

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549**

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**FORM 8-K**

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**CURRENT REPORT  
Pursuant to Section 13 or 15(d)  
of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): May 14, 2019**

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**PIERIS PHARMACEUTICALS, INC.**  
(Exact name of registrant as specified in its charter)

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**Nevada**  
(State or other jurisdiction of  
incorporation)  
255 State Street, 9th Floor  
Boston, MA

(Address of principal executive offices)

**001-37471**  
(Commission  
File Number)

**30-0784346**  
(IRS Employer  
Identification No.)

**02109**

(Zip Code)

**Registrant's telephone number, including area code: 857-246-8998**

**N/A**  
(Former name or former address, if changed since last report.)

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Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

Emerging growth company

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If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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**Item 7.01: Regulation FD Disclosure.**

Attached hereto as Exhibit 99.1 and incorporated by reference herein is the May 2019 Investor Presentation of Pieris Pharmaceuticals, Inc.

The information set forth under this “Item 7.01. Regulation FD Disclosure,” including Exhibit 99.1 attached hereto, shall not be deemed “filed” for any purpose, and shall not be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, regardless of any general incorporation language in any such filing, except as shall be expressly set forth by specific reference in such filing.

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**Item 9.01 Financial Statements and Exhibits**

(d) *Exhibits.*

99.1 [Investor Presentation, Dated May 2019.](#)

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**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

PIERIS PHARMACEUTICALS, INC.

Dated: May 14, 2019

/s/ Allan Reine

\_\_\_\_\_  
Allan Reine

Chief Financial Officer



# INVESTOR PRESENTATION

MAY 2019



# Forward Looking Statements

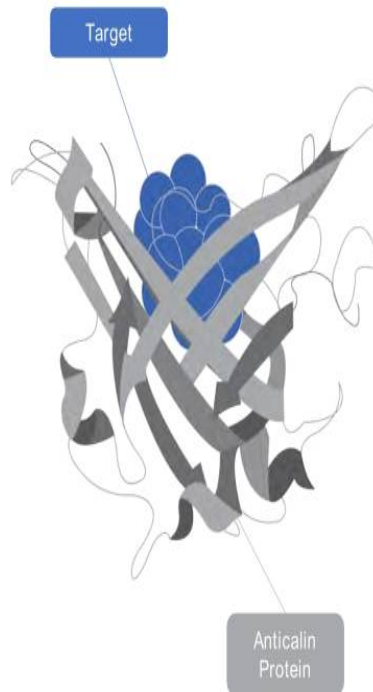
This presentation contains forward-looking statements as that term is defined in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Statements in this press release that are not purely historical are forward-looking statements. Such forward-looking statements include, among other things, 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. Actual results could differ from those projected in any forward-looking statements due to numerous factors. Such factors include, among others, our ability to raise the additional funding we will need to continue to pursue our business and product development plans; the inherent uncertainties associated with developing new products or technologies and operating as a development stage company; our ability to develop, complete clinical trials for, obtain approvals for and commercialize any of our product candidates, including our ability to recruit and enroll patients in our studies; our ability to address the requests of the FDA; competition in the industry in which we operate and market conditions. These forward-looking statements are made as of the date of this press release, and we assume no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law. Investors should consult all of the information set forth herein and should also refer to the risk factor disclosure set forth in the reports and other documents we file with the SEC available at [www.sec.gov](http://www.sec.gov), including without limitation the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 and the Company's Quarterly Reports on Form 10-Q.



# What are Anticalin<sup>®</sup> proteins?

## A Novel Therapeutic Class with Favorable Drug-Like Properties

- Derived from lipocalins (human extracellular binding proteins)
  - TLC and NGAL lipocalins used as "templates" for drug development
- Engineerable binding pocket for robust target engagement
- Monomeric, monovalent, small size (~18 kDa vs 150kDa mAbs)
- Can be formulated for inhalable delivery
- Can be formatted into novel bi/multispecific constructs
- Broad IP position



## Underpinned by a Powerful Drug Discovery Platform

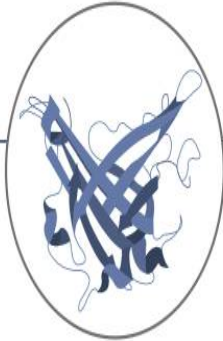
- Highly diverse libraries (>10<sup>11</sup>) of potential drug candidates...
- Automated high-throughput drug screening technology (phage display)...
- Extensive protein engineering know-how...
- ...resulting in high hit rates, quick-to-development candidates



# Company Snapshot

## Pipeline Highlights

- PRS-060: Inhaled IL4-R $\alpha$  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



## Projected Inflection Points

- Respiratory: Co-developed (AstraZeneca) inhaled IL4-R $\alpha$  antagonist (PRS-060) MAD phase 1 data, including FeNO reduction vs. placebo
- IO: Wholly-owned bispecific 4-1BB agonist (PRS-343) phase 1 data in 2019
- IO: 4-1BB/PD-L1 bispecific (PRS-344) IND in 2019

