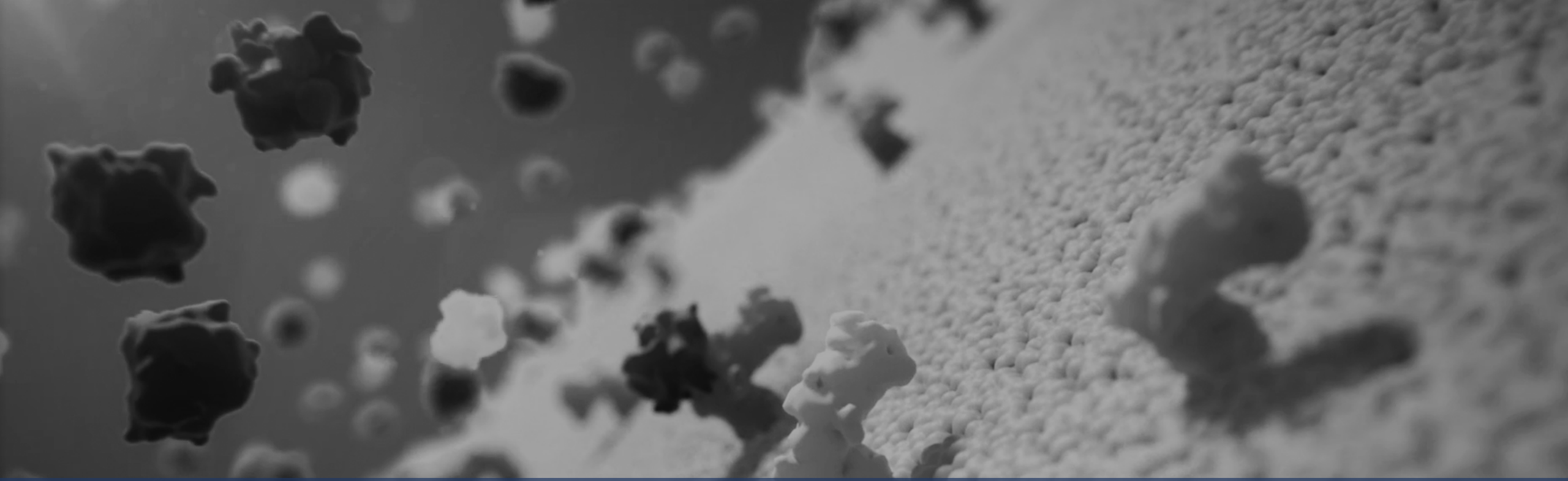
Co-Dev Option Requirements:
30-day opt-in period triggered upon both completion of Phase 2a trial and notice by AZ (must include product development plan & budget)

Two Opt-In Scenarios

Contractual Baseline (no cost sharing)
- Single digit up to mid-teen royalties for royalty term
- Same development milestones as 25% option; up to $1.9B in sales milestones

25% cost share with cost cap
- Single digit up to high-teen royalties for product lifetime
- Development milestones approximating 50% of development costs
- Potential $3.5B+ in sales milestones

50% cost share without cost cap
- Gross margin share percentage in mid-twenties for the product lifetime
- Development milestones approximating two-thirds of 25% option



PRS-220
Inhaled CTGF Antagonist

IPF is an Orphan Indication with Significant Unmet Need

3 to 5 years

– Median survival from the time of diagnosis
– Increasing prevalence as population ages

Only nintedanib & pirfenidone currently approved as standard of care; convey modest benefit with significant side effects. No new therapeutics have been approved since 2014

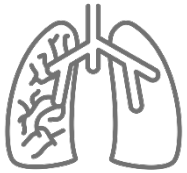
>$4B

– Current market sales of approved therapies
– High overall cost burden on the healthcare system

CTGF Is an Important Driver of Lung Fibrosis and a Clinically Validated Target in IPF

Despite clinical validation of CTGF antagonism, inefficiencies of pulmonary target engagement with injectable mAb leave significant room for improvement

CTGF is…



…a Key Driver of Fibrotic Lung Remodeling

CTGF increased in IPF lung tissue, regulates fibrotic remodeling

…a Clinically Validated Intervention Point

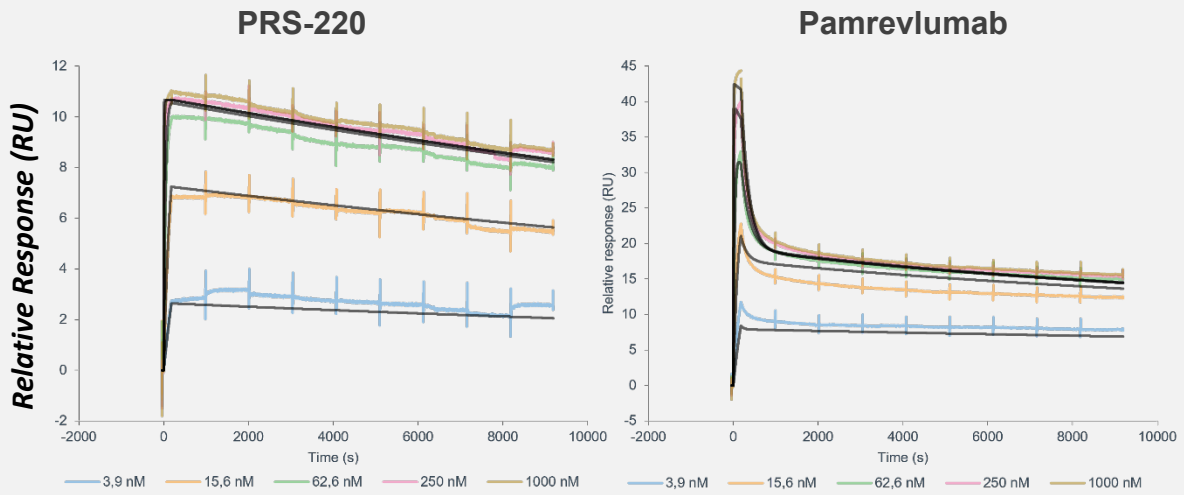
Pamrevlumab's Ph2 results provide clinical POC

