

# PULMATRIX Corporate Overview



August 2018

# Safe Harbor



This presentation contains forward-looking statements. All statements other than statements of historical fact contained herein, including statements regarding our business plans or strategies, projected or anticipated benefits or other consequences of our plans or strategies, projected or anticipated benefits from acquisitions to be made by us, or projections involving anticipated revenues, earnings or other aspects of our operating results, are forward-looking statements. Words such as “anticipates,” “assumes,” “believes,” “can,” “could,” “estimates,” “expects,” “forecasts,” “guides,” “intends,” “is confident that,” “may,” “plans,” “seeks,” “projects,” “targets,” and “would,” and their opposites and similar expressions, as well as statements in future tense, are intended to identify forward-looking statements. Forward-looking statements should not be read as a guarantee of future performance or results and may not be accurate indications of when such performance or results will actually be achieved. Forward-looking statements are based on information we have when those statements are made or our management’s good faith belief as of that time with respect to future events and are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in or suggested by the forward-looking statements. A discussion of these and other factors, including risks and uncertainties with respect to Pulmatrix, Inc. (the “Company”), is set forth in the Company’s filings with the Securities and Exchange Commission (“SEC”), including the Company’s most recently filed Annual Report on Form 10-K). Investors and security holders are urged to read these documents free of charge on the SEC’s website at <http://www.sec.gov>. Forward-looking statements contained in this presentation are made as of this date, and the Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise.

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**CAUTION: We have not received approval from the FDA, or any other regulatory entity, to market our therapeutic candidates in the United States or in any other jurisdictions. Our therapeutic candidates, including Pulmazole, PUR1800, and PUR0200 are classified by the FDA as investigational drugs and are limited by Federal (or United States) law to investigational use only that require additional studies to make definitive conclusions and claims about such candidates’ safety or efficacy.**

# Pulmatrix: Building Value by Meeting Important Unmet Medical Needs in ABPA and AECOPD



## ➤ **LEAD PROGRAM: iSPERSE™ Pulmazole Anti-Fungal**

- Pulmazole is inhaled Itraconazole for allergic bronchopulmonary aspergillosis (ABPA) – seeking to be the first to market inhaled anti-fungal in US and EU
- Reduced development risk as oral itraconazole (Sporanox) has been on the market for over 25 years
- Itraconazole use in ABPA, though effective, has limited utility given poor bioavailability and toxicity concerns
- Phase 1/1b study results demonstrated Pulmazole safety/tolerability and ability to achieve significantly higher lung exposure and lower plasma exposure than oral Sporanox, supporting the belief that Pulmazole could significantly improve upon known efficacy and safety profile of Sporanox
- Qualified Infectious Disease Product (QIDP) designation obtained in 2017 for ABPA and CF

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## ➤ **Second PROGRAM: iSPERSE PUR1800 Kinase Inhibitor**

- PUR1800 is a novel narrow spectrum kinase inhibitor (NSKI) for COPD first in class (US/EU) inhaled non-steroidal anti-inflammatory to treat acute exacerbations in COPD (AECOPD)
- NSKI in PUR1800 demonstrated anti-inflammatory activity, safety and tolerability in stable COPD patients

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## ➤ **Underlying iSPERSE Platform Technology Supports Future Value Growth**

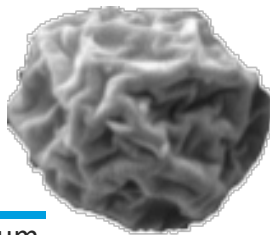
- iSPERSE dry powder technology significant patient experience and product opportunities
- iSPERSE intellectual property carries well into 2030's on platform and specific products

# iSPERSE™ Best-in-Class Engineered Particles Enable Development and Patient Care Advantages



## iSPERSE™ Differentiation

- **Small, dense, dispersible**, respirable particles
- **Highly efficient** inhaled delivery
- **Flow rate independent** performance (consistent delivery of high drug loads)
- **Scalable** platform
- **Broad IP** portfolio into 2030s



iSPERSE™

## Potential iSPERSE™ Advantages

- **Can be used with a broad range of drugs**, small molecule to biologic
- **Can be used with any device** (i.e., metered-dose, reservoir, or blister-based inhalers)
- **Requires low inspiratory flow** for penetration deep into lung based on high dispersibility
- **Can deliver large doses into lungs (tens of milligrams)** with high lung delivery efficiency
- **Avoids first-pass effect and systemic side-effects** with improved PK profile compared to oral delivery

iSPERSE™ Enables Sick Patients to Get More Effective Doses

# Robust Pipeline with Projected Significant Value Catalysts\*



Product Pipeline	Indication	2H 2018	2019	1H 2020	Milestone
<b>Pulmazole</b> <i>Anti-fungal</i>	Allergic Bronchopulmonary Aspergillosis (ABPA) in Patients with Asthma		Phase 2		Phase 2 4Q 2019
<b>PUR1800</b> <i>NSKI</i>	Acute Exacerbations of COPD (AECOPD)	★ 28-Day Tox	Phase 2a		Phase 2a 2Q 2020
<b>PUR5700</b> <i>NSKI</i>	Idiopathic Pulmonary Fibrosis (IPF)		Pre-Clinical		Pre-clinical

## Potential Future Revenue Opportunities

<b>PUR0200-US</b> <i>LAMA</i>	Chronic Obstructive Pulmonary Disease (COPD)		Phase 1		Out-Licensed to Vectura for U.S. 09/2017
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## Pulmazole – Inhaled Antifungal



Inhaled Itraconazole to Treat Allergic Bronchopulmonary Aspergillosis (ABPA) in Asthmatics

**“***I am very encouraged by the phase 1 results demonstrating that it is both feasible to administer itraconazole by inhalation and further that high levels of the drug may be achieved within the airways. I believe that Pulmazole has the potential to significantly improve upon both the efficacy and safety profile of oral Sporanox, and I look forward to working with the other members of the advisory board to assist Pulmatrix in advancing the development of Pulmazole to treat patients with fungal asthma, focusing initially on ABPA.”*