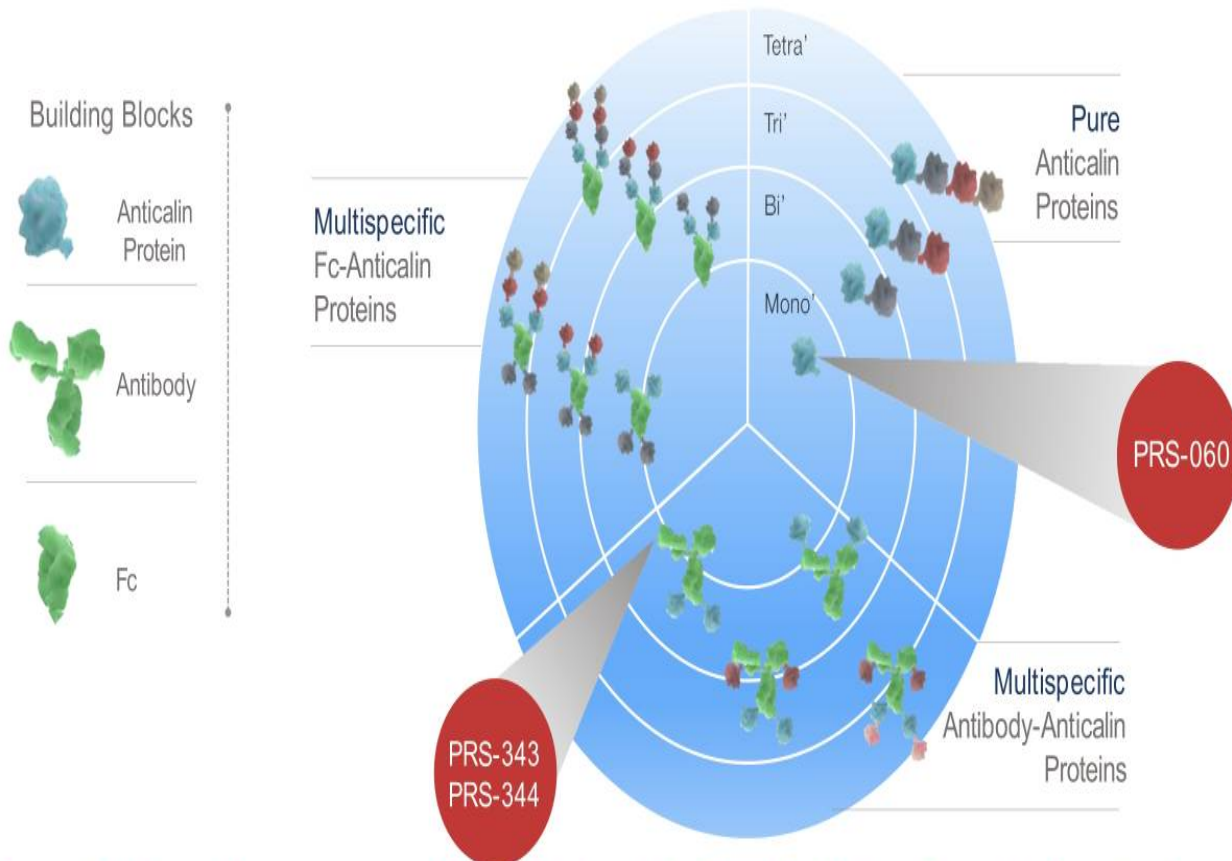


# Pipeline

RESPIRATORY							
CANDIDATE	TARGETS	PARTNER	COMMERCIAL RIGHTS	DISCOVERY	PRECLINICAL	PHASE I	PHASE II
PRS-060	IL4-R $\alpha$		Pieris Worldwide Profit-Share Option	▶			
Proprietary Programs	n.d.	n/a	Pieris Worldwide	▶			
AstraZeneca Programs*	n.d.		Pieris Worldwide Profit-Share Option*	▶			
*4 additional respiratory programs (2 active, 2 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	Pieris Worldwide	▶			
PRS-344	PD-L1/4-1BB		Pieris U.S. Rights	▶			
Servier Programs†	n.d.		Pieris U.S. Option†	▶			
Proprietary IO Programs	n.d.	n/a	Pieris Worldwide	▶			
Seattle Genetics Programs‡	n.d.		Pieris U.S. Option‡	▶			
†4 additional IO bispecific programs in collaboration with Servier, with Pieris retaining US rights for 2 of 5 programs							
‡3 bispecific programs (1 active, 2 forthcoming) in collaboration with Seattle Genetics, with Pieris retaining US rights for 1 program							
OTHER DISEASE AREAS							
CANDIDATE	TARGETS	PARTNER	COMMERCIAL RIGHTS	DISCOVERY	PRECLINICAL	PHASE I	PHASE II
PRS-080	Hepcidin		Major Markets Ex-ASKA Territories	▶			