…Potentially More Effective Targeted Locally

CTGF needs to be targeted directly in the lung to block pro-fibrotic function

Inhaled PRS-220 Has a Higher Affinity for CTGF Than Pamrevlumab and Is Well Suited for Inhaled Delivery

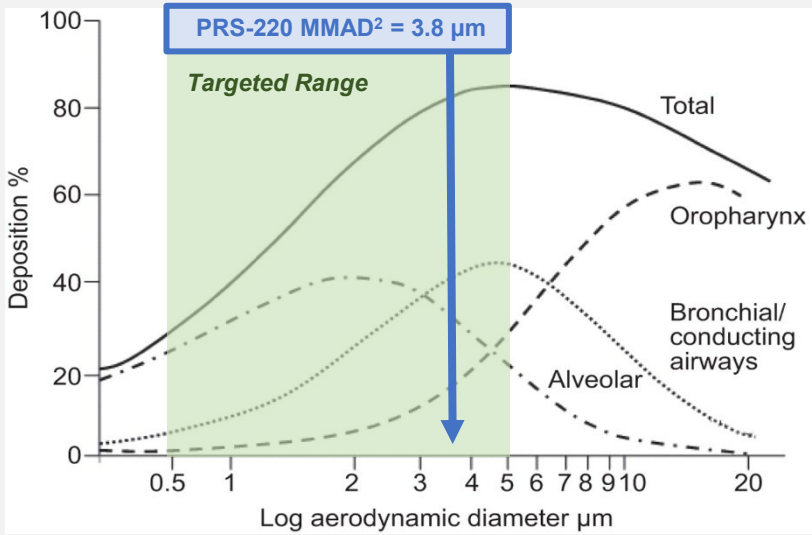
Superior Profile of PRS-220 Binding to CTGF Compared to Pamrevlumab Demonstrated by SPR[1]:



PRS-220 has Prolonged CTGF Binding through Slower Dissociation Rate

Desired Aerosol Performance for PRS-220:

Aerosol particles < 5 µm (fine particle fraction) have greatest potential for deposition in the lung



(adapted from Laube, European Respiratory Journal, 2011)

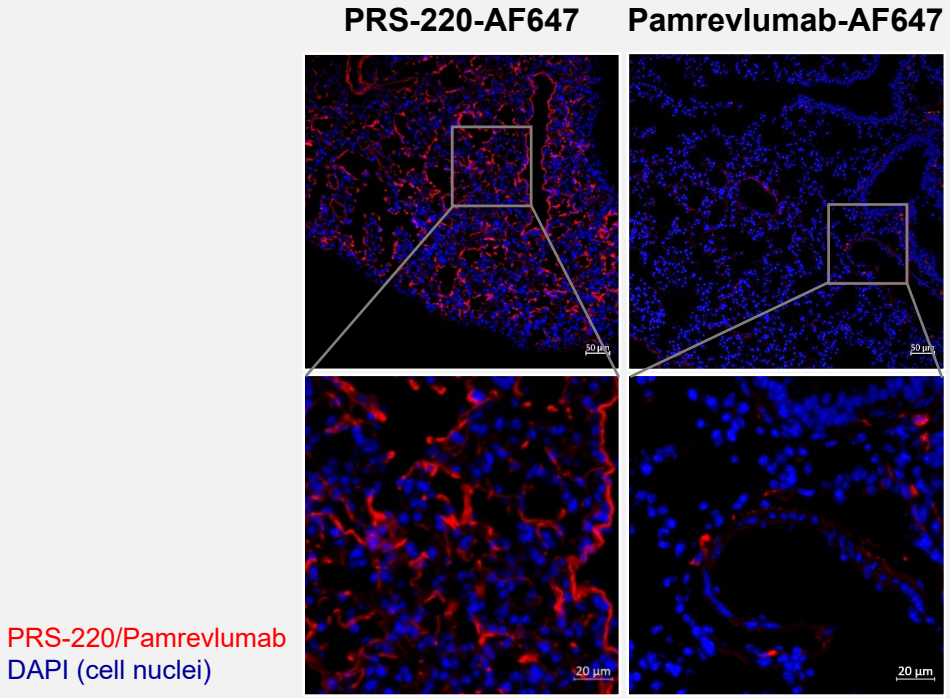
PRS-220 Aerodynamic Properties and Optimal Size Allow for Effective Lung Deposition

