Anticalin® Technology for Innovative Protein Therapeutics in Respiratory Disease and Immuno-Oncology

July 21, 2020

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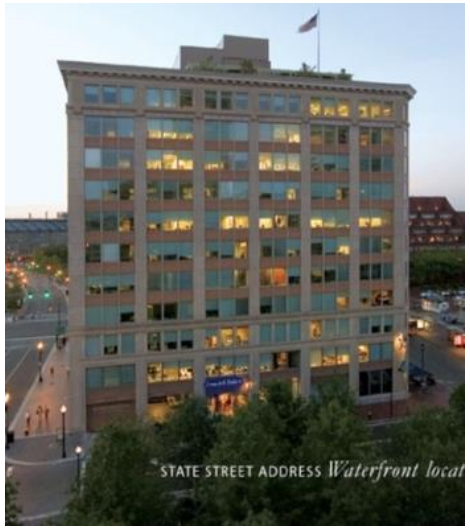
Pieris Pharmaceuticals

- **2001: Pieris is founded by Prof. Arne Skerra**
  - Anticalin technology
- **2014: Pieris Pharmaceuticals, Inc. goes public**
  - 2015: NASDAQ "PIRS"
- **2020: >100 employees across 2 sites**
  - Headquarters in Boston (MA), USA
    - Functions: Senior Management, Legal/IP, Clinical Operations and Quality Assurance
  - Research Hub in Hallbergmoos, Germany
    - Recently moved in from Freising
    - >9.000 m^2 office and lab space
    - Collaboration space available, biotech companies moving in 2020
    - Functions: Discovery, Technical Development, Pre-clinical, Translational as well as Finance, HR and IT

Pieris Pharmaceuticals GmbH
Hallbergmoos, Germany

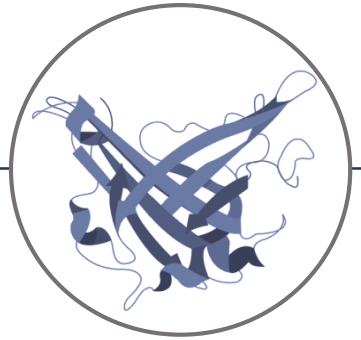


Pieris Pharmaceuticals Inc.
Boston, USA

Company Snapshot

Pipeline Highlights

- **PRS-060:** Inhaled IL4-Rα antagonist for moderate-to-severe asthma (partnered with AstraZeneca)
- **Next-generation respiratory:** Includes 4 discovery-stage inhaled therapeutics programs (2 proprietary, 2 partnered with AstraZeneca)
- **PRS-343:** 4-1BB/HER2 bispecific for solid tumors
- **PRS-344:** 4-1BB/PD-L1 bispecific (partnered with Servier)



Anchor Partnerships

- Validation through three anchor partnerships
- $120+M in upfront payments and milestones since January 2017
- Each partnership includes options for co-development & US-focused commercialization rights
- Value-driving opt-in for PRS-060 after phase 2a completion