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



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

# Partnerships



- PRS-060 + 4 additional novel inhaled Anticalin protein programs
- Retained co-development and co-commercialization (US) options on PRS-060 and up to 2 additional programs
- \$57.5M upfront & 2017 milestone
- ~\$2.1B in milestone potential, plus double-digit royalties
- AZ funds all PRS-060 development costs through post-phase 2a co-development opt-in decision
- Access to complementary formulation and device know-how for inhaled delivery



- PRS-344: PD-L1/4-1BB antibody-Anticalin bispecific
- 5-program deal (all bispecific fusion proteins)
- Pieris retains option for full U.S. rights for 3 out of 5 programs
- ~\$31M upfront payment, ~\$1.8B milestone potential
  - ✓ Two preclinical milestones achieved for PRS-344
- Up to low double-digit royalties on non-co-developed products



- 3-program partnership based on tumor-localized costimulatory bispecific fusion proteins
- Pieris retains opt-in rights for 50/50 global profit split and U.S. commercialization rights on one of the programs
- \$30M upfront payment, ~\$1.2B milestone potential
- Up to double-digit royalties on non-co-developed products

Strong Partners • Significant Cash Flow • Retained Commercial Rights



# Scientific and Clinical Advisory Boards

## SCIENTIFIC ADVISORY BOARD: ONCOLOGY

- E. John Wherry, PhD  
University of Pennsylvania
- Vijay Kuchroo, DVM, PhD  
Harvard Medical School
- Michael Curran, PhD  
MD Anderson Cancer Center
- Dario Vignali, PhD  
University of Pittsburgh
- Padmanee Sharma, PhD  
MD Anderson Cancer Center

## SCIENTIFIC ADVISORY BOARD: RESPIRATORY

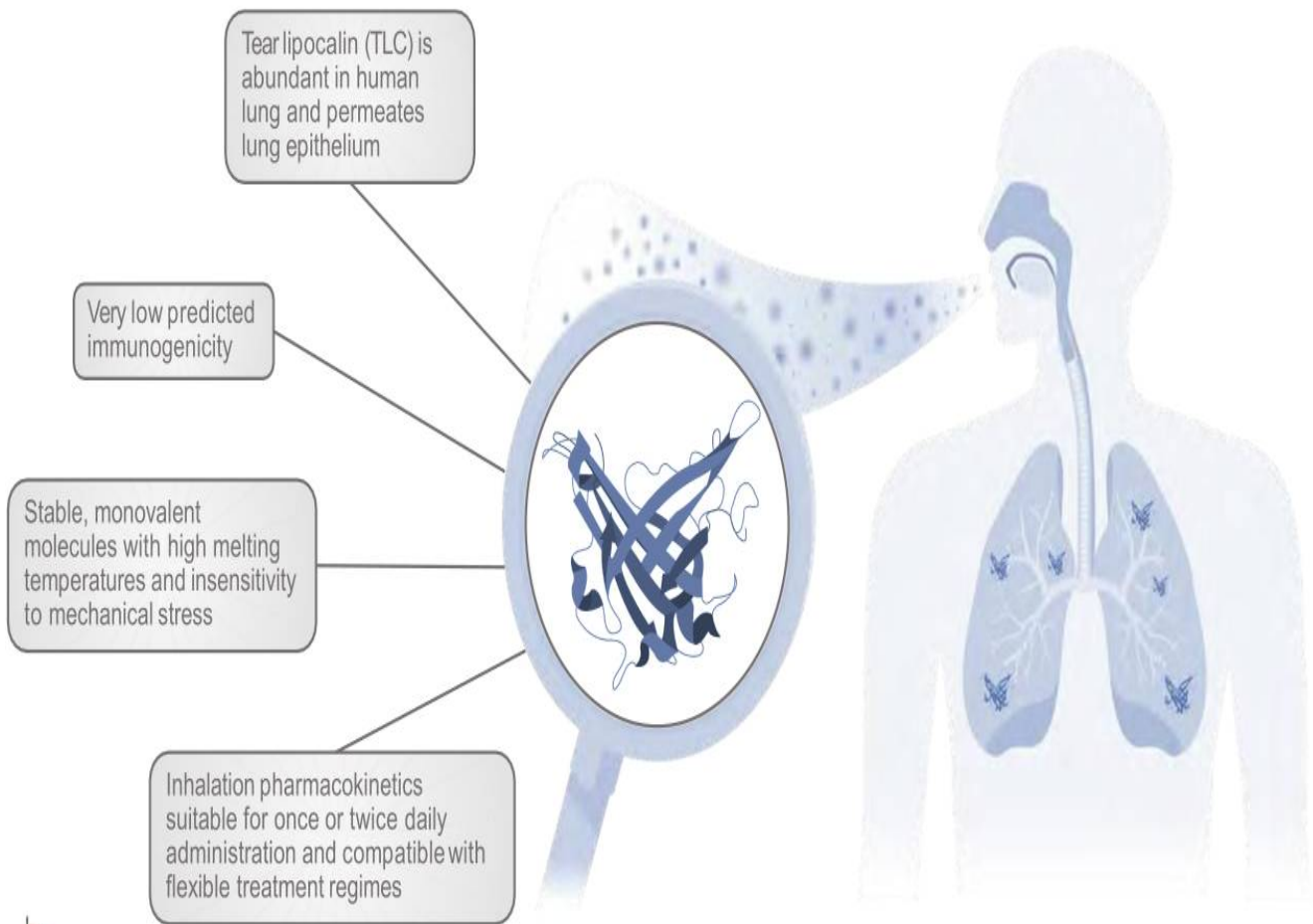
- Gary Anderson, PhD  
University of Melbourne
- Peter Barnes, FRS  
Imperial College
- Bruce Levy, MD  
Harvard University, Brigham and  
*Women's* Hospital
- Fan Chung, MD, DSc  
Imperial College
- Ian Adcock, PhD  
Imperial College
- Oliver Eickelberg, MD  
University of Denver
- Sally Wenzel, MD  
University of Pittsburgh Medical  
Center

