



# Corporate Overview

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## Developing New Therapies *for* Rare Respiratory Diseases

January 2023



# Safe Harbor Statement

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Savara Inc. (“Savara” or the “Company”) cautions you that statements in this presentation that are not a description of historical fact are forward-looking statements which may be identified by the use of words such as “expect,” “intend,” “plan,” “anticipate,” “believe,” and “will,” among others. Such statements include, but are not limited to, statements regarding the nature, strategy and focus of Savara; the Savara investment thesis; the timing, design and other matters related to clinical trials of our product candidate; the safety, efficacy and projected development timeline of our product candidate; the potential health benefits of our product candidate; our anticipated corporate milestones; the potential market size, commercial opportunity, and competitive landscape for our product; and the sufficiency of our resources to fund the advancement of our development program and potential sources of additional capital. Savara may not actually achieve any of its plans or product development goals in a timely manner, if at all, or otherwise carry out its current intentions or meet the expectations or projections disclosed in its forward-looking statements, and you should not place undue reliance on these forward-looking statements. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These forward-looking statements are based upon Savara's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, the risks and uncertainties related to the impact of the COVID-19 pandemic and geopolitical conditions on our business and operations; risks and uncertainties associated with the ability to project future cash utilization and reserves needed for contingent future liabilities and business operations; the availability of sufficient resources for our operations and to conduct or continue planned clinical development programs; the timing and ability of Savara to raise additional capital as needed to fund continued operations; the ability to successfully conduct clinical trials for our product candidate; the ability to successfully develop our product candidate; and the risks associated with the process of developing, obtaining regulatory approval for and commercializing drug candidates that are safe and effective for use as human therapeutics. The risks and uncertainties facing Savara are described more fully in Savara's filings with the Securities and Exchange Commission including our filings on Form 8-K and our Annual Report on Form 10-K for the fiscal year ended December 31, 2021.

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# Executive Leadership Team

**Matthew Pauls, J.D., M.B.A.**  
*Chair & Chief Executive Officer*

**Ray Pratt, M.D. FACP**  
*Chief Medical Officer*

**Dave Lowrance**  
*Chief Financial & Administrative Officer*

**Peter Clarke, Ph.D.**  
*EVP, Global Technical Operations*

**Scott Wilhoit**  
*EVP, Global Commercial*

**Anne Erickson**  
*SVP, Head of Global Business Operations*

**Charles LaPree**  
*SVP, Global Regulatory Affairs  
and Quality Assurance*

**Kate McCabe, J.D.**  
*SVP, General Counsel*



# Pursuing Transformative Therapies for Rare Respiratory Diseases

**Focused** on single Phase 3 program: molgramostim nebulizer solution (molgramostim) in autoimmune pulmonary alveolar proteinosis (aPAP)

- Recombinant form of human granulocyte-macrophage colony-stimulating factor (GM-CSF)
- Favorable efficacy and safety data generated from the first IMPALA trial
- Pivotal Phase 3 trial underway – builds on key learnings from IMPALA

**Seasoned** management team

- Deep experience in the development and commercialization of rare respiratory therapeutics and pulmonary medicines

**Capitalized** through major clinical and regulatory milestones

- ~\$134M\* in cash expected to fund company ~18-months beyond Phase 3 data read-out, beyond BLA filing, and through potential approval

**Quality** investor base

# Investment Thesis



**The molgramostim in aPAP clinical program has a high probability of success**



**As a novel inhaled biologic, molgramostim has the potential for a long-term, durable revenue stream**



**Significant global commercial opportunity**



**Strong balance sheet –funded through 2025**



# Molgramostim Key Highlights



## June 2019: IMPALA clinical trial results

- Randomized, double-blind, 24-week, placebo-controlled trial
- Primary endpoint of alveolar-arterial oxygen gradient (A-aDO<sub>2</sub>) not met
- Improvements in St. George's Respiratory Questionnaire (SGRQ) suggest molgramostim may improve health status in patients with aPAP

## Sept. 2020: IMPALA results published in *New England Journal of Medicine*



Data demonstrating synchronous improvement across multiple outcome measures that reflect physiological, clinical, radiologic, and biochemical disease manifestations provide strong support for a beneficial treatment effect of molgramostim in aPAP

## June-Aug. 2022: UK's Medicines and Healthcare Products Regulatory Agency (MHRA) awarded molgramostim Innovation Passport and Promising Innovative Medicine Designations



## End of 2Q 2021: First patient dosed in Phase 3 IMPALA-2 Trial

- Randomized, double-blind, 48-week, placebo-controlled trial
- Informed by key learnings from IMPALA trial

## Dec. 2019: FDA granted molgramostim Breakthrough Therapy Designation for aPAP



## May 2016: Phase 1 clinical trial of molgramostim:

May 2016, presented results from randomized, double-blind, 7-day, placebo-controlled trial at American Thoracic Society (ATS)

← 2016

2019

2020

2021

2022

Q1

Q2

Q3

Q4

Q1

Q2

Q3

Q4

Q1

Q2

Q3

Q4

Q1

Q2


Q3

Q4

# IMPALA-2 Key Milestones

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- Expect top line data readout end of 2Q 2024
- Upon a successful trial, Company plans to submit regulatory applications in the US, UK, EU, and Japan