Strong Partners • Significant Cash Flow • Retained Commercial Rights

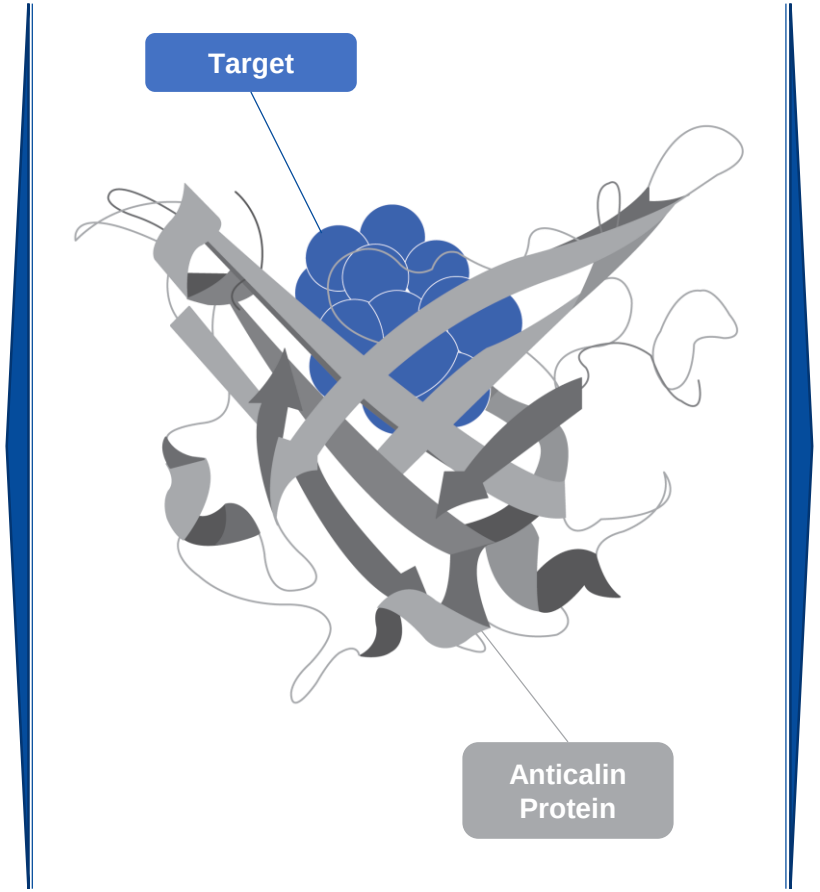
2020 Catalysts

- **Respiratory:**
  - ❑ PRS-060 phase 2a trial initiation
  - ❑ Data and rationale for advancement into IND-enabling studies for wholly-owned inhaled program
- **Immuno-Oncology:**
  - ❑ PRS-343 complete monotherapy and combination with atezolizumab phase 1 escalation data
  - ❑ PRS-343 initiation of 2nd line HER2+ gastric cancer PoC study, additive to SoC

The Anticalin® Protein Platform

A Novel Therapeutic Class with Favorable Drug-Like Properties

- **Human –** Derived from lipocalins (human extracellular binding proteins)
- **Small** – Monomeric, monovalent, small size (~18 kDa vs 150kDa mAbs)
- **Engineerable** binding pocket for robust target engagement
- **Stable** – Inhalable delivery
- **Simple** – Bi/multispecific constructs



Powerful Drug Discovery Platform

- Highly diverse libraries (>10^{11})
- Automated high-throughput screening
- Extensive protein engineering know-how

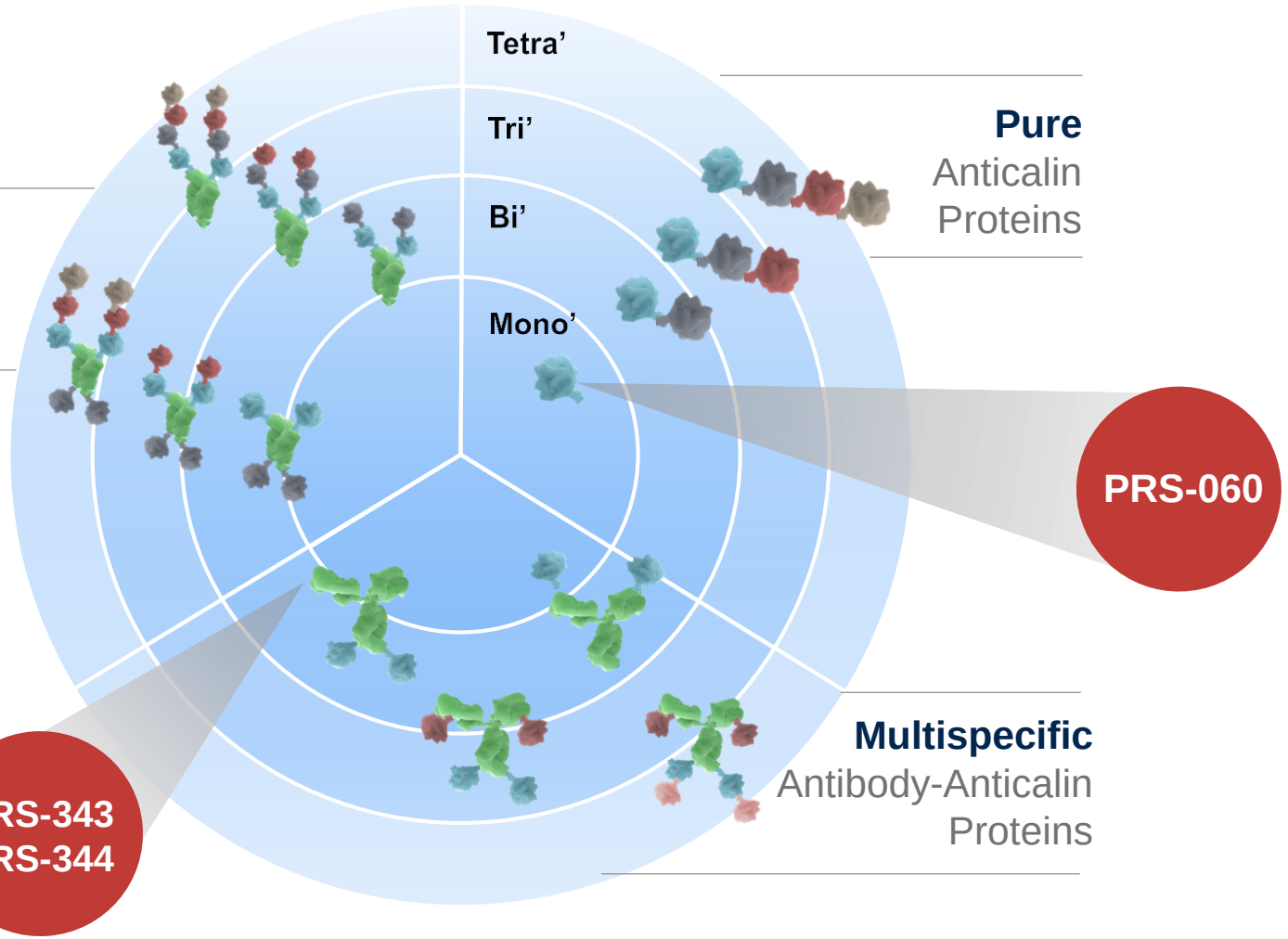
Translational Science Expertise to Deploy Platform in Meaningful Way