## CLINICAL ADVISORY BOARD: ONCOLOGY

- Sandra Swain, MD  
Georgetown University Cancer  
Center
- Noah Hahn, MD  
Johns Hopkins University School of  
Medicine
- David Ilson, MD, PhD  
Memorial Sloan-Kettering Cancer  
Center, Weill Cornell Medical College
- Funda Meric-Bernstam, MD, PhD  
Institute for Personalized Cancer  
Therapy, MD Anderson Cancer  
Center
- Mario Sznol, MD  
Yale University

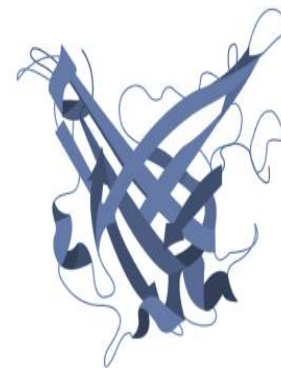


# Anticalin Technology Advantages: Differentiated Respiratory Platform



# PRS-060: IL-4R $\alpha$ Antagonist

Candidate	PRS-060
Function/MoA	Inhibiting IL4-R $\alpha$ (disrupts IL-4 & IL-13 signaling)
Indications	Moderate-to-severe asthma
<b>Development</b>	Phase 1 multiple-ascending dose trial ongoing
<b>Commercial Rights</b>	Co-development and U.S. co-commercialization rights, including gross margin share



PRS-060

# 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%)



All numbers reflect 2016 estimates.

Source: Artisan Healthcare Consulting analysis, including the following: CDC, Eurostat, Rabe (2004), Cazzoletti (2007), Colice (2012), Hekking (2015).



# IL-4Ra: Best-in-Class Efficacy for Uncontrolled Asthma

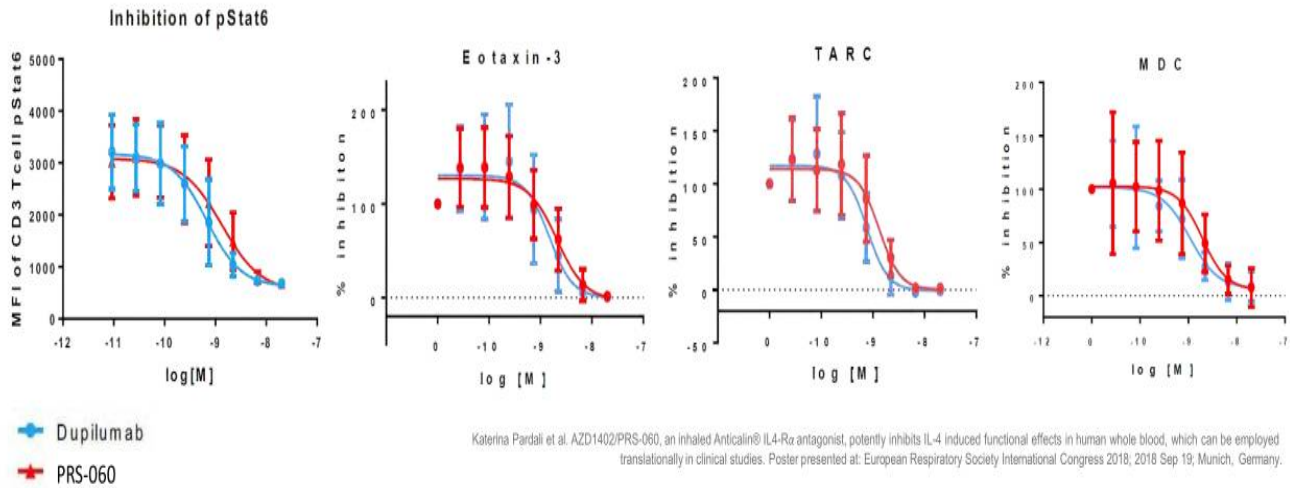
Superior data on lung function improvement, exacerbation reduction and steroid-sparing effects across all indicated biologics therapies