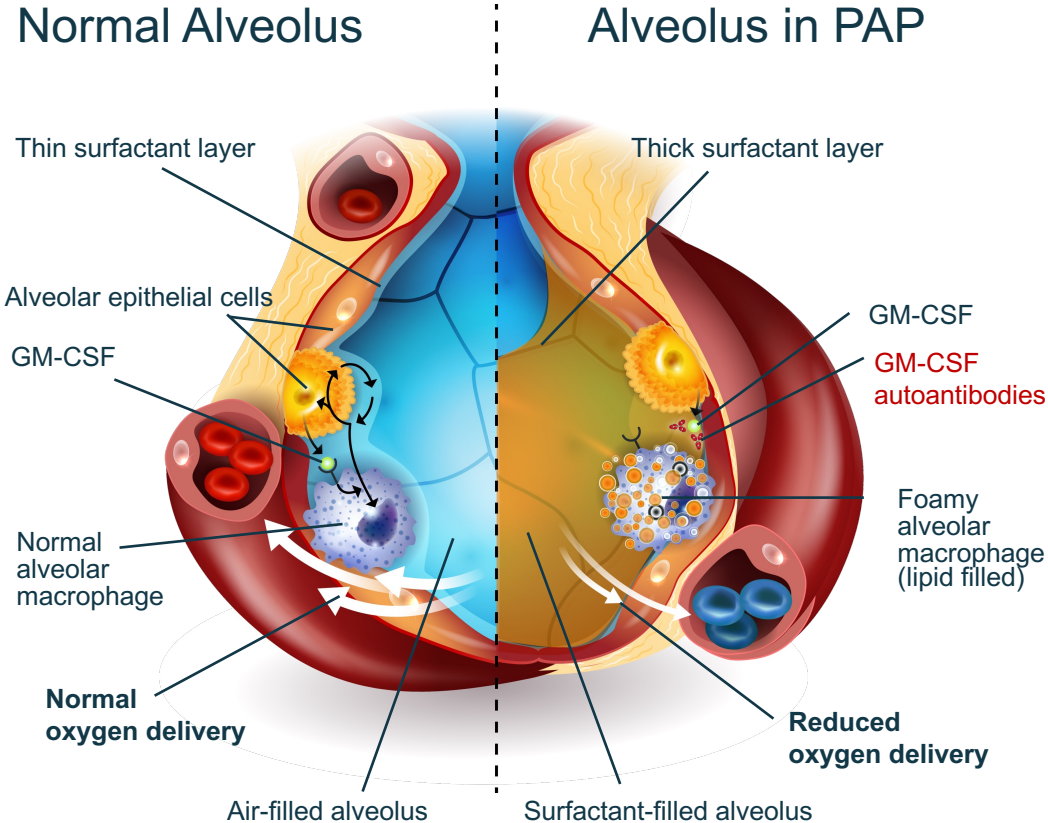
**Company operations  
funded through 2025  
(~18-months beyond  
anticipated IMPALA-2  
top line results)**

# Molgramostim

Molgramostim for Autoimmune Pulmonary  
Alveolar Proteinosis (aPAP)



# aPAP: A Disease of Alveolar Macrophage Dysfunction



## Alveolar macrophages

Need GM-CSF for maturation, expansion, and function (e.g., surfactant clearance)

## GM-CSF

Critical to alveolar homeostasis, structure, function, and host defense

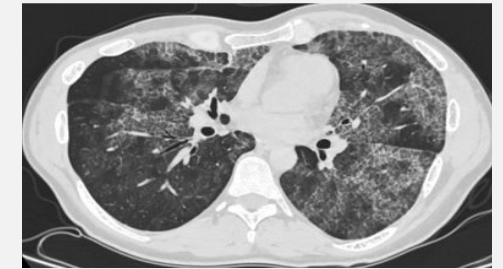
## aPAP

Caused by GM-CSF autoantibodies which block GM-CSF signaling and reduce surfactant clearance

Surfactant accumulation causes altered gas exchange in the lung, reduced blood oxygenation and, ultimately, hypoxemic respiratory failure

## aPAP PATIENT

Baseline  
(Week 0)



After  
Treatment  
(Week 24)



From IMPALA trial

# aPAP is a Rare, Long-Term, Chronic Disease

## Progressive Shortness of Breath



- Gas exchange in the lungs is impaired and patients may experience shortness of breath
- At first it occurs upon exertion, but as disease progresses, it can occur even when a person is at rest

## Cough and Episodes of Fever



- Cough, sputum production, and episodes of fever, especially if secondary lung infection develops

## Fatigue, Decreased Exercise Tolerance



- Fatigue and significantly reduced exercise capacity can dramatically impact the simplest of daily activities, e.g., getting winded walking up a flight of stairs