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

Key Value Driver:
Unique Formatting of Anticalin Protein-Based Drugs

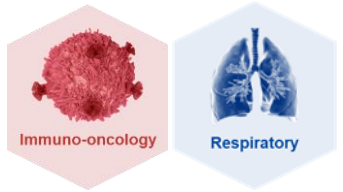
Building Blocks

- Anticalin Protein
- Antibody
- Fc



Potent Multi-Target Engagement • Novel Inhaled and Multispecific MoA • Favorable Drug-like Properties

Pipeline



RESPIRATORY							
CANDIDATE	**TARGETS**	**PARTNER**	**COMMERCIAL RIGHTS**	**DISCOVERY**	**PRECLINICAL**	**PHASE I**	**PHASE II**
PRS-060/AZD1402	IL4-Rα	AstraZeneca	Pieris Worldwide Profit-Share Option				
AstraZeneca Programs*	n.d.	AstraZeneca	Pieris Worldwide Profit-Share Option*				
Proprietary Programs	n.d.	n/a	Pieris Worldwide				
***4 additional respiratory programs (3 active, 1 forthcoming) in collaboration with AstraZeneca, 2 of which carry co-development and co-commercialization options for Pieris**							

IMMUNO-ONCOLOGY							
CANDIDATE	**TARGETS**	**PARTNER**	**COMMERCIAL RIGHTS**	**DISCOVERY**	**PRECLINICAL**	**PHASE I**	**PHASE II**
PRS-343	HER2/4-1BB	n/a	Pieris Worldwide				
	+ Anti-PD-L1	n/a					
PRS-344	PD-L1/4-1BB	SERVIER	Pieris U.S. Rights				
PRS-352	n.d.	SERVIER	SERVIER				
Proprietary IO Programs	n.d.	n/a	Pieris Worldwide				
Seattle Genetics Programs‡	n.d.	SeattleGenetics	Pieris U.S. Option‡				
‡3 bispecific programs (1 active, 2 forthcoming) in collaboration with Seattle Genetics, with Pieris retaining US rights for 1 program							

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RESPIRATORY

Anticalin Technology Advantages: Differentiated Respiratory Platform

Small size of 18-20kDa enables deep penetration into smaller airways and permeation of lung epithelium