Approved Intervention	FeNO	Exacerbation Rate	FEV <sub>1</sub>
Anti-IL-4R $\alpha$ (dupilumab)	Stat. sig. reduction in all comers, normalizes in ~70% of FeNO high patients, no increase following ICS/LABA withdrawal	High EO: 67% reduction on label (87% in Phase II)	Significant Change: 0.25L-0.32L in high EO population
Anti-IL-5 (benralizumab, mepolizumab, rezlizumab)	No change	51-53% on label for benralizumab and mepolizumab	Minimal change: 0.08L-0.16L
Anti-IgE (omalizumab)	No change	43% in post-approval pediatric study (not analyzed in registrational studies)	No change

# PRS-060 Potency Similar to that of Dupilumab

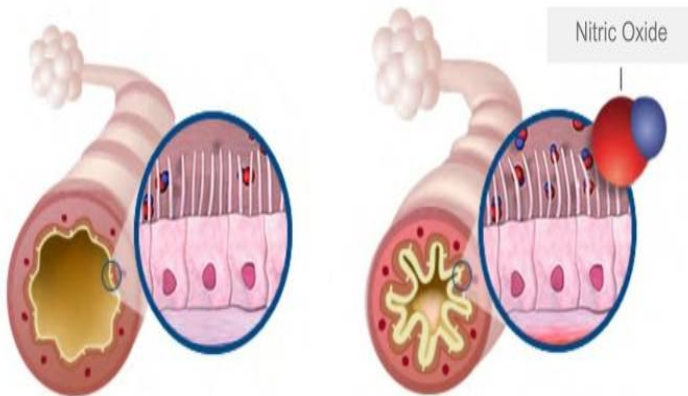
PRS-060 reduces levels of pSTAT6, Eotaxin-3, TARC and MDC comparably to dupilumab

Drug	IC <sub>50</sub> [nM] pSTAT6	IC <sub>50</sub> [nM] Eotaxin-3	IC <sub>50</sub> [nM] TARC	IC <sub>50</sub> [nM] MDC
PRS-060	1.3	2.1	1.3	2.0
Dupilumab	0.8	1.5	0.8	1.1



# FeNO is a Validated Biomarker in Allergic Asthma Interventions

Elevated fractional exhaled nitric oxide (FeNO) is a marker of allergic asthma



Normal epithelial cells release minimal NO

During airway inflammation, activated epithelial cells increase production of NO

Biologics that have demonstrated a meaningful reduction in FeNO (dupilumab, tezepelumab) have subsequently produced clinically-significant improvements in lung function and superior exacerbation improvements versus drugs that had no effect on FeNO

Dupilumab was recently approved by the EMA for severe asthma in patients with either high EOs OR high FeNO

We are exploring FeNO reduction versus placebo in a multi-dose ascending phase 1 study of PRS-060

Positive FeNO data from this study would support continued development to assess the potential to improve lung function (FEV1) in uncontrolled asthmatics

# PRS-060 Phase I Single Ascending Trial

## TRIAL

Healthy volunteers

Initiated in December 2017

Study completed in 2018

Pieris was the trial sponsor, with AstraZeneca reimbursing Pieris for all associated costs

## DATA

Safe and well-tolerated at all dose levels (0.25mg to 400mg) with no SAEs reported or ADAs detected

PK profile showed slow & prolonged absorption into systemic circulation after inhalation

Dose-dependent inhibition of systemic pSTAT6 confirms robust target engagement

Presenting poster at ATS 2019

# 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



Data will be presented at an upcoming medical conference



# PRS-343: 4-1BB/HER2 Bispecific

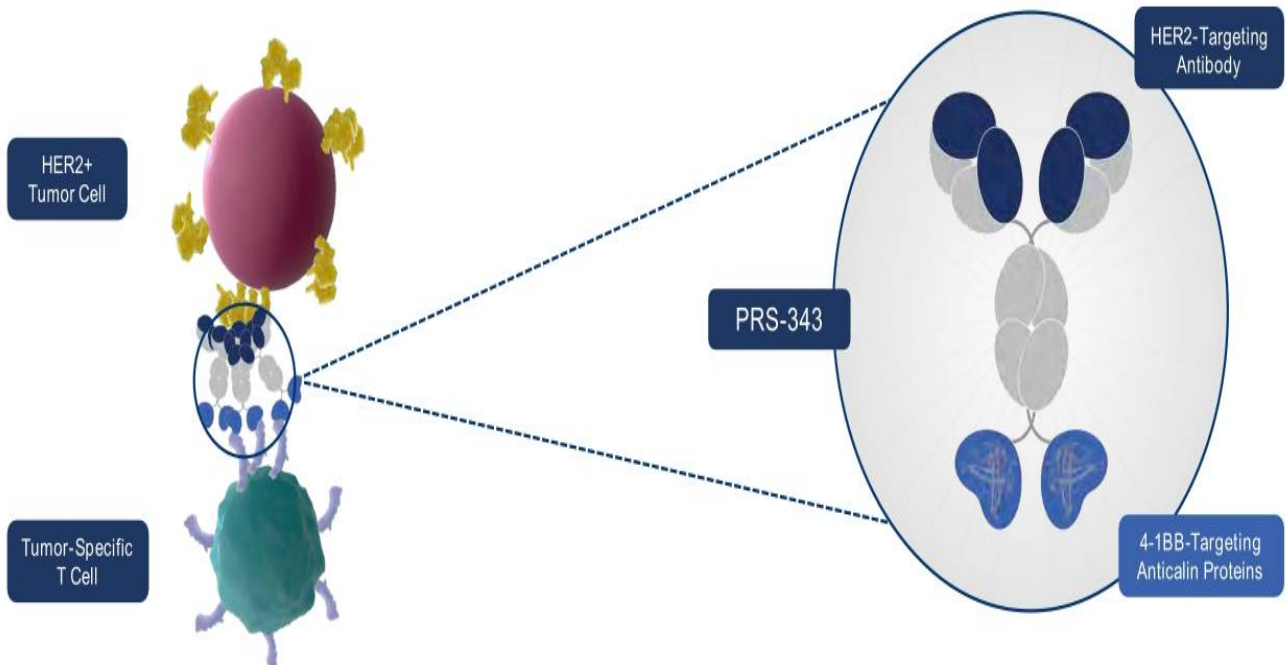
Candidate	PRS-343
Function/MoA	Tumor-targeted 4-1BB agonism, HER2 antagonism
Indications	HER2+ solid tumors
Development	Phase 1 ongoing
Commercial Rights	Fully proprietary