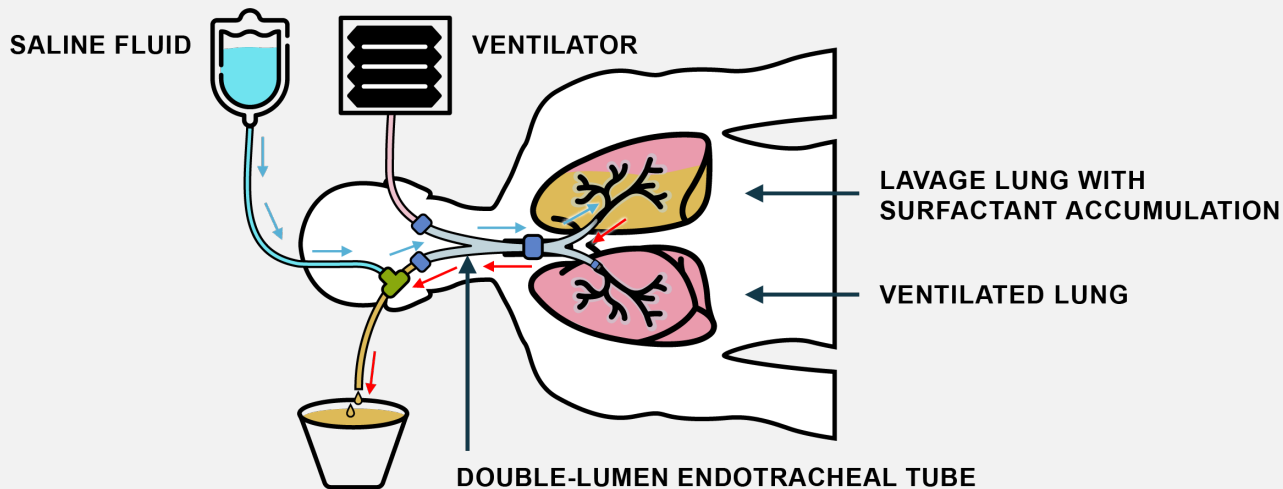
## Fibrosis and Lung Transplant



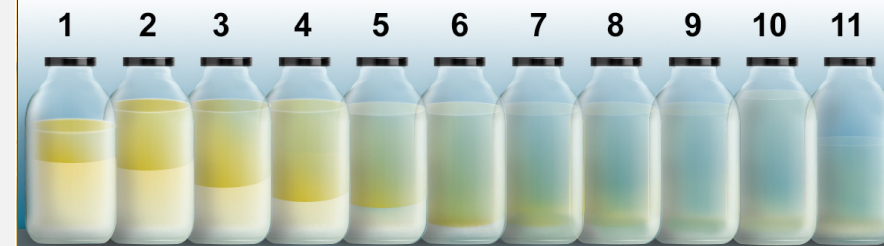
- In the long-term, the disease can lead to serious complications, including fibrosis, often leading to the need for lung transplantation

**There are no approved drugs for the treatment of aPAP.  
Only option is whole lung lavage, an invasive procedure.**

- Whole lung lavage is an invasive procedure to physically remove excess surfactant from the lungs and requires hospitalization
- Performed under general anesthesia by highly experienced physicians at certain sites



## Whole Lung Lavage is a Highly Invasive Procedure Performed in a Tertiary Center and is Not Standardized



Requires insertion of double-lumen endobronchial tube for lung separation

Treated lung is repeatedly filled with up to 15-50L of saline and then drained by gravity

Patient is percussed to emulsify the surfactant sediment

Saline is drained by gravity and continued until lavage fluid becomes clear

Sources: 1: Campo, Assessment and Management of PAP in a Reference Center, Orphanet Jour. of Rare Dis., 2013; 2: Campo, Nat. History of PAP Data from Italian Nat. Reference Center, ERJ, 2019.; Seymour, J. J. Pulmonary alveolar proteinosis: Progress in the First 44 Years, Am. J. Respir Crit. Care Med, 2002.

# Complications and Short-Comings of Whole Lung Lavage



## Potential Complications

- Rib fracture
- Hypoxia
- Pneumothorax (collapsed lung)
- Hydrothorax (fluid in pleural cavity)
- Superimposed infection
- Acute Respiratory Distress Syndrome (ARDS)



## Short Comings

- Treatment fails to address pathophysiology of disease
- Patients continue to experience symptomatic deterioration between procedures – and can require more than one whole lung lavage
- Rollercoaster ride of improvement and decline
- The procedure, performed under general anesthesia, is not standardized and remains highly operator-dependent

# Journey to Diagnosis Can Be Long and Misdiagnosis is Common

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**Due to aPAP's rarity and associated non-specific symptoms, patients are often misdiagnosed with more common pulmonary illnesses (e.g., recurrent pneumonia, chronic bronchitis, COPD, asthma)**



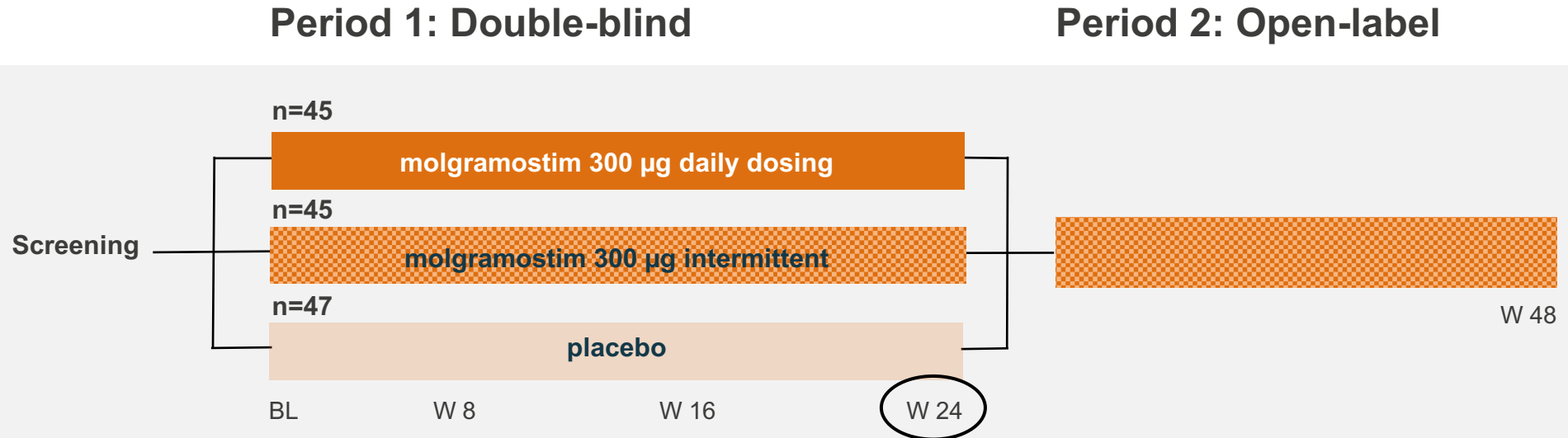
**Diagnostic tests typically conducted to rule-out other more common pulmonary diseases:**