– David Denning, MD

Professor of Infectious Diseases in Global Health and  
Director of the National Aspergillosis Centre, Manchester, UK



# PULM: Investment Opportunity

## Clinical Stage Antifungal

- Pulmazole is an inhaled reformulation of itraconazole in Ph2 for airway fungal infections
- Ph1/1b study demonstrated safety/tolerability in healthy normal volunteers dosed up to 14 days and asthmatics following single dose
- Ph1/1b results support belief that Pulmazole could significantly improve upon known efficacy and safety profile of Sporanox

## Clinical Data & Upcoming Milestones

- Phase 2 28-day proof-of-mechanism in ABPA patients scheduled to begin 4Q 2019 (FPI 4Q 2018)
- Phase 2 proof-of-concept efficacy/safety trial in ABPA patients scheduled to begin 2Q 2020



## Attractive Market Opportunity

- Up to \$1.5B U.S. in Asthma-ABPA and in other Aspergillus pulmonary disease (ex. Cystic Fibrosis – ABPA)\*
- Following 505(b)(2) pathway for registration as Sporanox has been on market for 25+ years
- Additional 5 years exclusivity with QIDP status

## Superior Technology and Team

- iSPERSE best-in-class particle engineering technology for lung delivery
- Clinical stage COPD assets (PUR0200 and PUR1800) with substantial follow on development opportunities
- Experienced management team and board with success in commercializing respiratory products

ABPA = Allergic Bronchopulmonary Aspergillosis; COPD = Chronic Obstructive Pulmonary Disease; FPI = First Patient In

\* Peak revenues expected at loss of market exclusivity, ~11 years post launch

# Pulmazole Has Potential to Transform the Standard of Care for ABPA



## Significant Product Opportunity

- Estimated **300K US** and **5M WW** ABPA patients
- No approved antifungal therapy available
- **Limited/no novel competition** anticipated for ABPA market

## Improving Upon Standard of Care

- Sporanox (oral itraconazole) use is limited due to poor bioavailability, safety/tolerability issues and drug-drug concerns associated with high oral plasma exposure

## Target Product Profile (TPP)

- Pulmazole is anticipated to provide **higher lung exposure** and **lower plasma exposure** than Sporanox, potentially improving both **efficacy** and **safety/tolerability**

## Ph1/1b Clinical Study Results

- Pulmazole was **safe** and **well tolerated** in SAD/MAD study in healthy normal volunteers and SD administration to asthmatics
- Pulmazole demonstrated **significantly higher lung exposure** than Sporanox in asthmatics, despite inhaling **1/10 of the dose** administered orally
- Pulmazole **plasma exposure** in asthmatics and healthy normal volunteers was **significantly lower** than that of Sporanox

## Pulmazole Clinical Value Drivers

- Investment required to deliver **Phase 2 28-day POM data** expected in **4Q 2019**
- Potential registration Phase 2b/3 POC trial start date 2Q 2020



# ABPA Represents a Large Addressable Antifungal Patient Population in Aspergillus Related Diseases



## ABPA is a Debilitating Disease

- ABPA in asthmatics is caused by hypersensitivity to *Aspergillus* species lung infection
- ~300K adult asthma ABPA patients in U.S. and ~5M worldwide
- Diagnostic criteria include:
  - High IgE (>1000 IU/mL)
  - Skin prick positivity to *Aspergillus*
  - Eosinophilia (>500 cells/ $\mu$ L)
  - Elevated IgE/IgG Antibodies to *Aspergillus*
  - Radiographic pulmonary opacities consistent with ABPA

## ABPA Pathophysiology

Healthy Lung



Diseased Lung



Persistence of *A. fumigatus* in the airways leads to local inflammation, mucus production, reduction in lung function and worsening of asthma symptoms. Untreated ABPA may result in pulmonary fibrosis, respiratory failure and potentially death.

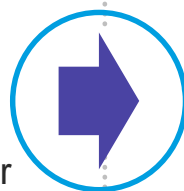


# ABPA Progression and Treatment Options

## ABPA is Treated by Allergists and Pulmonologists

### ABPA-Asthma Treatment Goals

- Symptom control of asthma or cystic fibrosis
- Prevent or treat pulmonary exacerbations
- Reduce or remit pulmonary inflammation
- Mitigate progression to end-stage fibrotic or cavitary disease



### Treatment is Limited Primarily to Steroids and Antifungal Therapy

- Oral steroid therapy is the standard of care for treating ABPA
- In patients with insufficient treatment response, antifungal therapy is added to steroid therapy for ~4 months
- Antifungals are sometimes used 1<sup>st</sup> line in conjunction with steroids

### Limited Treatment Options Impede Ability to Achieve Treatment Goals

- ~50% of ABPA patients have **inadequate response** to oral steroids alone
- ~20% of ABPA patients become **steroid dependent**
- Antifungal agents are believed to **reduce fungal burden** (antigen induces inflammatory response)
- Antifungal treatment **improves clinical outcomes** and can enable a reduction in steroid burden
- While the majority of antifungal use in ABPA is itraconazole, overall antifungal use is limited by safety/tolerability concerns

# Literature Establishes Strong Clinical Precedent for Itraconazole Use in ABPA



## Literature Indicates Antifungals Improve ABPA Outcomes



### preliminary report

#### Adjunctive Therapy of Allergic Bronchopulmonary Aspergillosis with Itraconazole\*

David W Denning, John F. Van Wye, M.D., Norman J. Lewiston, M.D., F.C.C.P., and David A. Stevens, M.D.