# 4-1BB (CD137): Validated Target in Need of Appropriate Drug

- Marker for tumor-specific T cells in TME
- Drives anti-tumor cytolytic activity
- Ameliorates T-cell exhaustion & critical for T-cell expansion
- Drives central memory T-cell phenotype

Systemically agonizing 4-1BB mAb (urelumab) has shown clinical activity yet caused significant toxicity

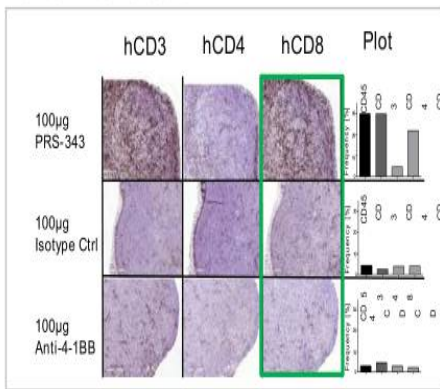


PRS-343 was designed for TME-specific 4-1BB activation\*

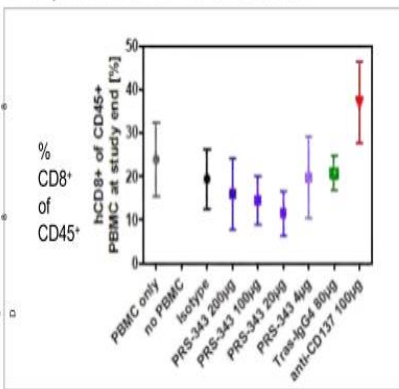
# PRS-343 Shows Localized Activity and Differentiation in Humanized Mouse Model

	CD8 <sup>+</sup> Proliferation in TME	Peripheral CD8 <sup>+</sup> Proliferation	Systemic Toxicity
PRS-343	Yes	No	No
4-1BB mAb	No	Yes	Yes
Isotype Control	No	No	No

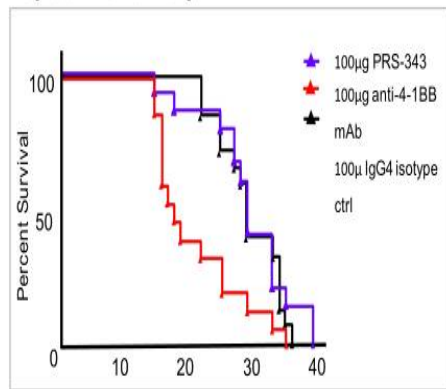
CD8<sup>+</sup> Proliferation in TME



Peripheral CD8<sup>+</sup> Proliferation



Systemic Toxicity



Experimental Design:

- SKOV-3 tumor cells grafted onto immune-deficient mice and grown to predetermined volume
- Human PBLs + control or PBLs + PRS-343 administered