- Imaging
- Pulmonary function tests
- Secondary PAP testing
- Transbronchial biopsy and cytological analysis of bronchoalveolar lavage fluid



# IMPALA Clinical Trial Design

○ = Primary efficacy analyses



## Primary Endpoint\*

- Change from baseline in A-aDO<sub>2</sub>

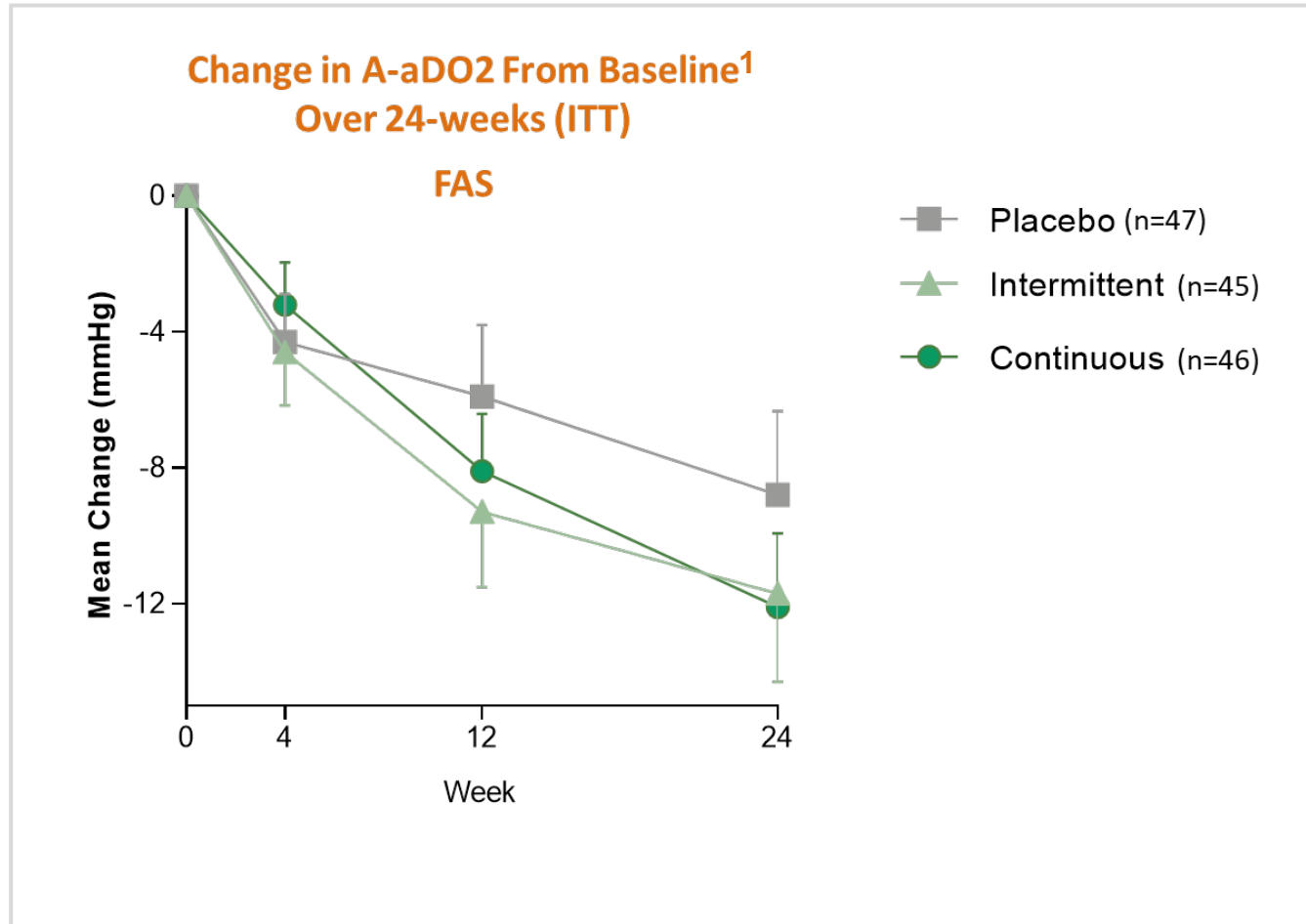
## Secondary Endpoints\*\*

- 6-minute walk distance
- SGRQ
- Time to whole lung lavage/requirement for whole lung lavage

\*Primary analysis: Continuous dose vs. placebo

\*\*Secondary endpoints: Analyzed in parallel and corrected for multiplicity

# IMPALA Trial Did Not Meet the Primary Endpoint



1: Trapnell, Inhaled Molgramostim Therapy in aPAP, NEJM, 2020.