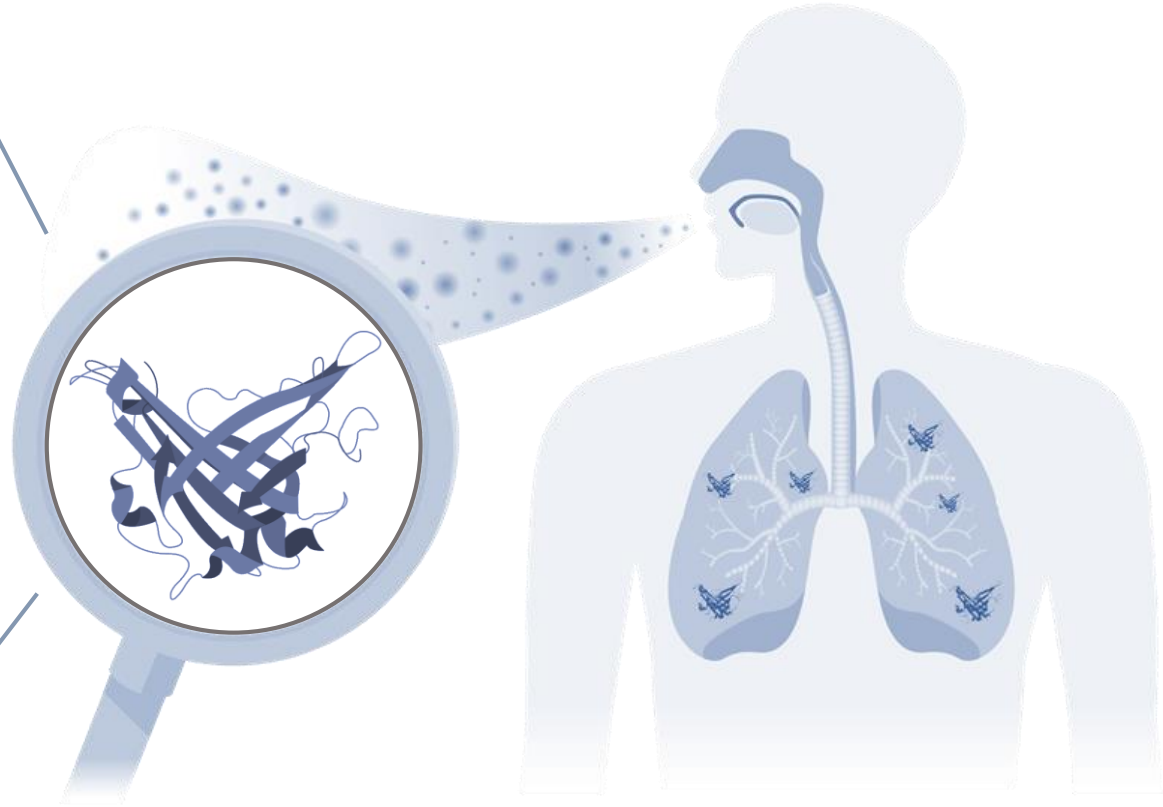
High stability of Anticalin® proteins with high melting temperatures and insensitivity to mechanical stress

Inhalation pharmacokinetics suitable for once or twice daily administration – compatible with flexible treatment regimes

Formulation for lung delivery demonstrated as **nebulized and dry powder** application

Low immunogenicity – Tear lipocalin (TLC) “template” is abundant in human lung and permeates lung epithelium

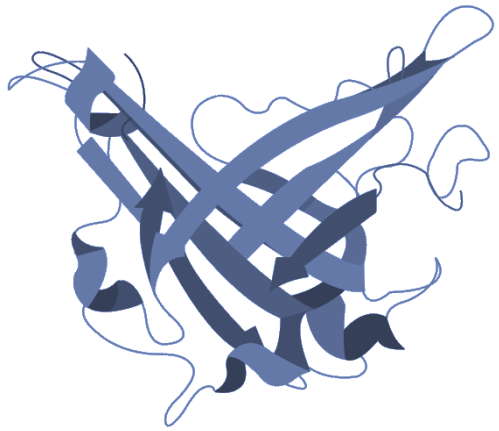
Modularity and multispecific capability offers further differentiation to improve efficacy and broaden patient populations



PRS-060: IL-4Rα Antagonist

Respiratory

Candidate	PRS-060
Function/MoA	Inhibiting IL4-Rα (disrupts IL-4 & IL-13 signaling)
Indications	Moderate-to-severe asthma
Development	Phase 1 multiple-ascending dose trial ongoing; phase 2a to begin in 2H2020
Commercial Rights	Co-development and U.S. co-commercialization rights, including gross margin share