### 1991, Denning et al.

Itraconazole improved pulmonary function, decreased corticosteroid use and total IgE in 6 patients with ABPA (3 cystic fibrosis and 3 asthma)



Expert Review of Respiratory Medicine

#### Developments in the diagnosis and treatment of allergic bronchopulmonary aspergillosis

Ritesh Agarwal, Inderpaul S Sehgal, Sahajal Dhooria & Ashutosh N Aggarwal

### 2018, Agarwal et al.

In acute stage treatment naive ABPA patients, monotherapy itraconazole is effective in considerable number with less side-effects compared to prednisolone



Journal of Asthma

#### A pilot RCT of nebulized amphotericin for maintenance of remission in patients with allergic bronchopulmonary aspergillosis

Babu Ram M.Sc, Ashutosh N. Aggarwal MD, DM, Sahajal Dhooria MD, DM, Inderpaul Singh Sehgal MD, DM, Mandeep Garg MD, Digambar Behera MD, Arunakote Chakrabarti MD & Ritesh Agarwal MD, DM

### 2016, Ram et al.

Nebulized amphotericin B reduced exacerbations compared to nebulized budesonide in a study in 21 patients

The New England Journal of Medicine

#### A RANDOMIZED TRIAL OF ITRACONAZOLE IN ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS

DAVID A. STEVENS, M.D., HONARD J. SCHWARTZ, M.D., JEANNETTE Y. LEE, PH.D., BRUCE L. MOSKOWITZ, M.D., DENNIS C. JEROME, M.D., ANTONINO CATANZARO, M.D., DAVID M. BAMBERGER, M.D., ALLISON J. WEINMANN, M.B., B.S., CARMELOTTA U. TUAZON, M.D., MARC A. JUDSON, M.D., THOMAS A.E. PLATTS-MILLS, M.D., PH.D., AND ARTHUR C. DEGRAFF, JR., M.D.

### 2000, Stevens et al.

Itraconazole improved pulmonary function, and decreased steroid use and total IgE in a randomized double-blind trial with 55 patients

#### Anti-inflammatory effect of itraconazole in stable allergic bronchopulmonary aspergillosis: A randomized controlled trial

Peter Alexander Blanch Wark, BMed, PhD, FRACP; Michael John Hensley, MBBS, PhD, FRACP, FAFPHM; Nicholas Saitos, MBBS, FRACP, FRCP, FCCP; Michael James Boyle, MD, FRACP, FRCPA; Ruth Christina Tonaguzzi, Grad Dip Clin Epidemiol; Jodie Louise Simpson, BSc (Hons); Patrick McElduff, PhD; and Peter Gerard Gibson, MBBS, FRACP; Newcastle, Australia, and Manchester, United Kingdom

### 2003, Wark et al.

Itraconazole decreased total IgE and the exacerbation frequency in a randomized, double-blind trial with 29 patients

**Pulmazole is Anticipated to Improve Upon Sporanox Outcomes (FEV<sub>1</sub>, Exacerbation Rate, Asthma Control and Steroid Burden) Demonstrated in Clinical Literature**

Source: Denning. *Chest*.1991; 100:813; 116(6):1665; Stevens. *NEJM*.2000;342(11):757; Wark. *J Allergy Clin Immuno*. 2003;111; 952; Agarwal *Chest* 2018; doi: 10.1016/j.chest.2018.01.005; Ram. *Journal of Asthma*. 2016:517; Physician Interviews; ClearView Analysis.; FEV<sub>1</sub> = Forced Expiratory Volume in 1 Second

# Randomized Placebo Controlled Studies Support Efficacy of Oral Sporanox in Asthma-ABPA



## 2000, Stevens et al. *New England Journal of Medicine*

- **Design:**
  - Part 1: 200 mg Sporanox BID vs PBO for 16 weeks (n=55)
  - Part 2: open label, all patients received 200 mg Sporanox QD (n=50)
- **Results:**
  - 46% response rate in Sporanox group vs 19% response rate in placebo group (p=0.04)
  - Greater improvements in lung function (FEV<sub>1</sub>, FVC, PEF) noted in Sporanox treatment group versus placebo

## 2003, Wark et al. *Journal of Allergy & Clinical Immunology*

- **Design:** 200 mg oral Sporanox bid vs PBO for 16 weeks (n=29)
- **Results:**
  - Sputum eosinophils (35% decrease/week first 4 weeks) and serum IgE (6% decrease/week) significantly reduced
  - Clinically significant improvement in FEV<sub>1</sub> following 16 weeks of treatment (9.8% treatment difference between groups (p=0.5, likely due to small sample size)
  - Fewer exacerbations requiring oral corticosteroids in those treated with Sporanox (p=0.03)

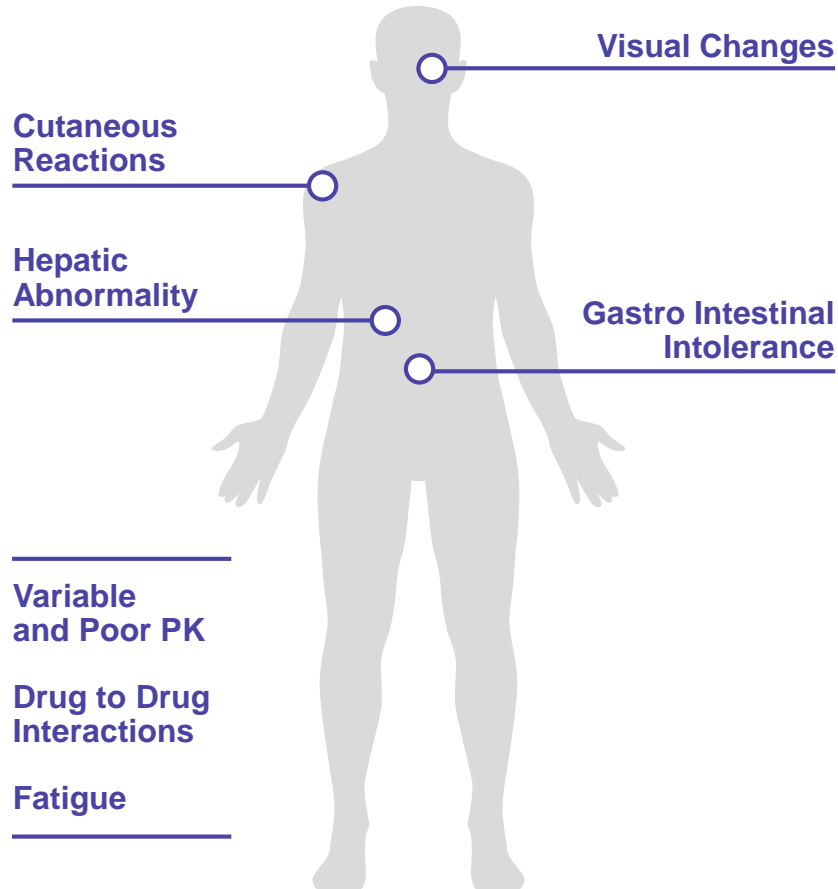
## Stevens & Wark Studies — Key Takeaways