## Continuous Once Daily Dosing Regimen (OD)

Full Analysis Set (FAS)\*  
Estimated treatment difference of  
-4.6 mmHg (p=0.17)

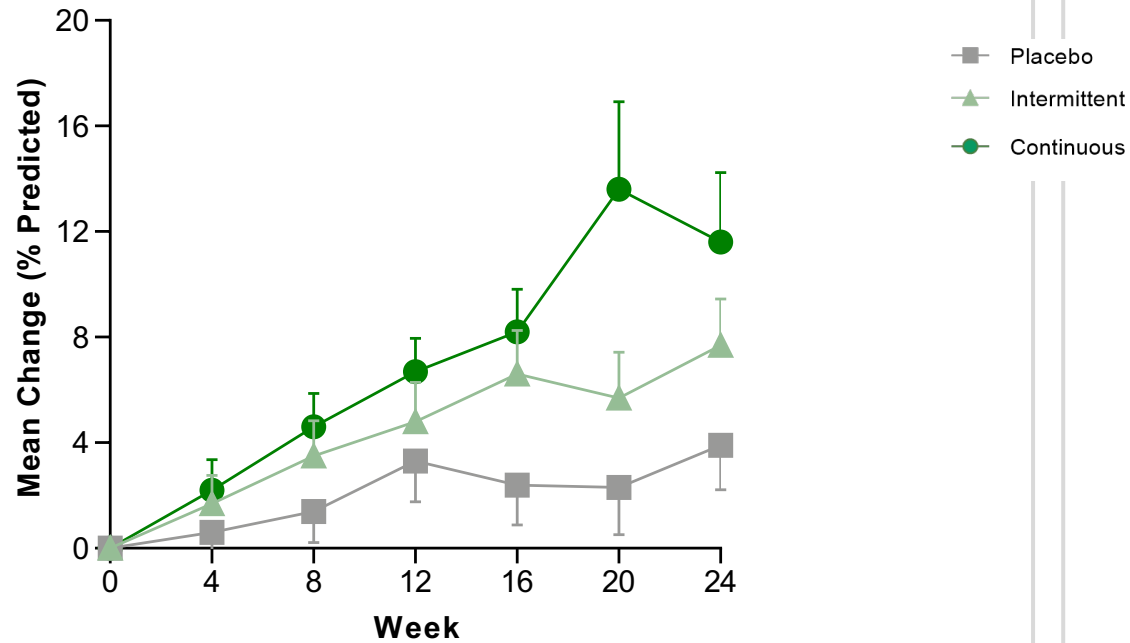
Revised FAS†  
Estimated treatment difference of  
-6.5 mmHG (p=0.025)

\*Protocol specified analysis (ITT).

†Revised analysis excludes 4 patients using supplemental oxygen during testing (placebo: n=2, intermittent: n=1, continuous: n=1).

# IMPALA: DLCO and SGRQ Showed Robust Improvement with Continuous Once Daily (OD) Dosing Regimen

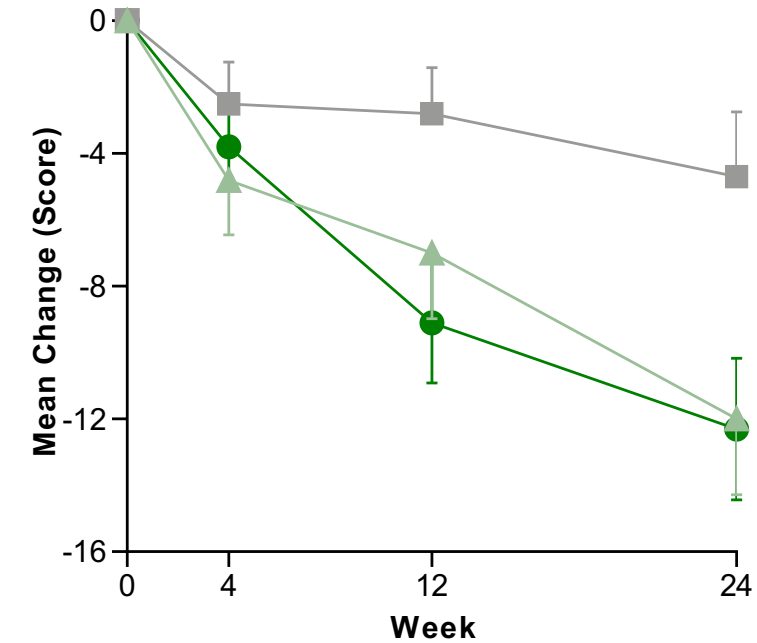
Change in Diffusion Capacity for Carbon Monoxide (DLCO) From Baseline Over 24-weeks<sup>1</sup> (FAS)



OD estimated treatment difference of 7.9% predicted (p=0.007)

IMPALA-2 Primary Endpoint

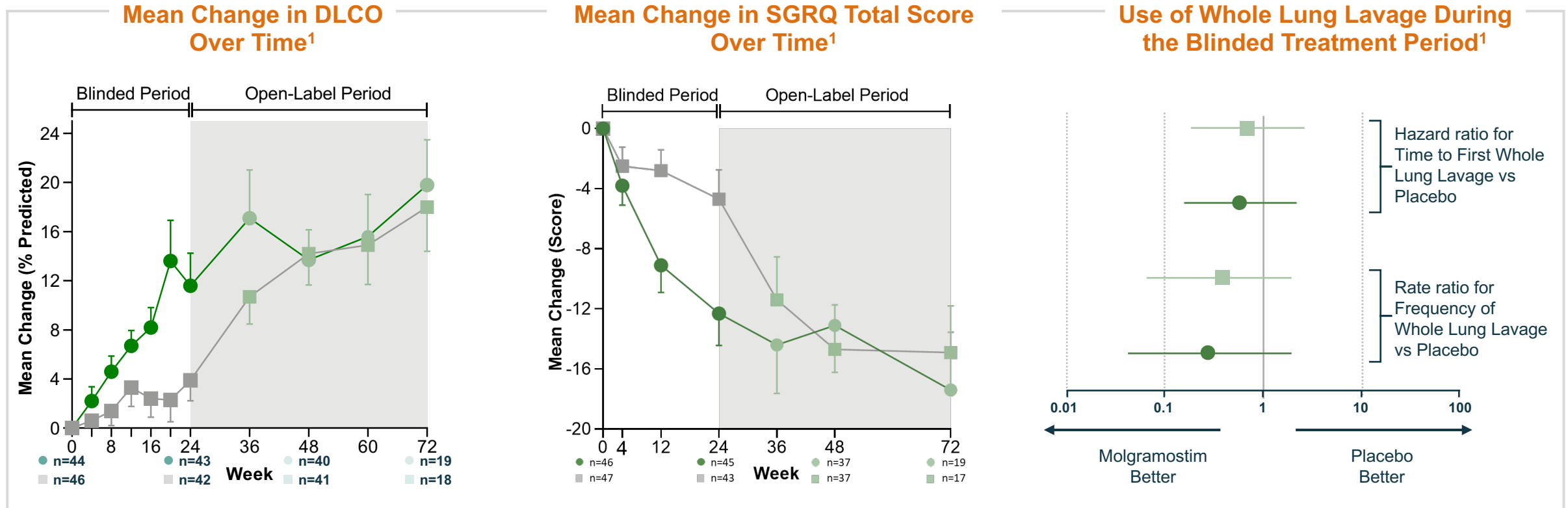
Change in St. George's Respiratory Questionnaire (SGRQ) From Baseline Over 24-weeks<sup>1</sup> (FAS)