PRS-060

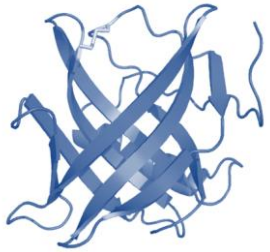
AZD1402/PRS-060

First-in-Class Inhaled IL4Rα Antagonist For Treatment of Moderate-to-Severe Asthma

PRS-060/AZD1402: Inhaled Anticalin® protein for treatment of moderate-to-severe asthma

Systemic exposure with s.c. **mAbs** targeting IL-4Rα

Inhaled **Anticalin®** protein to maximize effects of IL-4Rα blockade in the lung



IL-4Rα-targeting Anticalin® protein

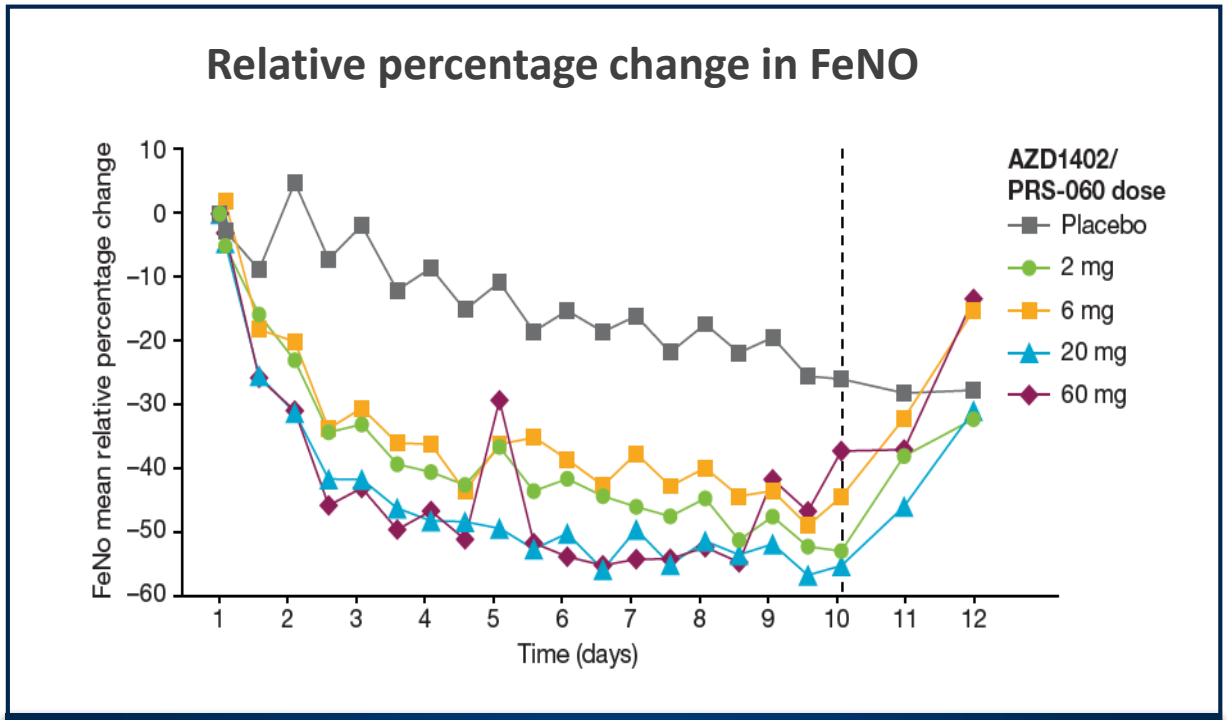
- Lead program in a strategic respiratory alliance with AstraZeneca
- Target population of moderate to severe, uncontrolled asthmatics in US & EU: ~ 12 Mio patients

- Proof of concept for targeting IL-4Rα in asthma has been achieved with dupilumab (Regeneron/Sanofi), an antibody given by **subcutaneous injection**
- Dupilumab has been approved for the treatment of moderate-to-severe eosinophilic asthma[1]
- AZD1402/PRS-060 targeting IL-4Rα is being developed as an **inhaled treatment** for moderate-to-severe asthma to maximize effects in the lung
- AZD1402/PRS-060 is **highly potent** (20pM)
- **Strong preclinical data package,** demonstrating *in vitro* and *in vivo* efficacy following pulmonary delivery