[1]SPR = Surface Plasmon Resonance

[2]MMAD = Mass Median Aerodynamic Diameter

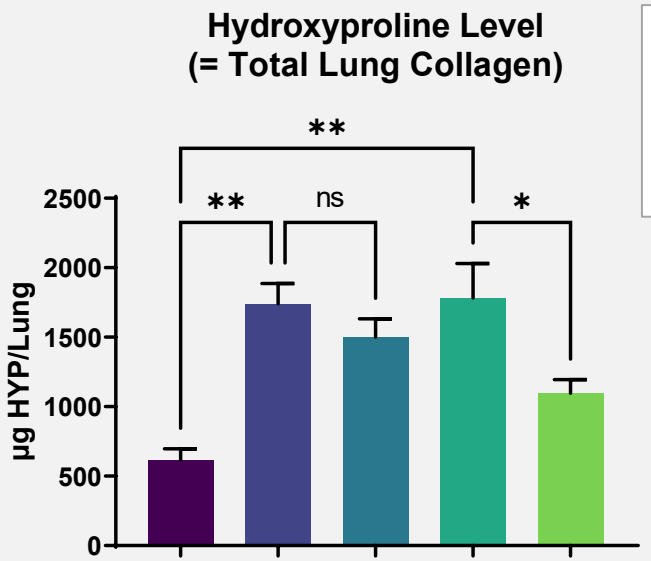
Inhaled PRS-220 Has Both Superior Lung Biodistribution and Anti-Fibrotic *in vivo* Activity Compared to Systemically Administered Pamrevlumab

Lung Imaging of Single Dosing of PRS-220 Delivered by OA[1] vs. Pamrevlumab Delivered by IV[2] in Healthy Mice:



PRS-220 Provides Significantly Greater Exposure and Lung Penetration Compared to Systemically Delivered Antibody

In Vivo Efficacy of Inhaled PRS-220 in Silica-Induced Lung Fibrosis Mouse Model:



Inhaled PRS-220 Shows Significant Reduction of Collagen Deposition in the Lung Compared to Systemically Administered Pamrevlumab

[1]Oropharyngeal Aspiration
[2]Intravenous Delivery

PRS-220 Has Potential to be Best-in-Class CTGF Inhibitor

Pamrevlumab's positive Ph2 data (PRAISE trial) provided strong clinical precedent for CTGF. However, PRS-220 is expected to block CTGF more efficiently and offer superior convenience compared to systemically administered pamrevlumab

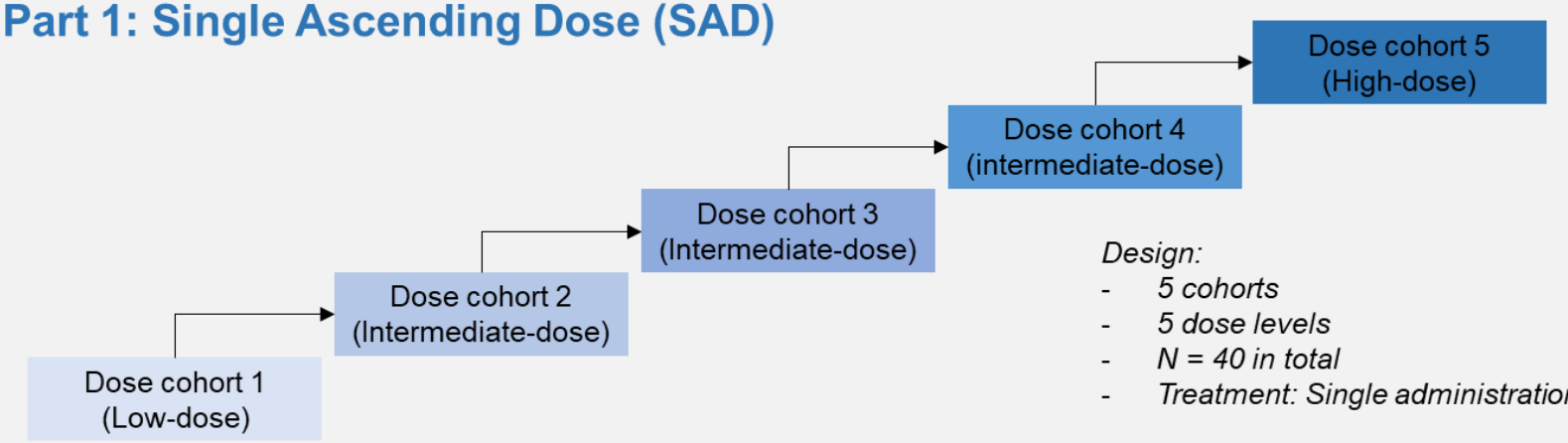
	PRS-220	Pamrevlumab
CTGF Target Engagement	✓	✓
Superior Potency[1]	✓	✗
Higher Lung Exposure[1]	✓	✗
Avoidance of Systemic Target Sink	✓	✗
Convenient Route of Administration	✓	✗
Combinability w/ SoC	✓	✗