OD estimated treatment difference of 7.6 points (p=0.01)

IMPALA-2 Secondary Endpoint

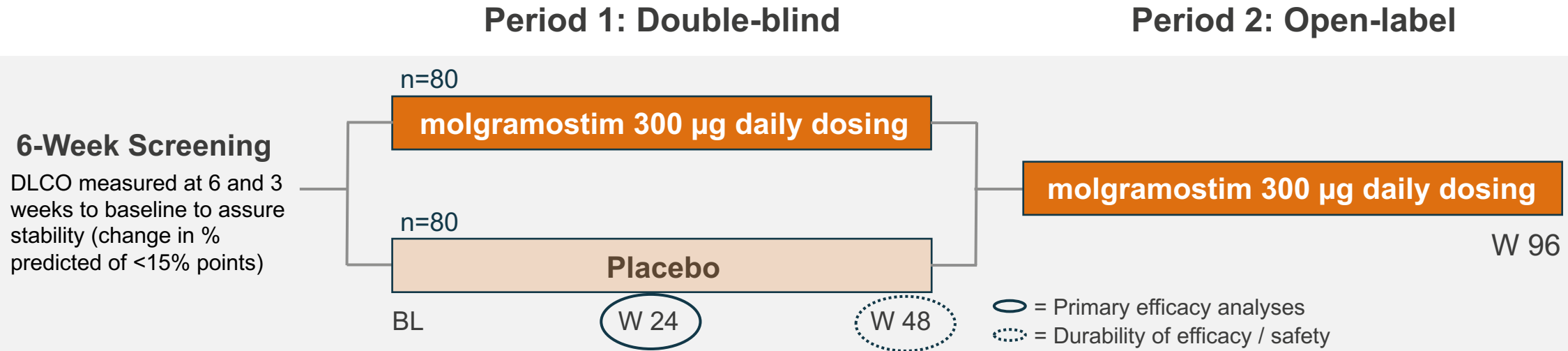
# IMPALA Open-Label Data Show Sustained Effect, or Continued Improvement, after Longer-Term Drug Exposure



● Continuous molgramostim    ■ Placebo    ● Intermittent molgramostim

Dosing schedules for blinded and open-label periods were different.  
All patients received intermittent molgramostim during open-label period.

# Phase 3 IMPALA-2 Trial Design Leverages Key Learnings from IMPALA



## Primary Endpoint

- Change from baseline in DLCO
  - 90% powered to detect 5.7% predicted difference with standard deviation of 11

## Secondary Endpoints

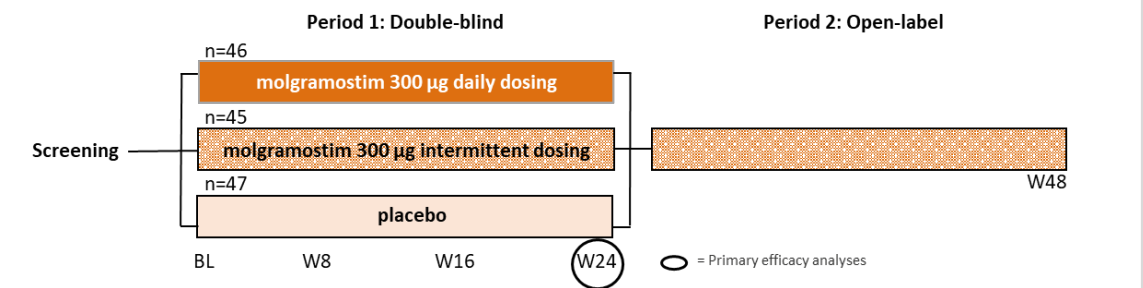
- SGRQ Total Score
- SGRQ Activity Score
- Exercise capacity using treadmill test

IMPALA-2 is being conducted at ~50 sites across ~18 countries. Patients needing whole lung lavage will have procedure prior to screening.