- Both clinical trials support inclusion of Sporanox into current ABPA treatment guidelines
- Key biomarkers of ABPA activity can be reduced as early as 4 weeks of treatment
- Both studies show improvements in FEV<sub>1</sub> at 16 weeks, a potentially approvable endpoint
- Both studies are the foundation for Pulmazole Phase 2 POM and Phase 2b/3 POC development plan

# Pulmazole Potentially Addresses the Significant Limitations of Oral Antifungals in ABPA



## Antifungal Limitations



## Physician Feedback Supports Pulmazole as a Preferred Treatment

- Antifungals reduce both exacerbations and chronic steroid use
- Sporanox has been on the market for 25+ years and is the preferred antifungal
- Oral antifungal dose dependent side-effects can be significant restricting physician use and variability in lung concentration limit the ability to maximize therapeutic effect
- Physicians desire additional antifungal treatment options
- Inhalation of itraconazole directly to the airways should allow for higher exposure where *Aspergillus* is present
- Pulmazole profile would lead to significant treatment adoption

# Pulmazole Has Up to \$1.5B Peak Revenue Potential in the U.S.

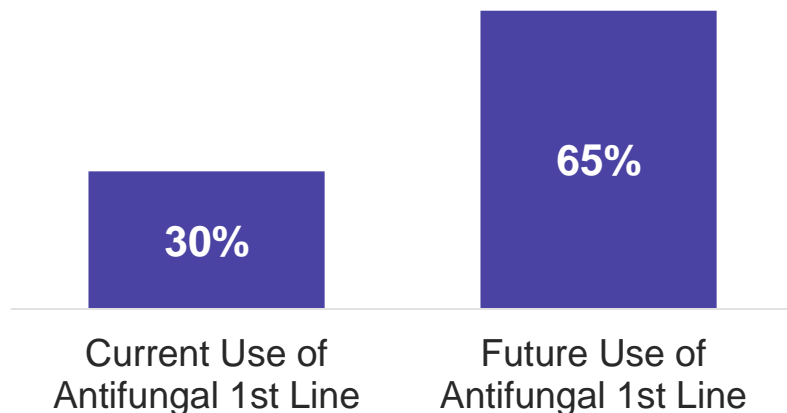


## Payers and Physicians Interviewed See Logic in Pulmazole Value Proposition

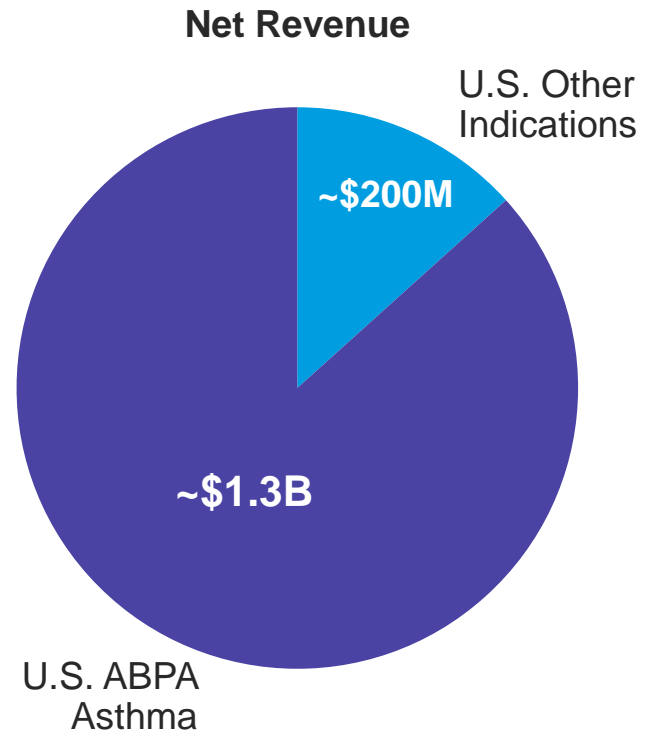
- Payers suggested **~70%** market access\*\*\*
- Payers indicated **~\$40K/year** asthma biologic price with restrictions to specialty use and label
- Physicians indicated **67%** addressable market penetration with Pulmazole\*\*

## 1<sup>st</sup> Line Antifungal Usage May More than Double

% of Antifungal Use 1<sup>st</sup> Line with Steroids



## Pulmazole U.S. Peak Revenue Forecast\*



Source: Physician Interviews; Payer Interviews; ClearView Analysis. \*Also includes discount for patient compliance, patient persistence, and gross-to-net adjustment; \*\* Estimate based on ClearView Analysis, which included qualitative physician surveys and interviews; \*\*\* Estimate based on ClearView Analysis, which took into account uninsured patients, patients who are unwilling to pay, and projected access restrictions placed by payers; \* Peak revenues expected at loss of market exclusivity, ~11 years post launch

# Phase 1/1b Data Highlights Potential of Pulmazole to Improve Upon Clinical Utility of Oral Sporanox



## Ph1/1b Study SUCCESSFULLY Met All Endpoints

### Phase 1/1b : Safety, Tolerability & PK Study in Healthy Normal Volunteers and Asthmatics

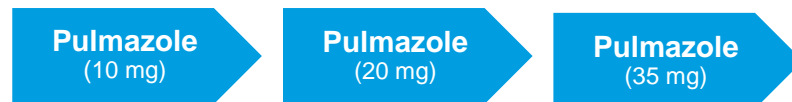
#### Part 1: Single Ascending Dose

Healthy Normal Volunteers (n=6/cohort): Optional 4<sup>th</sup> cohort of 35 mg



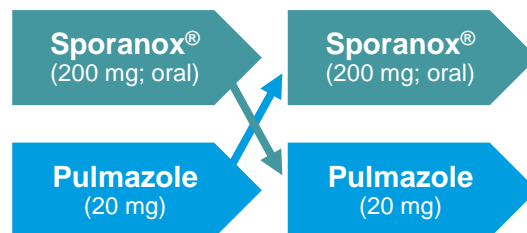
#### Part 2: Multiple Ascending Dose

Healthy Normal Volunteers (n=5-6/cohort)