1. Lancet. 2016 Jul 2;388(10039):31-44

AZD1402/PRS-060

Phase 1 MAD study: Robust FeNO Reduction and a Promising Clinical Profile



- Pulmonary target engagement and the overall profile demonstrates suitability for continued development as an inhaled therapy for asthma

- MAD study in mild asthmatics with elevated FeNO levels; inhaled PRS-060/AZD1402 or placebo bid. for a 10-day period
- AZD1402/PRS-060 **safe and well tolerated** at all dose levels in the phase 1 MAD study; no treatment-related serious AEs
- Pulmonary target engagement determined by inhibition of FeNO levels at all evaluated doses
- **Rapid onset** of FeNO reduction (after a single dose) and sustained until dosing completion
- **Significant inhibition of FeNO** at a delivered dose of 2 mg, where there is minimal systemic target exposure suggests that pulmonary target engagement is sufficient to reduce airway inflammation

Summary Respiratory

- Inhaled biologics represent an attractive approach to address unmet medical needs in respiratory diseases with significant commercial opportunity
- Pieris' Anticalin® technology is a highly efficient platform and offers unique advantages for the development of inhaled biologics including favorable drug-like properties
- Pieris has defined respiratory diseases as a key strategic focus area and is committed to building, developing and eventually commercializing a pipeline of inhaled Anticalin®-based drugs

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IMMUNO-ONCOLOGY

4-1BB Agonism Offers Promise of Strong & Durable Clinical Benefit
Pieris' Bispecifics Drive Desired Effect Locally in the Tumor Microenvironment

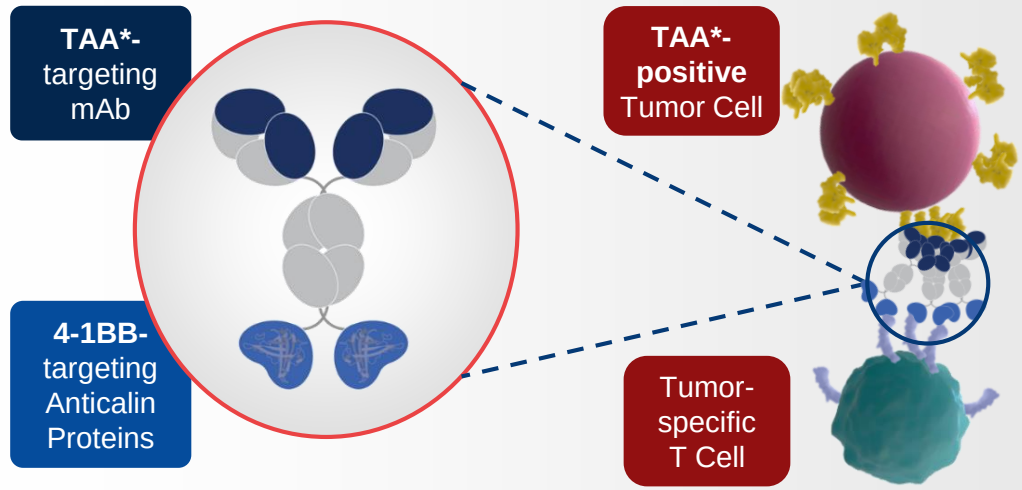
Immuno-oncology

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

- ✓ Increased T cell proliferation & enhanced cytotoxicity
- ✓ Central memory formation[1]
- ✓ Enhanced mitochondrial function & metabolic fitness[2]
- ✓ Enhanced anti-tumor activity via both innate & adaptive immunity[3]

…Offer Important Anti-Tumor Benefits

- ➢ Turn cold tumors hot
- ➢ Increased number of cytotoxic T cells
- ➢ Potent and durable anti-tumor response
- ➢ Survival of T cells in immunosuppressive TME



* *Tumor-associated antigen*

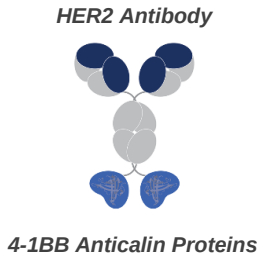
Tumor-localized MoA of Pieris' 4-1BB-based bispecifics enables full immune activation while avoiding systemic toxicities

1. *Bartkowiak and Curran, In Preparation.*
2. *Teijeira and Melero, CIR. 2018.*
3. *Bartkowiak and Curran, Front Oncol 2015*