1. Based on preclinical models

PRS-220 Phase 1 Study Ongoing; Data Expected 2H 2023

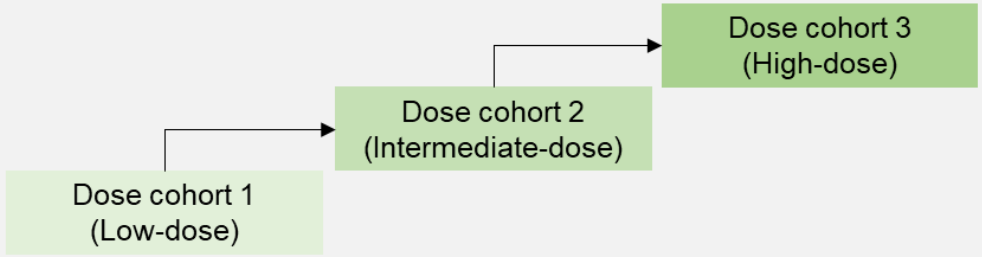
Study of single and multiple doses of PRS-220 administered by oral inhalation in healthy subjects

Part 1: Single Ascending Dose (SAD)

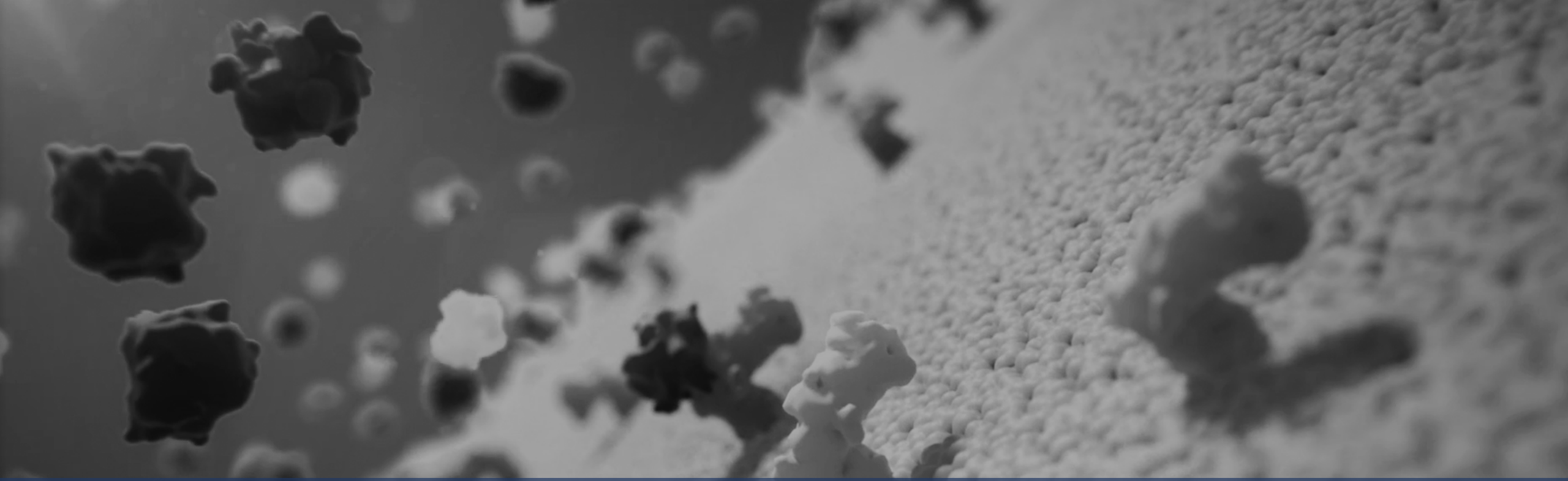


Design:
- *5 cohorts*
- *5 dose levels*
- *N = 40 in total*
- *Treatment: Single administration*

Part 2: Multiple Ascending Dose (MAD)