#### Part 3: Single Dose Crossover

Asthmatics (n=16)



### Parts 1 and 2 in HNIV

- ✓ Demonstrated **safety** and **tolerability** of Pulmazole administered up to 14 days
- ✓ Following inhalation of Pulmazole, total **systemic exposure** over 24 hours is **~100-400 fold lower** than that expected with Sporanox

### Part 3 SD in Stable Asthmatics

- ✓ Demonstrated **safety** and **tolerability** of Pulmazole administered as a single dose in asthmatics
- ✓ **~50 fold higher lung exposure** following inhalation of Pulmazole compared to Sporanox despite inhaling only 1/10 the dose
- ✓ **~85 fold lower plasma exposure** than oral Sporanox



# Global Thought Leaders in ABPA and Asthma on the Pulmazole Clinical Advisory Board (CAB)



**Ritesh Agarwal, MD, DM** – Professor of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India

**David Denning, FRCP, FRCPath, FIDSA, FMedSci** – Professor of Infectious Diseases in Global Health; President, Global Action Fund for Fungal Infections; Director, National Aspergillosis Centre, Manchester, UK

**Cendrine Godet, MD** – Doctor of Infectious Diseases and Pulmonary Medicine at Poitiers University Hospital, France; Coordinator of the French National Board for Chronic Fungal Infection and Secretary of the European CPA-net Board for Chronic Pulmonary Aspergillosis

**Richard B. Moss, MD** – Professor Emeritus, Pediatrics-Pulmonary Medicine at Stanford University School of Medicine, Stanford, CA

**David A. Stevens, MD, FACP, FAAM, FIDSA** – Professor Emeritus, Infectious Diseases and Geographic Medicine at Stanford University School of Medicine, Stanford, CA; President, California Institute for Medical Research, San Jose, CA

**Peter Wark, BMed PhD FRACP ThorSoc** – Conjoint Professor, Centre for Healthy Lungs, University of Newcastle & Department of Respiratory and Sleep Medicine John Hunter Hospital, New Lambton NSW, Australia

**William J Calhoun, MD** – Professor and Vice Chair for Research, Divisions of Pulmonary, Critical Care and Sleep, and Allergy/Immunology. Department of Medicine at University of Texas Medical Branch, Galveston TX

**Mario Castro, MD, MPH, FCCP** – Professor of Medicine, Pediatrics, and Radiology, Division of Pulmonary and Critical Care Medicine at the Washington University School of Medicine in St. Louis, MO

**Jonathan Corren, MD** – Associate Clinical Professor of Medicine and Pediatrics, David Geffen School of Medicine at UCLA, Los Angeles, CA

**Russell Settipane, MD** – Clinical Professor of Medicine at Brown Medical School, Director of the Allergy & Asthma Center, Providence, RI; Associate Editor of Allergy & Asthma Proceedings and the Journal of Precision Respiratory Medicine, President Eastern Allergy and Eastern Pulmonary Conferences

**Michael Wechsler, MD, MMSc** – Professor of Medicine, Director, NJH Cohen Family Asthma Institute, Dept. of Medicine, National Jewish Health, Denver, CO

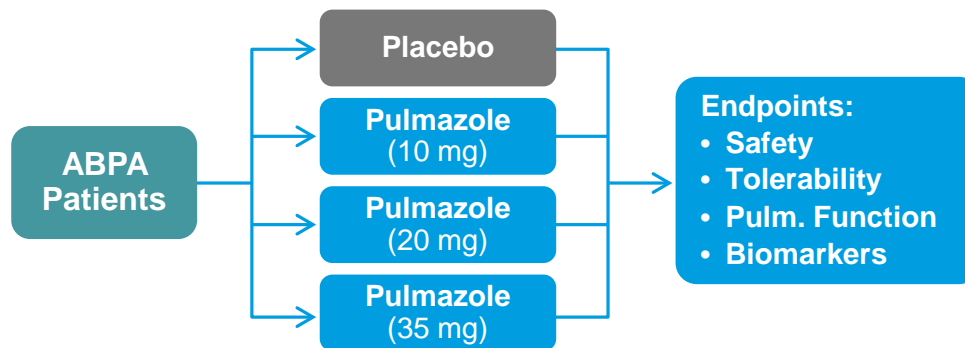


# Phase 2 Scheduled to Begin 4Q 2018 and Expected to Support Proof of Mechanism in Patients with Asthma-ABPA



## 28-day Safety, Tolerability, Pulmonary Function and Biomarker Study in Asthmatic ABPA Patients

Randomized, double-blind, placebo controlled study (1:1 randomization; each cohort n = 16).



### Primary Endpoint

- Safety & Tolerability

### Other Endpoints

- Plasma and sputum PK
- Pulmonary Function (FEV<sub>1</sub>)
- Sputum and plasma eosinophils
- IgE and IgG (specific to *A. fumigatus* antigens) plasma concentrations
- Aspergillus burden in sputum
- Disease control (ACQ-6)
- FeNO



### Patient Profile

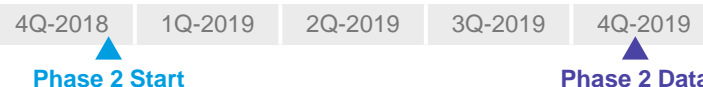
- Moderate-to-severe asthmatics (M/F, ages 18-65) confirmed/stable ABPA, diagnosed with ABPA
- Exacerbation and steroid use entry criteria

### Anticipated Outcomes and Value Catalysts



- Establish safety and tolerability of Pulmazole over 4 weeks in patients with ABPA
- Reductions in relevant biomarkers of inflammation in ABPA increase confidence that longer treatment will achieve clinically significant improvements in Phase 2b/3
- Evaluating impact on microbiology including Aspergillus burden in sputum, further substantiating link between fungal burden and other biomarkers / efficacy
- Demonstrate directional improvement in FEV<sub>1</sub> as a potentially approvable endpoint