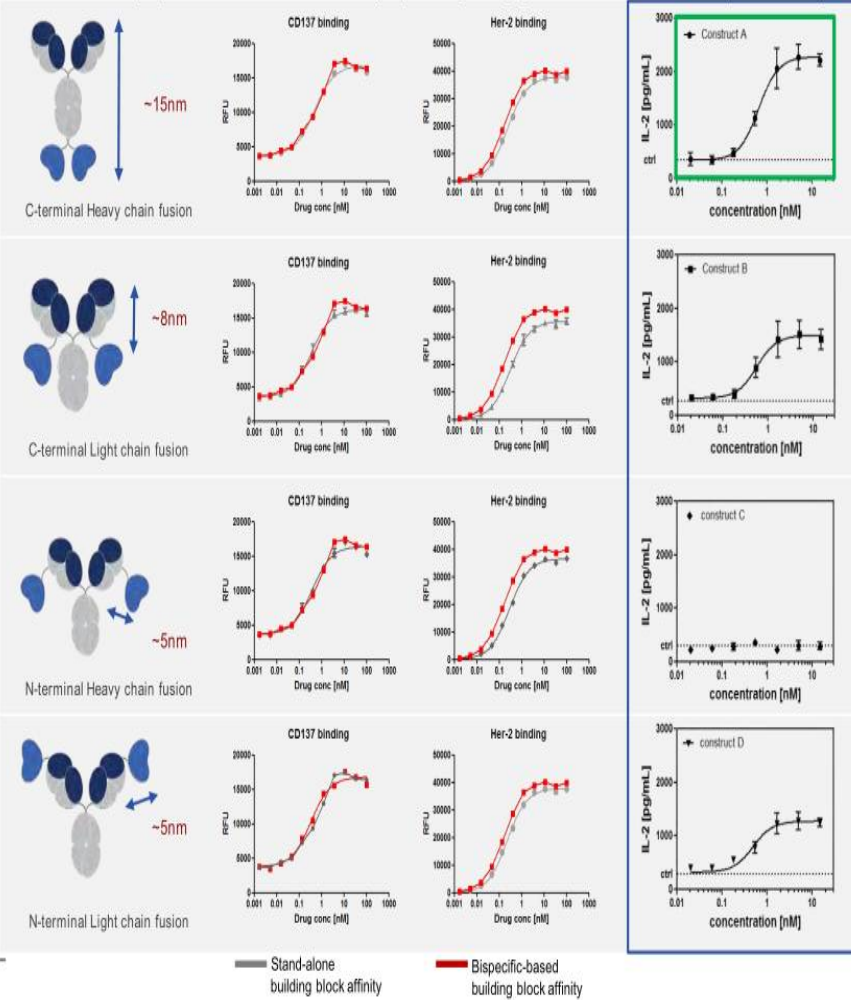


# Anticalin Technology Advantages: Well-Equipped for Targeted IO Agonism

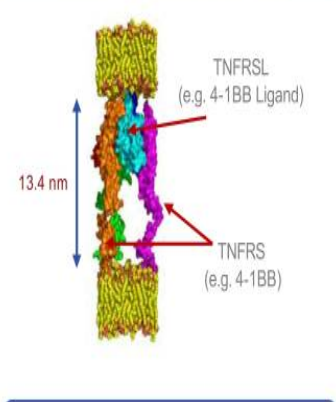
A Varied Immune Synapse...

...Does Not Materially Impact Target Engagement...

