areteia therapeutics

# Pioneering a new era in inflammatory airway disease

Areteia Therapeutics is a clinical stage I&I biotechnology company committed to putting respiratory patients in better control of their disease—and back in control of their lives— with **the first potential oral drug for eosinophilic asthma**

January 2024

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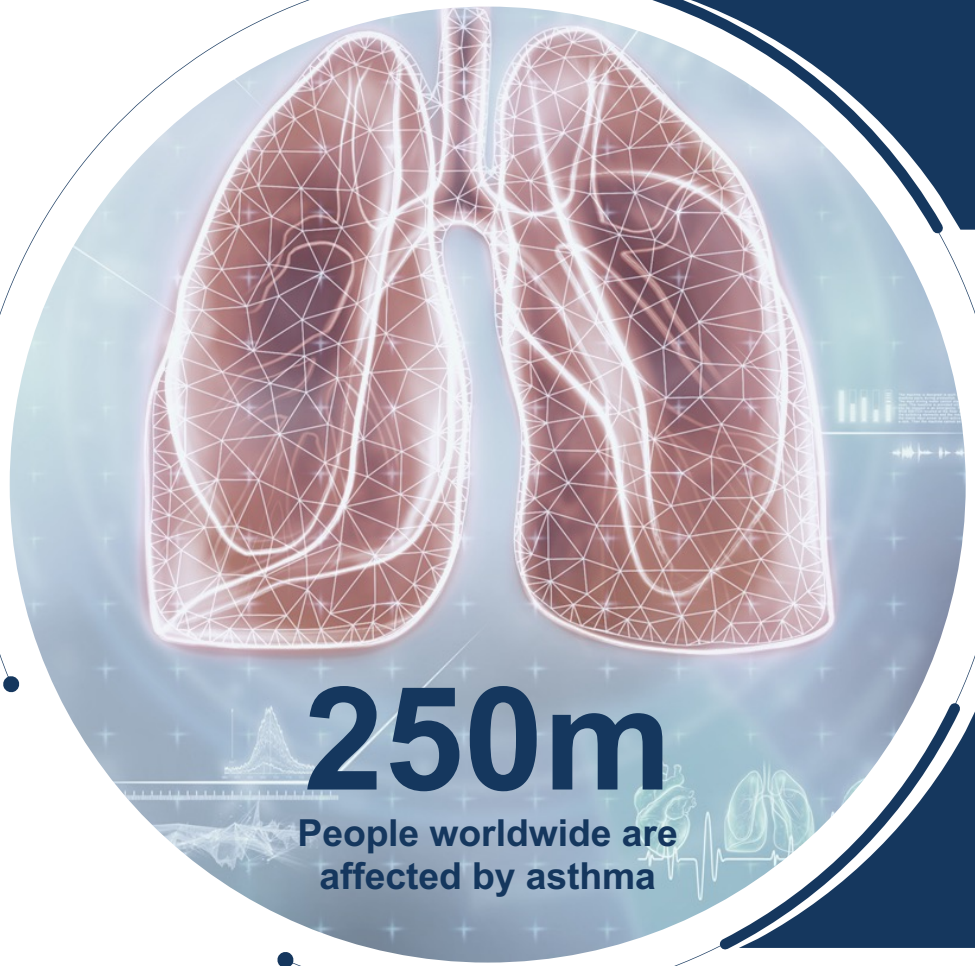
# Areteia Therapeutics: Advancing the first-ever oral therapy for eosinophilic airway disease

Key takeaways




Multi-billion-dollar **market opportunity upstream of biologics**

**First-in-class oral for eosinophilic asthma in Phase 3**

Experienced, well financed team **executing on FDA and EMA aligned development path**