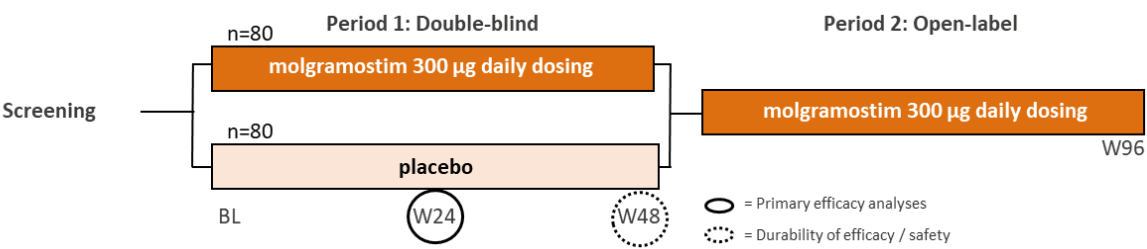
# Clinical Trial Design: IMPALA vs. IMPALA-2

## IMPALA



|   |   |
|---|---|
| <b>PRIMARY ENDPOINT:</b><br>(surrogate endpoint)        | Gas Exchange: A-aDO <sub>2</sub>                          |
| <b>SECONDARY ENDPOINTS:</b><br>(direct patient benefit) | SGRQ Total<br>6-minute walk distance<br>Whole lung lavage |
| <b>DEVICE:</b>  | Pari e-Flow Nebulizer System                              |
| <b>NUMBER OF TRIAL SITES:</b>                           | 34  |
| <b>GEOGRAPHIES:</b>                                     | 18 countries<br>N. America, Europe, Japan, S. Korea       |
| <b>ENROLLMENT DURATION:</b>                             | ~32 months  |
| <b>SUPPLEMENTAL OXYGEN:</b>                             | Allowed as background and during efficacy measure (n=4)   |
| <b>DISEASE SEVERITY:</b>                                | Stable moderate to severe disease                         |

## IMPALA-2



|   |   |
|---|---|
| <b>PRIMARY ENDPOINT:</b><br>(surrogate endpoint)        | Gas Exchange: DLCO  |
| <b>SECONDARY ENDPOINTS:</b><br>(direct patient benefit) | SGRQ Total<br>SGRQ Activity<br>Exercise capacity test using treadmill |
| <b>DEVICE:</b>  | Pari e-Flow Nebulizer System  |
| <b>NUMBER OF TRIAL SITES:</b>                           | ~50   |
| <b>GEOGRAPHIES:</b>                                     | ~18 countries<br>N. America, Europe, Japan, S. Korea                  |
| <b>ENROLLMENT DURATION:</b>                             | ~20 months  |
| <b>SUPPLEMENTAL OXYGEN:</b>                             | Allowed as background, NOT during efficacy measure                    |
| <b>DISEASE SEVERITY:</b>                                | Stable moderate to severe disease                                     |

# Molgramostim Regulatory Landscape

## MOLGRAMOSTIM IN aPAP REGULATORY DESIGNATIONS

- Orphan Drug Designation, Europe (eligible for 10 years exclusivity)
- Orphan Drug Designation, US (eligible for 7 years exclusivity)
- Fast Track Designation, US
- Breakthrough Therapy Designation, US
- Innovation Passport Designation, UK
- Promising Innovative Medicine Designation, UK

## IMPALA-2

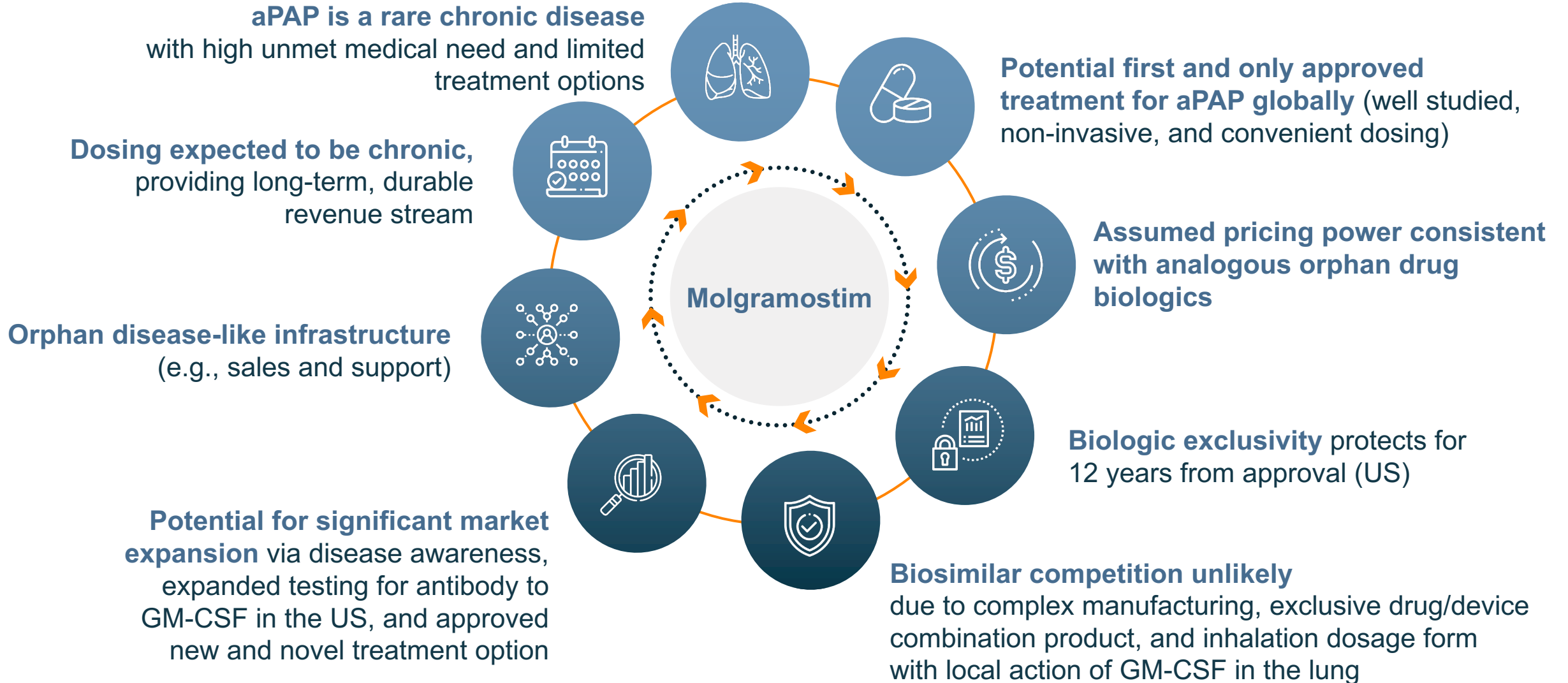
- Trial design endorsed by regulatory authorities in the US, Canada, Japan, South Korea, and the countries in Europe where the trial is being conducted