FeNO = Fractional Exhaled Nitric Oxide; PK = Pharmacokinetics; ACQ-6 = Asthma Control Questionnaire 6

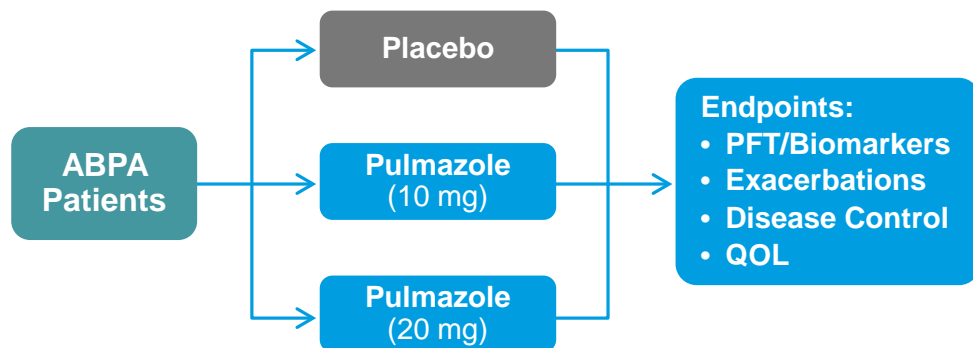


# Phase 2b/3 Proof of Concept Trial Powered to Show Improvement in FEV<sub>1</sub>



## Phase 2b/3: POC Efficacy/Safety Trial in Asthmatic ABPA Patients

Randomized, double-blind, placebo controlled study (n=85 per arm). 16 weeks dosing with 16 weeks follow-up.



### Patient Profile

- Moderate-to-severe asthmatics (M/F, ages 18-65) confirmed/stable ABPA, diagnosed with ABPA
- Exacerbation and steroid use entry criteria

### Primary Efficacy Endpoint

- FEV<sub>1</sub>

### Secondary Endpoint

- Disease control (ACQ-6)
- Exacerbation (frequency/timing)
- Steroid use

### Exploratory Biomarkers

- Sputum/plasma eosinophils
- IgE and IgG (specific to *A. fumigatus* antigens) plasma concentrations
- Aspergillus burden in sputum
- FeNO

### Anticipated Outcomes and Value Catalysts



- Demonstrate clear efficacy signal in FEV<sub>1</sub> and/or exacerbations (clinically relevant endpoints)
- Establish safety and tolerability of Pulmazole over 32 weeks in patients with ABPA
- Substantiate correlation between clinical outcomes and ABPA biomarkers and fungal burden in lungs

2Q-2020

3Q-2020

4Q-2020

1Q-2021

2Q-2021

3Q-2021

4Q-2021

Phase 2b/3 Start

Phase 2b/3 Data

## PUR1800 – Narrow Spectrum Kinase Inhibitor (NSKI)



Inhaled P38, Syk, Src Kinase Inhibitor to Treat Acute Exacerbations in COPD (AECOPD)

# PUR1800 (NSKI): Prescribers Predict PUR1800 Will Become Integral to Standard of Care



## The PUR1800 Advantage

<b>Target Product Profile</b>	<ul style="list-style-type: none"> <li>• SOC* + Placebo vs. SOC* + PUR1800</li> <li>• Acute treatment, not prevention, paradigm</li> <li>• 4-week treatment period and 24-week follow up period</li> <li>• Primary Endpoint: &gt;100ml FEV<sub>1</sub> improvement vs. SOC</li> </ul>
<b>Unmet Need in AECOPD</b>	<ul style="list-style-type: none"> <li>• Steroid resistant AECOPD</li> <li>• Steroidal lack of efficacy in viral and/or bacterial driven AECOPD</li> <li>• 20%–50% treatment failure or only partial response with oral steroids</li> </ul>
<b>PUR1800 Value Drivers</b>	<ul style="list-style-type: none"> <li>• Acting across 3-kinase, expected efficacy in viral, bacterial and eosinophilic driven AECOPD</li> <li>• Non-steroidal, inhaled anti-inflammatory with low systemic exposure</li> </ul>

## Prescriber Reported PUR1800 Utilization

Treatment Option	Current Use	Expected Use
PUR1800 (plus oral corticosteroids and/or antibiotics)	0%	~35%
Oral Corticosteroids + Antibiotics	~58%	~34%
Antibiotics Alone	~13%	~10%
Oral Corticosteroids Alone	~25%	~18%
No Treatment	~4%	~3%

Source: Physician Interviews; Physician Quantitative Survey; ClearView Analysis. Physician Reported Utilization in Moderate-to-Severe Acute Exacerbations.

\* Standard of Care (SOC) is oral corticosteroids with or without antibiotic

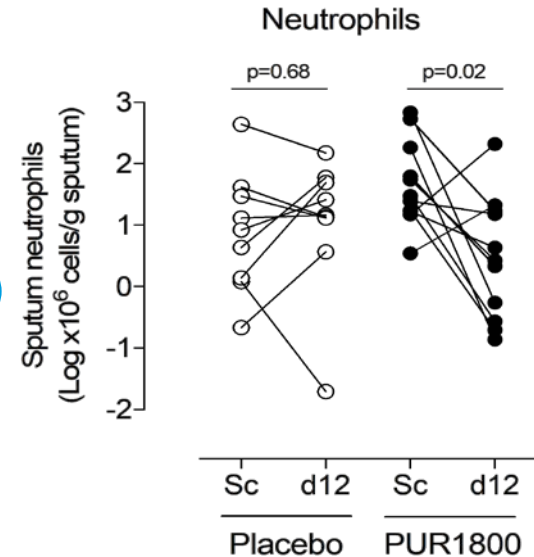
# PUR1800: Inhaled NSKI Has Up to \$2.4B Peak Revenue Potential in the U.S.