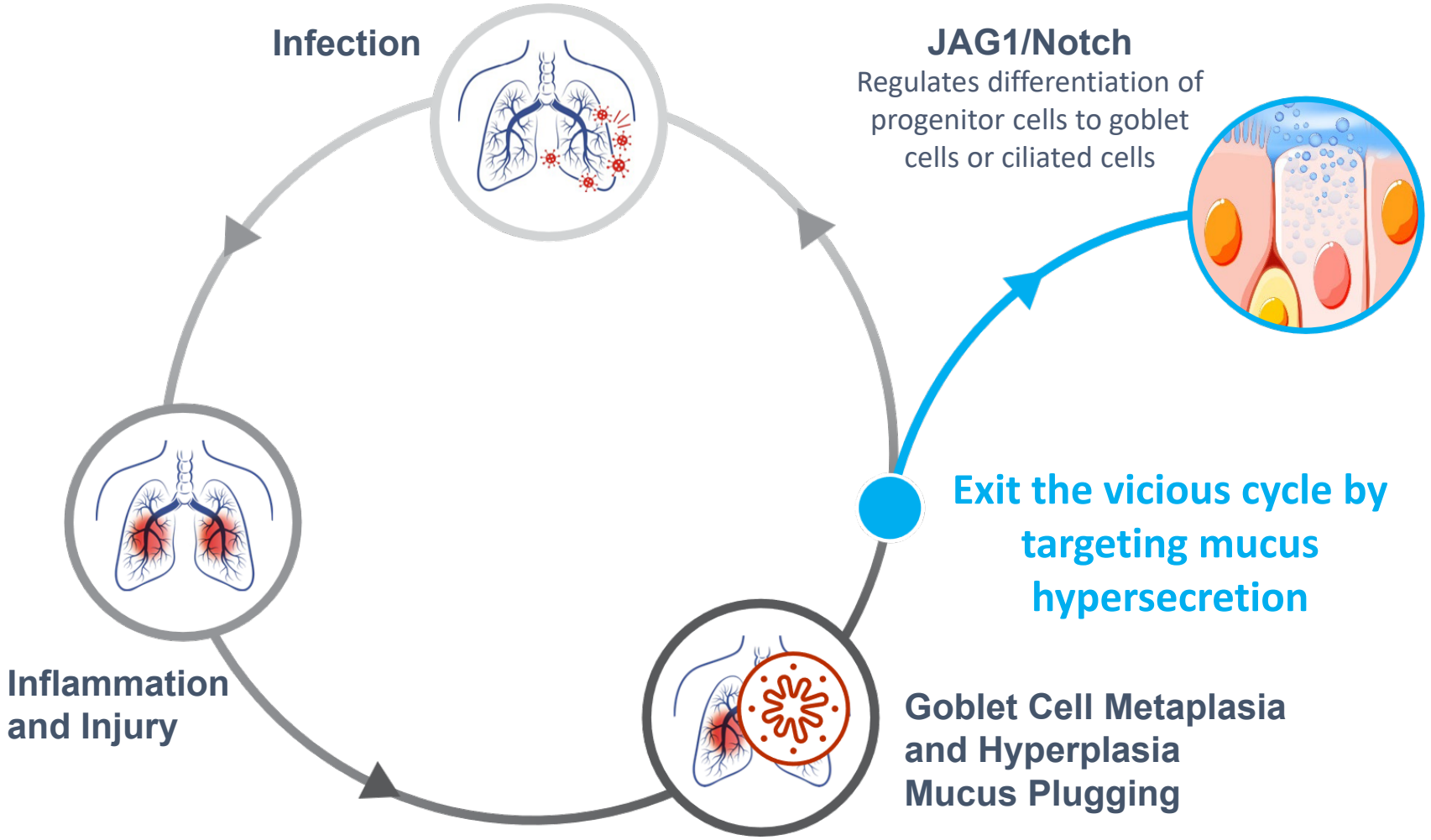


Design:
- *3 cohorts*
- *3 dose levels*
- *N = 24 in total*
- *Treatment duration: 28 days*



PRS-400
Inhaled Jagged-1 Antagonist

PRS-400 Designed to Disrupt Master Regulator of Mucus Production, Regardless of Insult



Mucus Hypersecretion is Pathogenic to Muco-obstructive Lung Diseases

Why inhaled route of administration may be necessary:

- The Jagged-1/Notch signaling pathway has fundamental roles in multiple other organs and a systemically administered intervention may have undesirable side effects.
- Low systemic bioavailability of antagonist avoids undesired disruption of Notch signaling throughout the body.

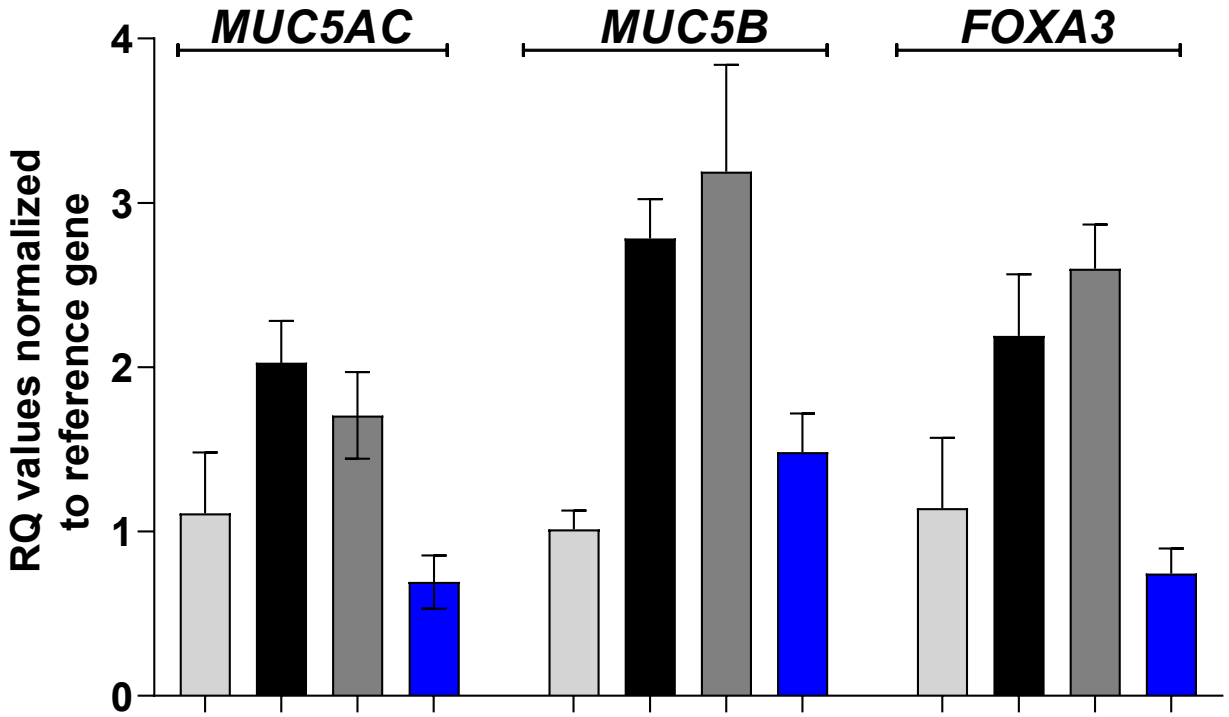
Wide range of muco-obstructive diseases are potentially addressable by PRS-400:

Both chronic and acute disease caused by Goblet Cell Metaplasia and Hyperplasia are potentially addressable by PRS-400, including:

COPD-CB	NCFB	CF	Asthma	PCD	CRS
Large global prevalence and high burden of disease; many patients remain symptomatic despite SOC treatment	*Growing prevalence with limited treatment options*	*Rare disease with high unmet need in patients unresponsive to or ineligible for CFTR modulators*	*Large global prevalence and unmet need for patients with ICS/OCS resistance and high mucus burden*	*Rare disease with no disease-modifying therapies*	*Few treatment options available, particularly for patients without nasal polyps*

COPD-CB = Chronic Obstructive Pulmonary Disorder with Chronic Bronchitis, NCFB = Non-CF Bronchiectasis, CF = Cystic Fibrosis, PCD = Primary Ciliary Dyskinesia, CRS = Chronic Rhinosinusitis

PRS-400 Prevents Cytokine-induced Goblet Cell Metaplasia and Mucus Hypersecretion *Ex Vivo* (Air Liquid Interface Cultures)

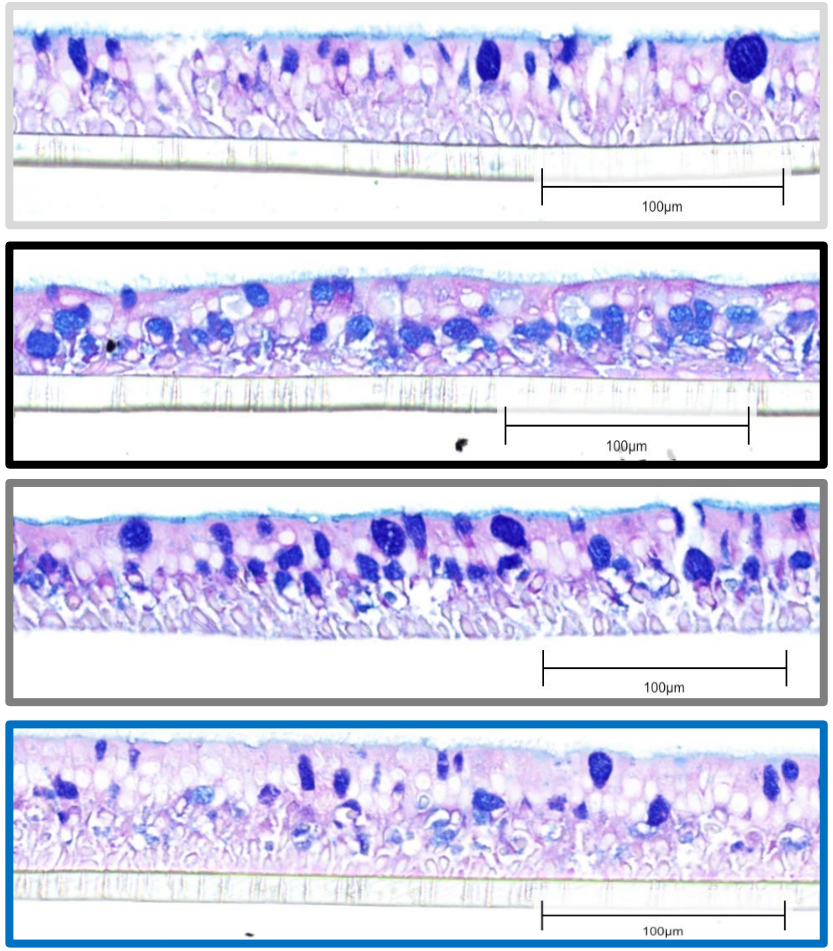


Un-challenged

huIL-17A-challenged

Anticalin control

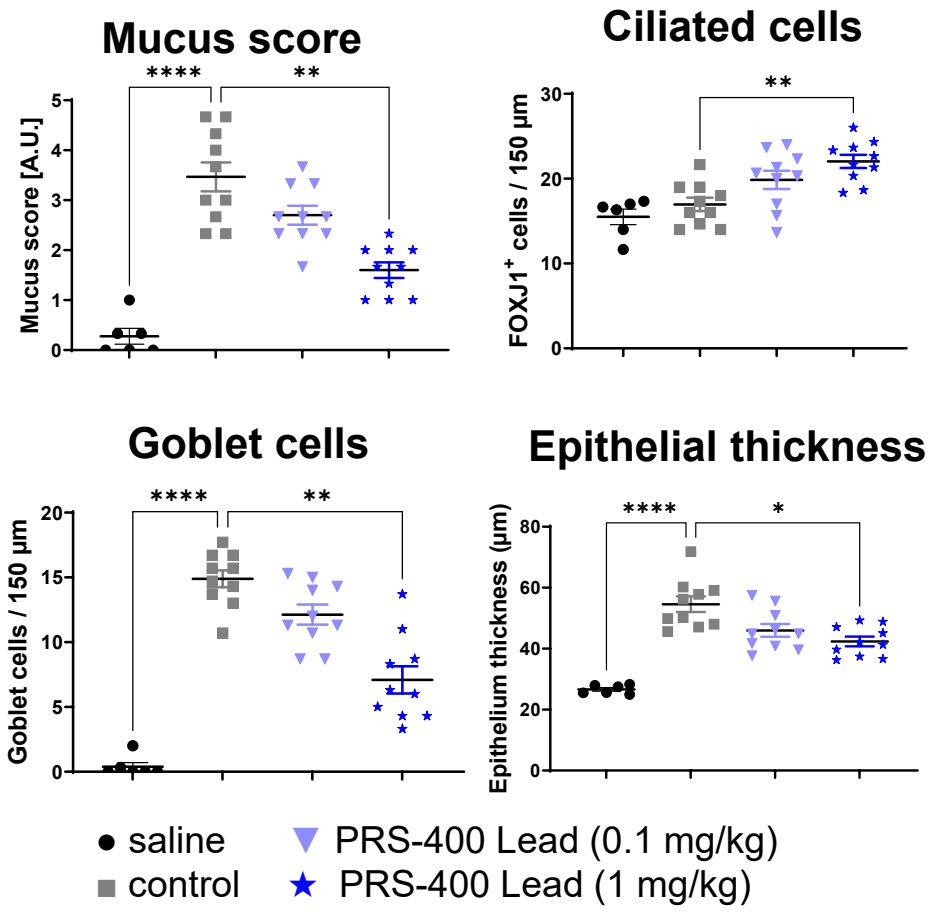
PRS-400 Lead



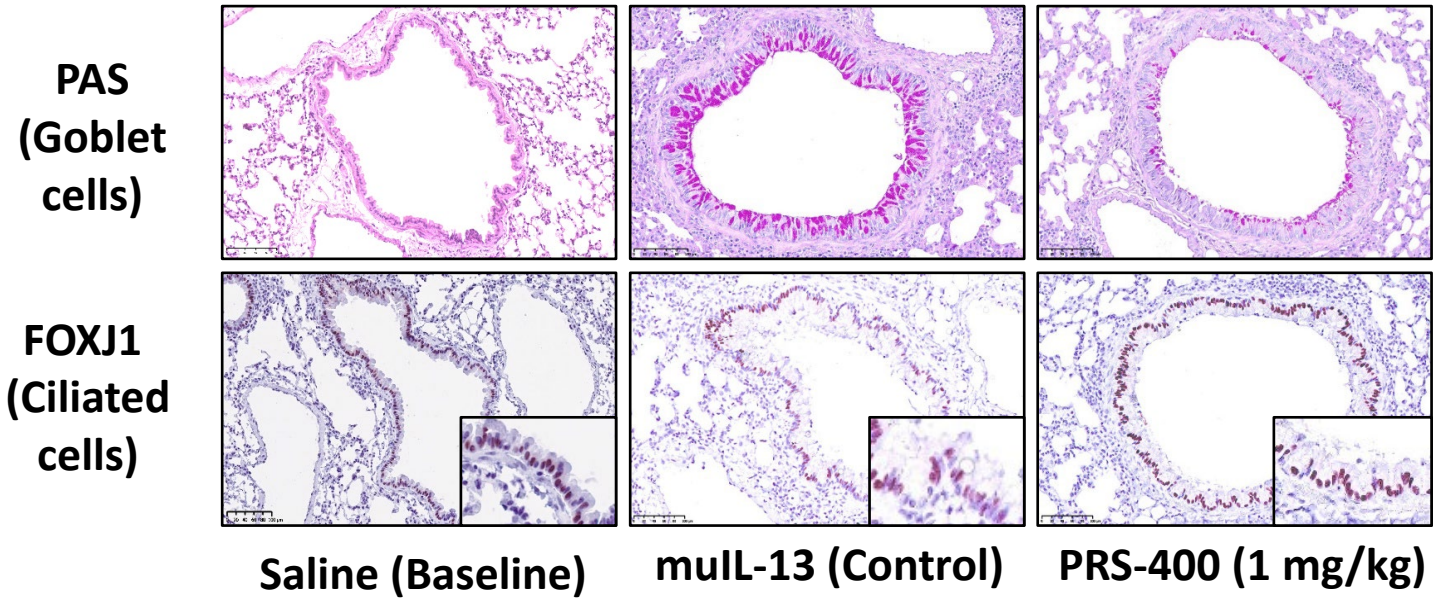
AB-PAS staining

PRS-400 lead candidate reduces the number of goblet cells (purple, mucus-filled cells – images at right) and mucin gene expression in IL-17A-stimulated ALI cultures (shown on graphs above).