## BIOLOGIC EXCLUSIVITY

- Upon Biologics License Application (BLA) approval FDA would grant 12 years marketing exclusivity

# Commercial Outlook

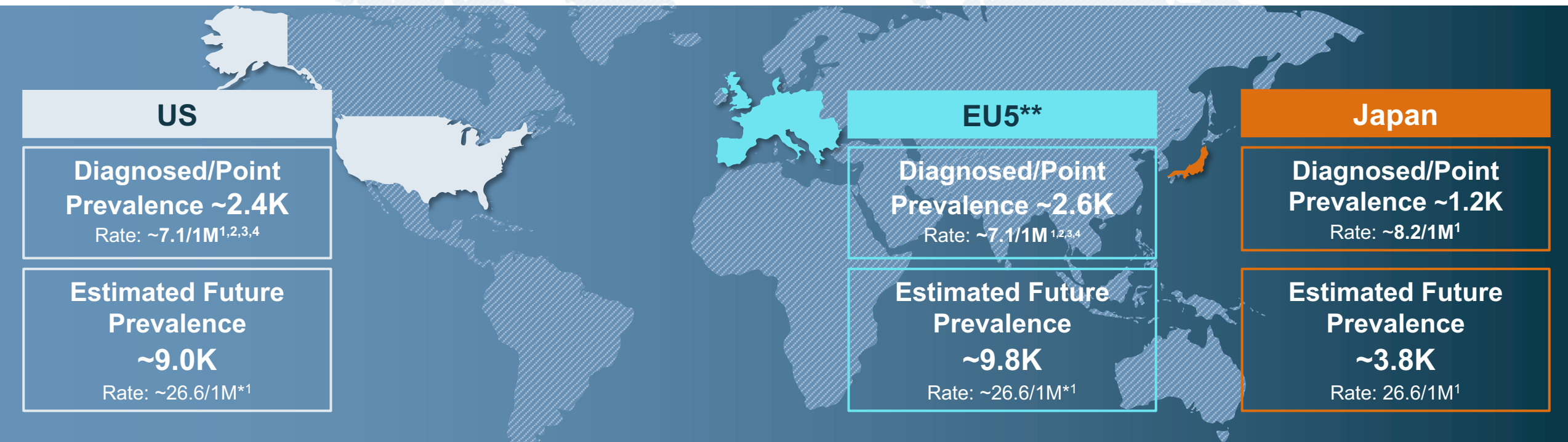
# Significant Global Commercial Opportunity





# Current Market Opportunity is Robust and has Significant Potential for Growth

Current projected patient population is **~6K**. With increased anti-GM-CSF antibody testing, the potential addressable population could be **greater than 20K**



Diagnosed prevalence expected to grow given anticipated increased awareness and market shaping efforts with a new approved agent

Sources: 1. Kitamura et al (2019); 2. McCarthy et al, (2018); 3. Medicare FFS and IBM MarketScan (2019) - Trinity EvidenceFirst Analysis; 4. Campo et al, (2013); \*High diagnosed prevalence rate in the Niigata region (Kitamura et al., 2019 - 26.6/1M) of Japan can be used as a proxy for true prevalence given high rates of GM-CSF antibody testing

\*\*EU5: France, Germany, Italy, Spain, UK



# In Japan, a Simple Blood Antibody Test is Routinely Performed to Diagnose aPAP



- Research advances have led to the development of a highly effective, simple blood test that can diagnose aPAP
- 100% sensitivity and 100% specificity
- Distinguishes aPAP from other respiratory diseases
- Not yet widely available in the US and EU
- Once widely available in the US and EU, it could improve accuracy and reduce time to diagnosis

## Analog: Pulmozyme® (dornase alpha)

### Pulmozyme®

- Prototype inhaled biologic
- Approved by the FDA in 1993
- No biosimilar available

Pulmozyme is a registered trademark of Genentech

# Financials

- **Well capitalized**
  - ~\$134M in cash (as of 9/30/22)
  - Cash **runway extends ~18-months** beyond anticipated IMPALA-2 top line results
- **Strong investor support with coverage from 6 equity research analysts**

## ANALYST COVERAGE

|                          |                       |
|--------------------------|-----------------------|
| Evercore ISI             | Liisa Bayko, MSC, MBA |
| H.C. Wainwright          | Andrew Fein           |
| Jefferies                | Suji Jeong, PhD       |
| Ladenburg Thalmann & Co. | Michael Higgins       |
| Oppenheimer              | Francois Brisebois    |
| Piper Sandler            | Yasmeen Rahimi, PhD   |

# Financial Highlights

# Investment Thesis



**The molgramostim in aPAP clinical program has a high probability of success**



**As a novel inhaled biologic, molgramostim has the potential for a long-term, durable revenue stream**



**Significant global commercial opportunity**



**Strong balance sheet –funded through 2025**





# Thank You

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