IO Pipeline Builds on Proven Biology and Technology

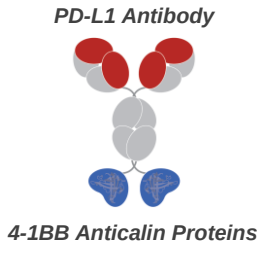
PRS-343
HER2/4-1BB

- **First tumor-targeted 4-1BB-based bispecific** to enter clinic
- Ongoing two Phase 1 studies as monotherapy & in combination with atezolizumab (PD-L1)
- Promising initial clinical data showing **monotherapy activity**, including **PR and CR** as well as **multifold increase of CD8+ tumor-infiltrating lymphocytes**
- Phase 2 in 2L HER2+ gastric cancer to start in 2H 2020



PRS-344
PD-L1/4-1BB

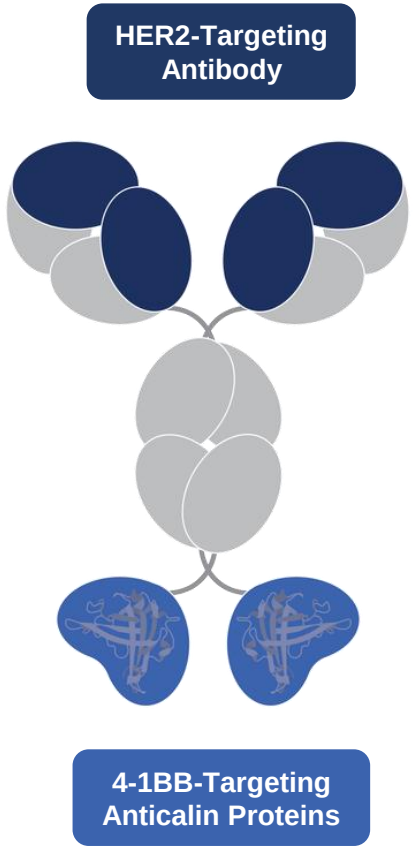
- Combines **two synergistic & independent anti-tumor MoAs:** tumor-targeted 4-1BB activation and PD-L1 checkpoint inhibition
- **IND-enabling studies** ongoing
- **Large commercial opportunity** across multiple tumor types



PRS-343: Proprietary Lead IO Asset

Immuno-oncology

Candidate	PRS-343
Function/MoA	Tumor-targeted 4-1BB agonism and HER2 antagonism
Indications	HER2+ solid tumors
Development	Initiating phase 2 in second line gastric in 2H2020
Commercial Rights	Fully proprietary



PRS-343 Demonstrates Strong Monotherapy Activity –
Three Partial and One Complete Response in Dose Escalation

Immuno-oncology

Monotherapy Data as of May 06, 2020, up to cohort 11B (CR in higher dose cohort)

Cohort	11b	11	10	9	Total
Best Response	8 mg/kg, Q2W	8 mg/kg, Q3W	5 mg/kg, Q3W	2.5 mg/kg, Q3W	
Response Evaluable Patients	7	4	5	5	21
PR	3	-	-	-	3
SD	3	3	2	2	10
ORR	**43%**	0%	0%	0%	**14%**
DCR	**86%**	75%	40%	40%	**62%**

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PRS-343 Clinical Case Study Monotherapy

Immuno-oncology

Monotherapy: Gastric Cancer Patient with Confirmed PR

- Cohort 11b | 8 mg/kg Q2W
- 80-year old female; initial diagnosis on June 2017
- Gastric Adenocarcinoma Stage 4
- Metastasis to liver, lymph node, and adrenal glands
- HER2 3+; PD-L1 positive (CPS=3)
- NGS: ERBB2 amplification, TP53 mutation, alteration of CDK12 and SF3B1
- Started PRS-343 Treatment March 26, 2019

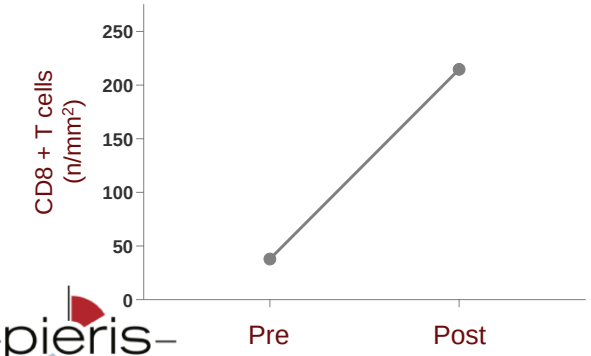
Oncology Treatment History	Duration	Best Response
Trastuzumab, Pembrolizumab + Capecitabine / oxaliplatin	July 2017 – June 2018	Stable Disease
Nivolumab with IDO1 inhibitor (investigational drug)	Aug 2018 – Jan 2019	Stable Disease