# ~$8B asthma biologics market

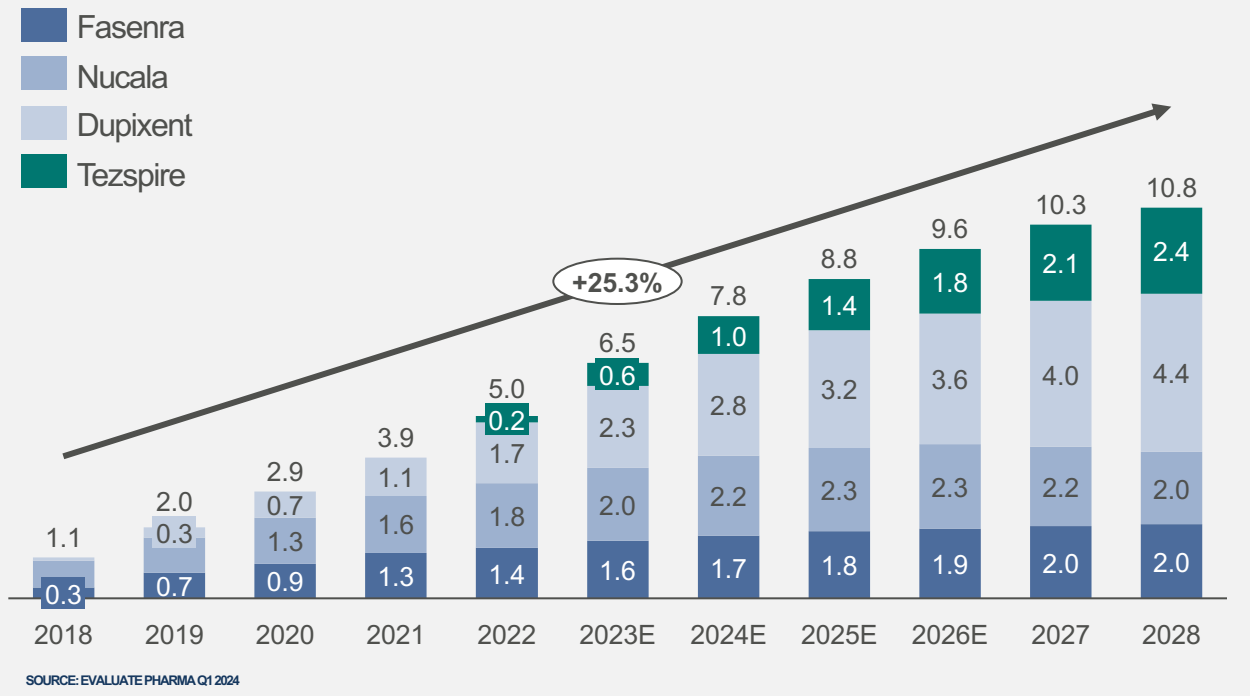
Market growing to $11B by 2028, driven by IL-5's and Dupixent

## Advanced therapy landscape in moderate-severe asthma

### Key Marketed Assets

| Molecule | MoA | Indication |
|---|---|---|
| Fasenra (benralizumab) | IL-5 mAb | Severe eosinophilic asthma, age 12+ (6+ Nucala) |
| Nucala (mepolizumab) | IL-5 mAb | |
| Dupixent (dupilumab) Injection 200mg · 300mg | IL-4 / IL-13 mAb | Mod/sev eosinophilic or OCS-dependent asthma, age 12+ |
| Tezspire (tezepelumab-ekko) | Anti-TSLP mAb | Severe asthma of any phenotype |
| Xolair Omalizumab FOR SUBCUTANEOUS USE 75 mg • 150 mg | Anti-IgE mAb | Mod/sev allergic asthma age 6+ |