## Large Addressable AECOPD Burden

- ~16M COPD patients in the U.S.
- 77% experience at least one exacerbation annually
- ~18M moderate-to-severe AECOPD episodes annually
- > 20% corticosteroid treatment failure rate in moderate-to-severe AECOPD patients
- PUR1800 potentially has efficacy across the spectrum of causes of AECOPD

Clinical Precedent with this NSKI in Phase 1/1b COPD



## PUR1800 Up to \$2.4B U.S. Peak Revenue\* Opportunity in AECOPD

### PUR1800 Market Opportunity

- Up to 35% expected use\*\*, in addition to standard of care (oral corticosteroids plus/minus antibiotic)

### Pricing Potential & Market Access

- 70% payer market access\*\*\* with minimal use restrictions
- Targeting \$650 per incident launch price

Source: Aaron SD et al. *N Engl J Med*. 2003; 348(26): 2618-25. CDC Behavioral Risk Factor Surveillance System, 2013. Celli BR et al. *Eur Respir J* 2007; 29: 1224–1238. Chronic obstructive pulmonary disease (COPD): Fact sheet. (2014, May). Chronic obstructive pulmonary disease (COPD): Fact sheet. (2014, May). Hurst JR et al. *N Engl J Med* 2010; 363(12): 1128-38. Soriano JB et al. *Chest*, 2013; 143(3): 694-702. Wise RA, et al. *Chronic Obstr Pulm Dis* (Miami). 2017; 4(1): 7-20. EST001 Study with 35 healthy subjects and 30 subjects with moderate-to-severe COPD

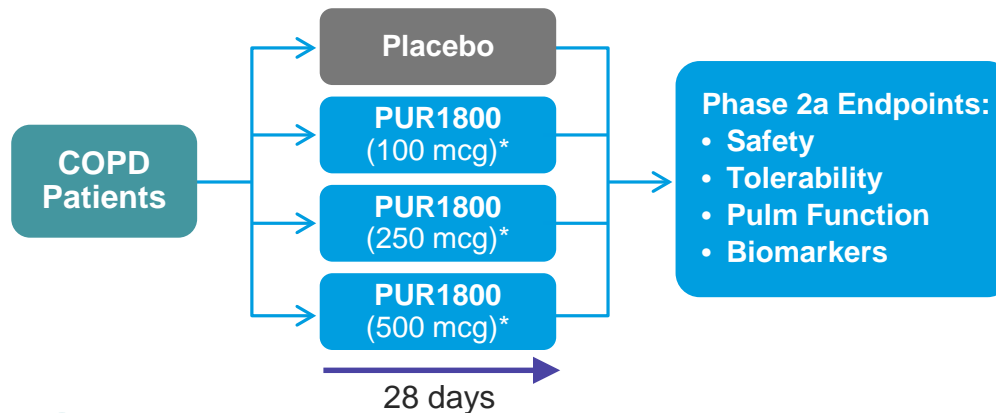
\*Also includes discount for patient compliance, patient persistence, and gross-to-net adjustment; \* Peak revenues expected at loss of market exclusivity, ~14 years post launch; \*\* Estimate based on ClearView Analysis, which included qualitative physician surveys and interviews; \*\*\* Estimate based on ClearView Analysis, which took into account uninsured patients, patients who are unwilling to pay, and projected access restrictions placed by payers; NSKI = Narrow Spectrum Kinase Inhibitor; AECOPD = Acute Exacerbations of COPD

# PUR1800 Phase 2a Study in Stable COPD (RV1162 to PUR1800 Bridging Study)



## Safety/Tolerability and PK Study of iSPERSE PUR1800 (NSKI) in Stable Moderate-Severe COPD Patients

### Randomization (1:1)



### Primary Endpoint

- Safety & Tolerability

### Other Endpoints

- Single dose PK profile
- Multiple dose PK profile over 14 and 28 days
- Pulmonary function
- Exploratory biomarkers
  - Target engagement
  - Sputum biomarkers



### Patient Profile

- Moderate-to-Severe COPD Patients
- $30\% \leq FEV_1 < 80\%$ ; n=60; 12–15 patients per arm

225 mcg iSPERSE PUR1800  $\approx$  500 mcg Janssen RV1162 Lactose Blend (based on predicted lung deposition)

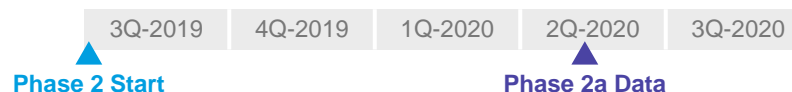
\*Doses to be administered daily for 28 days and confirmed following 4Q 2018 completion of GLP tox study

### Anticipated Outcomes and Value Catalysts



- Establish safety and tolerability of PUR1800 over 4 weeks in patients with stable COPD
- Evaluate kinase target engagement and biomarker activity to demonstrate anti-inflammatory effect

FEV<sub>1</sub>: Forced Expiratory Volume in 1 Second



## PUR0200 – Long Acting Muscarinic Agonist (LAMA)



Inhaled Tiotropium Bromide for Treatment of Chronic Obstructive  
Pulmonary Disease (COPD)

# PUR0200: Out-License Creates Revenue Stream and Further Prioritizes Pulmazole and PUR1800



We Believe PUR0200 is an Improved Version of the Spiriva® HandiHaler®



*Equivalent Lung Exposure at 80% Nominal Dose*

## Unmet Needs

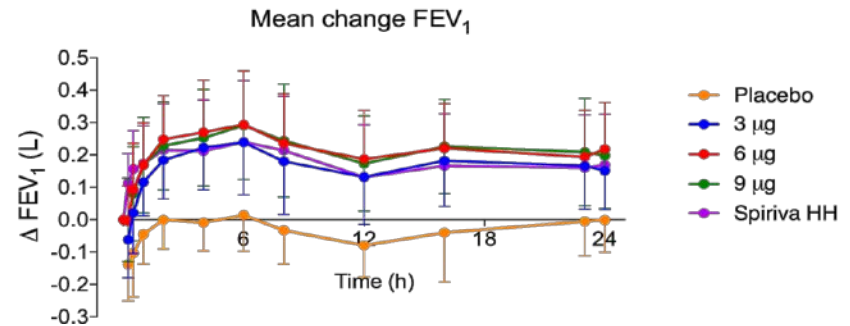
- Spiriva® \$3.5B WW revenues in 2016
- Spiriva lacks a dry-powder multi-dose inhaler in the U.S.
- In the rest of world, there is a need for therapeutically equivalent, lower cost products