PRS-400 Dose-dependently Reverses Goblet Cell Metaplasia and Mucus Hypersecretion *In Vivo*



non-parametric Kruskal-Wallis followed by Dunn's Multiple comparison test.
* p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001, **** p ≤ 0.0001



- **Lead candidate significantly reduces mucus score, goblet cell numbers and epithelial thickness, as well as increases the number of ciliated cells**
- **Results establish proof of mechanism for lead candidate in muco-obstructive disease, where mucus is pathogenic**

In Comparison to Competitors, Potential for PRS-400 to Have Disease- Modifying Impact With Reduced Systemic Toxicity Risk

	PRS-400 Inhaled Jagged-1 Inhibitor	**AMG 430** Systemic Anti-Jagged-1 Antibody	**MUC5AC Targeted Inhaled RNAi / Antisense Oligonucleotides**
Reduces MUC5AC	✓	✓	✓
Normalizes MUC5B	✓	✓	✗
Disease Modifying *(Restoring Epithelial Homeostasis)*	✓	✓	✗
Reduces Systemic Toxicity Risk *(Jagged-1)*	✓	✗	**N/A**

Development Candidate Nomination in H2 2023

Financial Overview (as of 3/31/23)

$48.4M	$0.00	74.5M
Cash, Cash Equivalents & Investments	Debt	CSO

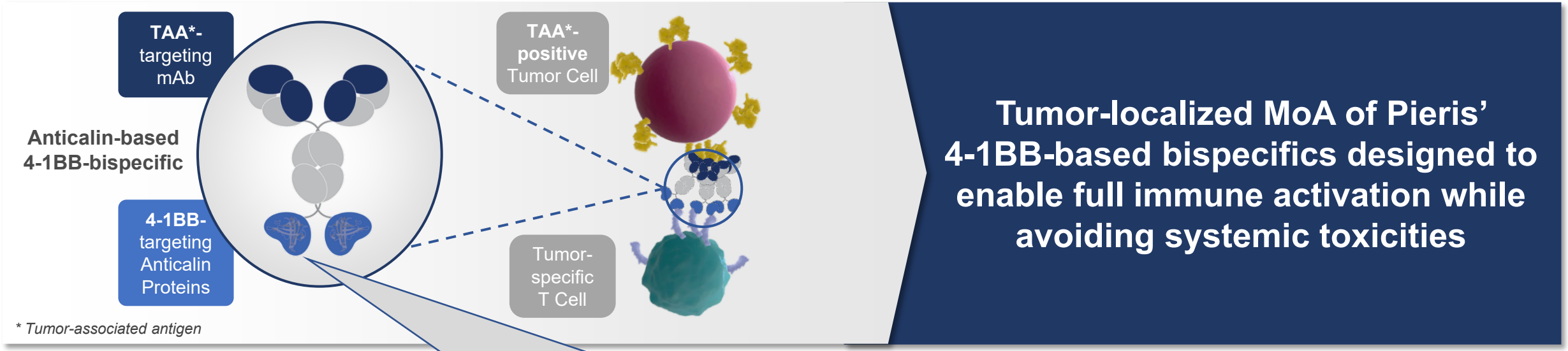
>$175M non-dilutive capital from partnerships since 2017

~$17M[1] grant announced in 2021

[1] *Calculated based on the June 25, 2021, noon buying rate of €1.00 to U.S. $1.1938*

Immuno-oncology

Anticalin Proteins are Also Well Suited to Build Mabcalin™ Bispecific Immune Agonists to Treat Cancer



Tumor-localized MoA of Pieris' 4-1BB-based bispecifics designed to enable full immune activation while avoiding systemic toxicities

- Monomeric, monovalent Anticalin proteins can be genetically fused to full-length mAbs → Mabcalin (antibody-Anticalin) proteins
- Several 4-1BB-engaging Mabcalin proteins have been manufactured under GMP for clinical development

Pieris' IO Bispecifics Pipeline is Driven by Partnerships and Offers Future Milestone and Royalty Upside

Program	Target	Indication	Discovery	Preclinical	Phase 1	Phase 2	Partner
cinrebafusp alfa*	4-1BB/HER2	HER2+ GC					
PRS-344/ S095012	4-1BB/PD-L1	n.d.	~50% co-dev cost share				SERVIER moved by you
PRS-346/ SGN-BB228	4-1BB/CD228	n.d.					Seagen
PRS-342/ BOS-342	4-1BB/GPC3	n.d.					BOSTON pharmaceuticals
SGN programs‡	n.d.	n.d.					Seagen

* *Announced stopping enrollment in 3Q22 due to strategic reasons, including focus on respiratory portfolio; spin-out and partnering discussions ongoing*

‡ *Two additional active bispecific programs in collaboration with Seagen, with Pieris retaining a U.S. co-promotion option in one of the programs in the collaboration*

Successful track record of partnering 4-1BB assets for value

225 Franklin Street
Boston, MA 02110
USA

Zeppelinstraße 3
85399 Hallbergmoos
Germany

Nasdaq: PIRS

IR: investors@pieris.com
BD: bd@pieris.com
www.pieris.com

SUPERIOR MEDICINES THROUGH EFFICIENT BIOLOGY