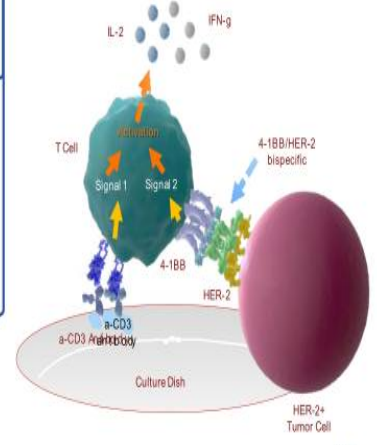
...But Impacts Efficacy



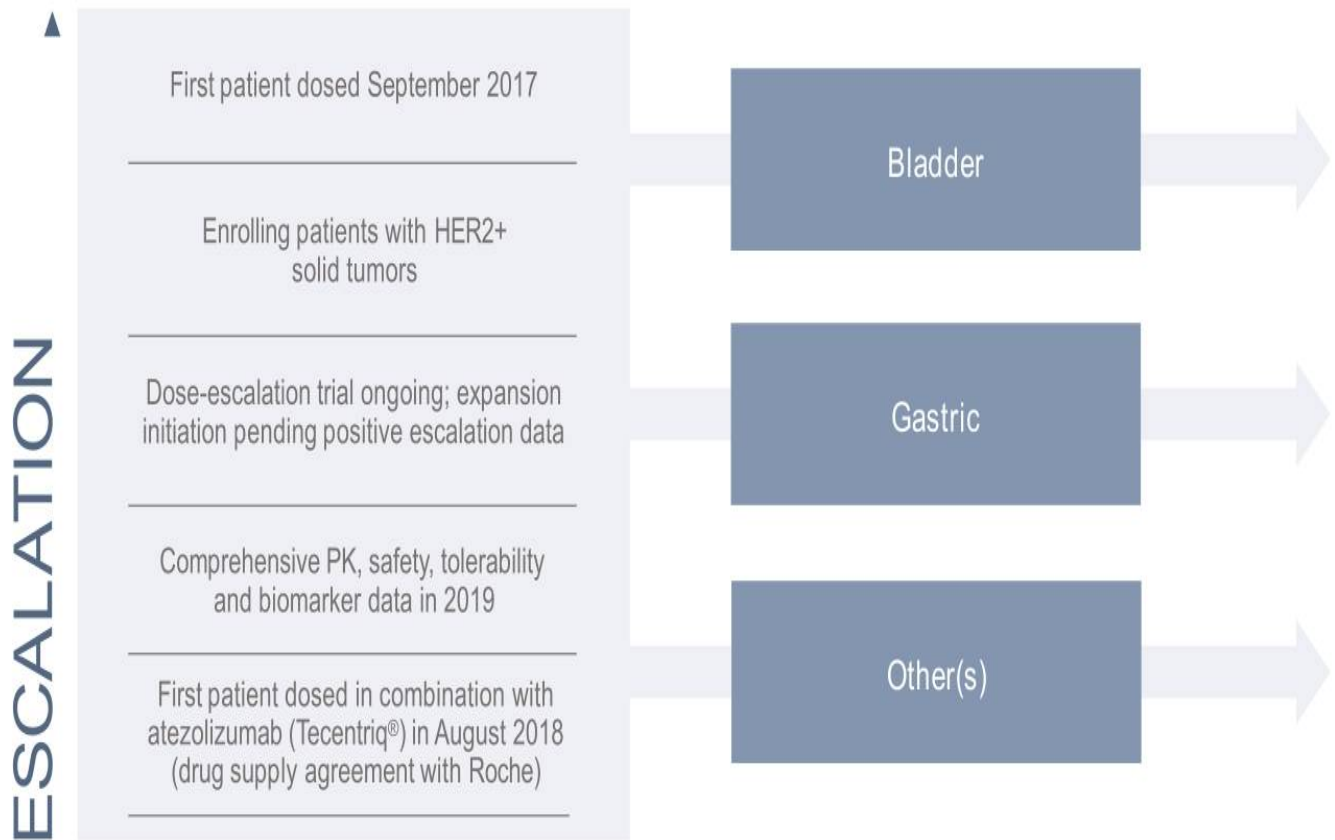
## The Natural Immune Synapse



## Efficacy Experimental Design

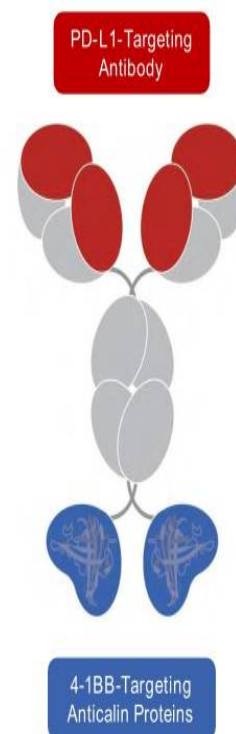


# PRS-343 Phase 1 Escalation and Expansion Trials



# PRS-344: 4-1BB/PD-L1 Bispecific

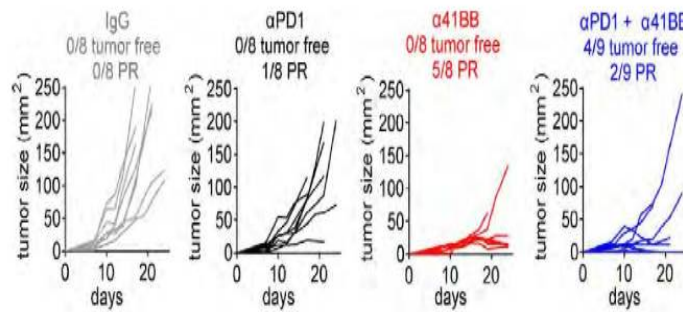
Candidate	PRS-344
Function/MoA	Localized 4-1BB agonism with PD-L1 antagonism
Indications	N.D.
Development	2019 IND expected (in co-dev with Servier)
Commercial Rights	Opt-in for co-development with full U.S. commercial rights; royalty on ex-U.S. sales



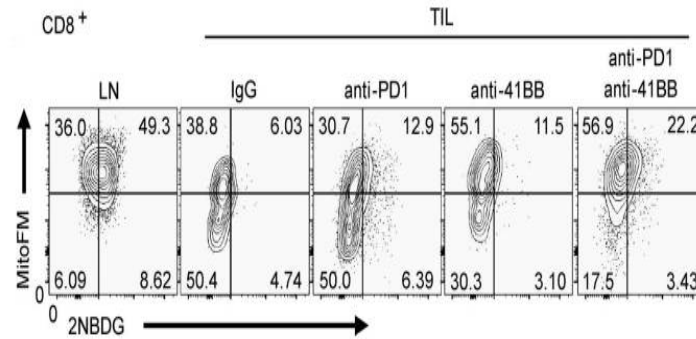
# PRS-344 Drives Synergistic IO Biology

- Combines the benefits of tumor-localized 4-1BB agonism with PD-L1 blockade
- Pan-tumor opportunity
- Publications support preclinical rationale of the combination, as evidenced below:

## Synergistic Response of PD-1+4-1BB Combination Demonstrated In Preclinical Models



PD-1+4-1BB combo demonstrates robust preclinical anti-tumor activity



4-1BB agonism enhances mitochondrial function in T cells

Adapted Menk et al. JEM (2018)

# Financial Overview (As of 3/31/19)

\$110.8 M

Cash & Cash  
Equivalents



\$0.0

Debt



50.9 M

CSO



**\$120+ M** non-dilutive capital since January 2017

## Pieris Pharmaceuticals

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Germany

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