Lesions	Lesion Site	Lesion Size (mm)				
		Baseline	C2	C3	C4	C6
% Change from Baseline in target lesions		-	-17%	-36%	-42%	-42%
Non-target	-	Present	Present	Present	Present	2 out 3 Absent

CD8+ T Cell Numbers Increase Post-Treatment

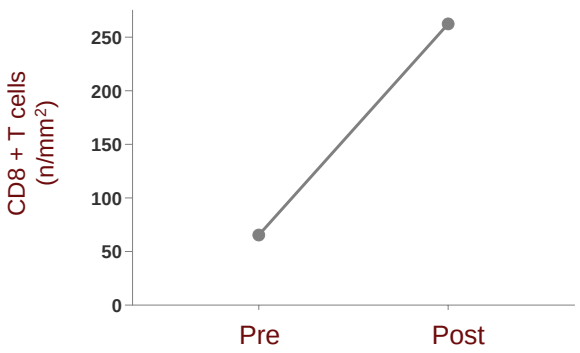
Tumor

CD8 fold change: 5.7 CD8 pre [n/mm^2]: **38**

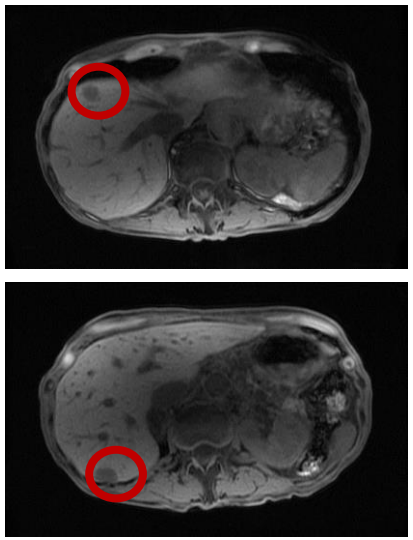


Stroma

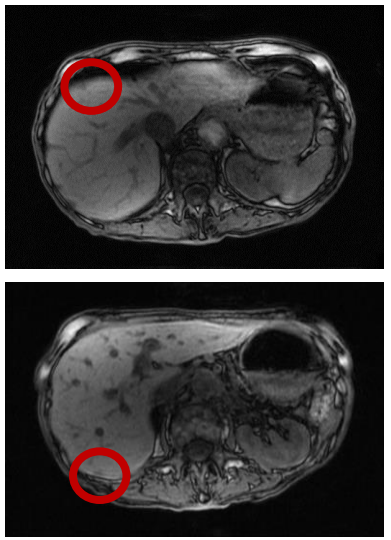
CD8 fold change: 4 CD8 pre [n/mm^2]: **66**



Baseline



Cycle 4



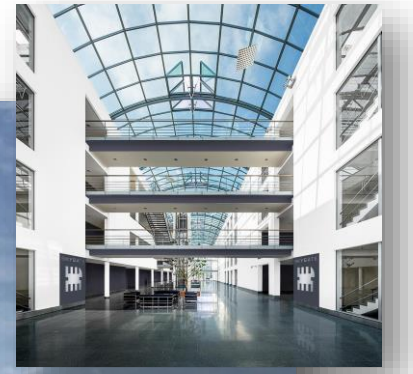
Summary Immuno-Oncology

- Pieris is developing a portfolio of **next-generation IO multispecifics**, both clinical and preclinical stage
- **PRS-343** has demonstrated early **clinical proof-of-concept for tumor-targeted 4-1BB agonism** with Pieris Anticalin-based bispecifics
- Pieris' is developing additional 4-1BB-based bispecifics, some of which are in late preclinical development
- Additional **preclinical programs include various MoAs** (Treg depletion, dual checkpoint inhibition, tumor-localized cytokine agonism and armored CAR-T cells)

Pieris is exploring both ***strategic and asset-focused partnerships on its 4-1BB-based bispecific programs*** as well as research collaborations on other discovery and preclinical-stage programs

Pieris Pharmaceuticals GmbH

New State-of-the-art Facility @ Hallbergmoos



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