## Vectura Deal Structure & Future Activity

- Out-licensed PUR0200 and PUR0200 combination products for U.S.
- \$1M milestone and revenue share
- No further investment by Pulmatrix to develop and commercialize
- Pursuing PUR0200 ex-U.S. out-license

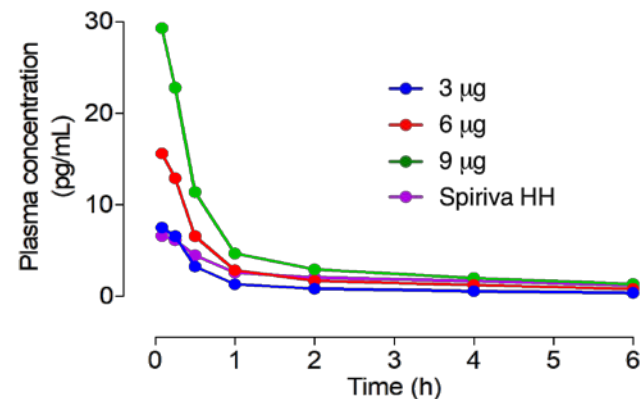
## PUR0200 Improves Lung Function in COPD at Low Doses (6x as Potent as Spiriva®)

n = 60 COPD PATIENTS



## PUR0200 Shows Comparable Systemic Exposure to Spiriva® at a Lower Dose

n = 60 COPD PATIENTS





## Summary



# Robust Pipeline with Projected Significant Value Catalysts\*



Product Pipeline	Indication	2H 2018	2019	1H 2020	Milestone
<b>Pulmazole</b> <i>Anti-fungal</i>	Allergic Bronchopulmonary Aspergillosis (ABPA) in Patients with Asthma		Phase 2		Phase 2 4Q 2019
<b>PUR1800</b> <i>NSKI</i>	Acute Exacerbations of COPD (AECOPD)	★ 28-Day Tox		Phase 2a	Phase 2a 2Q 2020
<b>PUR5700</b> <i>NSKI</i>	Idiopathic Pulmonary Fibrosis (IPF)		Pre-Clinical		Pre-clinical

## Potential Future Revenue Opportunities

<b>PUR0200-US</b> <i>LAMA</i>	Chronic Obstructive Pulmonary Disease (COPD)			Phase 1	Out-Licensed to Vectura for U.S. 09/2017
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# Experienced Leadership Team With Experience to Execute and Deliver Value



## Management Team



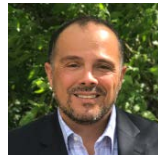
**Robert Clarke, PhD**  
CEO



**Bill Duke, MBA**  
CFO



**David Hava, PhD**  
CSO



**Ted Raad, MBA**  
CBO



**Jim Roach, MD**  
CMO

## Strong Background in Product Development and Commercialization

- Proven fundraising and capital management ability
- Experienced R&D team focused on pulmonary drug delivery and the role of inhaled particles
- Commercialization and partnership experience

## Board of Directors



**Mark Iwicki**  
Chairman



**Matthew Sherman**  
BOD



**Terry McGuire**  
BOD Investor



**Steve Gillis, PhD**  
BOD Investor



**Michael Higgins**  
BOD-Audit Chair



**Amit Munshi**  
BOD

## Diverse Collective Experience at Leading Respiratory Companies



# Pulmatrix is Positioned to Create Significant Value in the Near Term



## Investment Thesis

- ✓ Compelling Ph1/1b data demonstrating high itraconazole lung concentration and low plasma concentration with Pulmazole compared to Sporanox
- ✓ Ph2a proof of mechanism clinical study readout in 4Q 2019 with product exceeding \$1B in peak revenue potential
- ✓ Pulmazole is a “de-risked” 505(b)(2) program
- ✓ Rigorous clinical development plans developed in collaboration with global thought leaders in ABPA, asthma and COPD
- ✓ Robust product portfolio, including PUR5700 and PUR1800 with billions of peak revenue potential in major pulmonary diseases like COPD and IPF
- ✓ Underlying iSPERSE™ intellectual property carries well into 2030’s with additional patent protection through specific drug development



# Glossary of Terms

- **ABPA** – Allergic Bronchopulmonary Aspergillosis
- **ACQ-6** – Asthma Control Questionnaire 6
- **AECOPD** – Acute Exacerbations of Chronic Obstructive Pulmonary Disease
- **CAB** – Clinical Advisory Board
- **CF** – Cystic Fibrosis
- **COPD** – Chronic Obstructive Pulmonary Disease
- **FeNO** – Fractional Exhaled Nitric Oxide
- **FEV<sub>1</sub>** – Forced Expiratory Volume in 1 Second
- **FPI** – First Patient In
- **FVC** – Forced Vital Capacity
- **HNV** – Healthy Normal Volunteers
- **IgE** – Immunoglobulin E Antibodies
- **IgG** – Immunoglobulin G Antibodies
- **IP** – Intellectual Property
- **KOL** – Key Opinion Leader
- **MAD** – Multiple Ascending Dose
- **MAPK** – Mitogen-Activated Protein Kinases
- **MOA** – Mechanism of Action
- **NSKI** – Narrow Spectrum Kinase Inhibitor
- **PBO** – Placebo
- **PEF** – Peak Expiratory Flow
- **PK** – Pharmacokinetics
- **POC** – Proof of Concept
- **POM** – Proof of Mechanism
- **Pulmazole** – PUR1900
- **qPCR** – Quantitative Polymerase Chain Reaction
- **SAD** – Single Ascending Dose
- **SD** – Single Dose
- **Spiriva HH** – Spiriva® HandiHaler® (18 µg dose)
- **Sporanox** – Oral Itraconazole 200mg

# PULMATRIX Corporate Overview



August 2018