### Projected WW asthma biologics revenue to 2028 ($B)

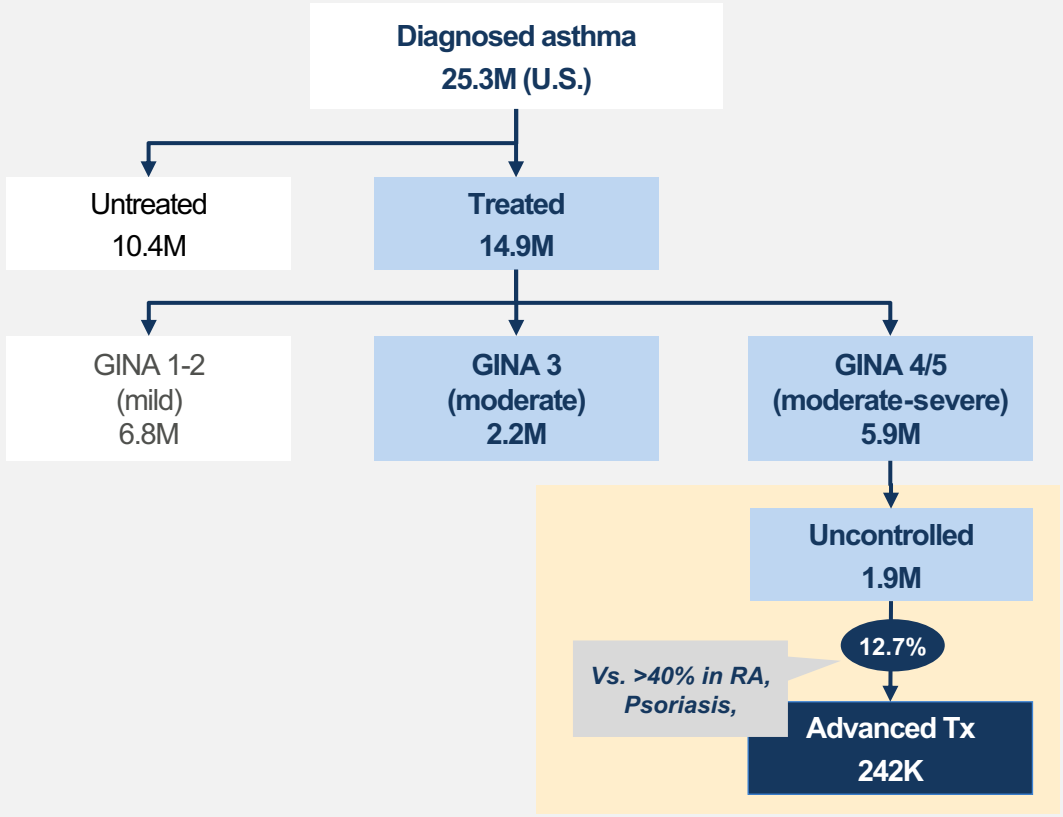



SOURCE: EVALUATE PHARMA Q1 2024

# Biologic therapies dramatically underpenetrated

Fewer than 13% of moderate-severe patients currently receive a mAb – driving significant unmet need

## A large, undertreated market…




## …with significant medical and economic unmet need

- >50% of moderate-severe patients have *eosinophilic* phenotype
- ~2.5M moderate-severe *eosinophilic* asthma patients in US, ~4.5M across U.S., EU
- >30% moderate-severe patients uncontrolled
- >50% of severe asthmatics hospitalized >1x/yr
- 2M+ annual ER visits
- $28B addressable healthcare spend (U.S.)

## ...and multiple barriers to broad mAb adoption

- Injection fear
- Patient refusal
- Burden of product administration / logistics
- Access to specialist prescribers / cost

SOURCE: Trinity Market Research, Datamonitor, Evaluate Pharma 2022
Identified in qualitative / quantitative market research conducted by Trinity Associates in Q1, 2021; validated by independent market research by Areteia

# Introduction to dexpramipexole

## Key takeaways from clinical data to-date

### Validated target

Elevated blood and tissue eosinophils (EOS) drive significant unmet need in multiple immunologic conditions

- Eosinophilic asthma: 60% of moderate-severe asthma cases (4.5 mm+ U.S./EU patients)

### Validated Pathway

Mechanism of Action: Eosinophil maturation inhibitor → blood and tissue eosinophil depletion → validated in asthma by IL-5 successes

### Consistent, biologic-like efficacy

Potent and selective eosinophil lowering in blood and tissue across multiple populations

### Consistent, robust safety and tolerability

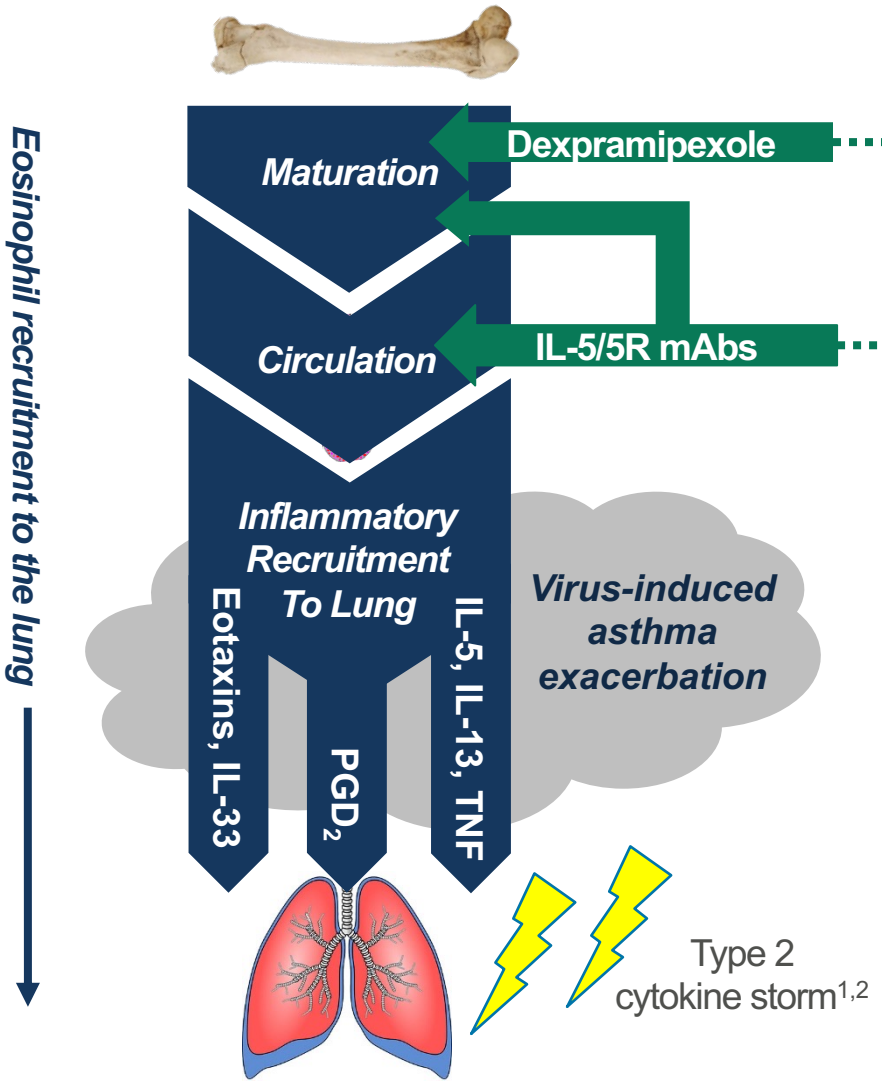
Favorable safety profile from 1,300+ patients over 10+ years of large-scale clinical research

### Ph. 3 started in asthma

Phase 2 demonstrates clear dose response with biologic-like lung function improvement

# Validated Target

## Clinical benefits of lowering eosinophils validated in asthma by recent successes



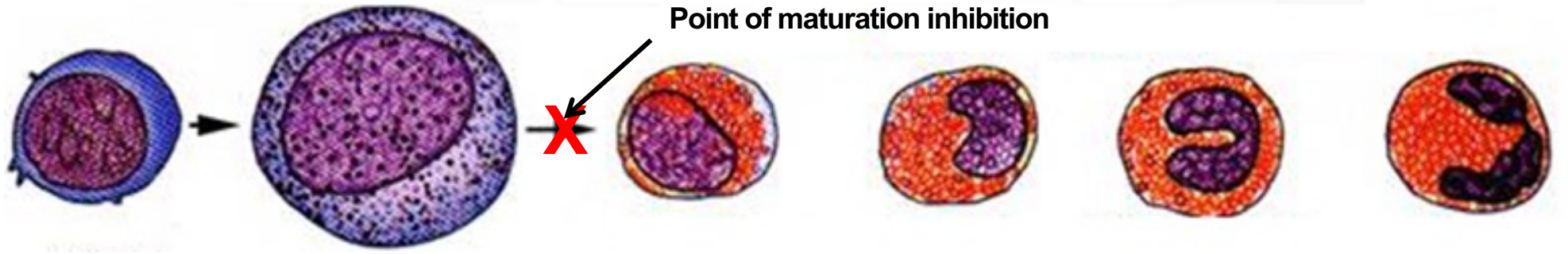

| MoA | Molecule | ↓ Blood Eos | ↓ Exacerbations |
|---|---|---|---|
| EMI | Dexpramipexole[6] | -80%, -94% | Ph. 3 |
| IL-5/5R mAbs | Mepolizumab[3] (Nucala) | -86% | - 53% |
| | Benralizumab[4] (Fasenra) | -99% | - 51% |
| | Reslizumab[5] (Cinqair) | -92% | - 54% |


1. Calhoun, JCI (1994)
2. Jackson, AJRCCM (2014)
3. Ortega, NEJM (2014)
4. Bleecker, Lancet, (2016)
5. Castro, Lancet Resp Med (2015); Cinqair product label
6. Phase 2: Asthma and CRSwNP

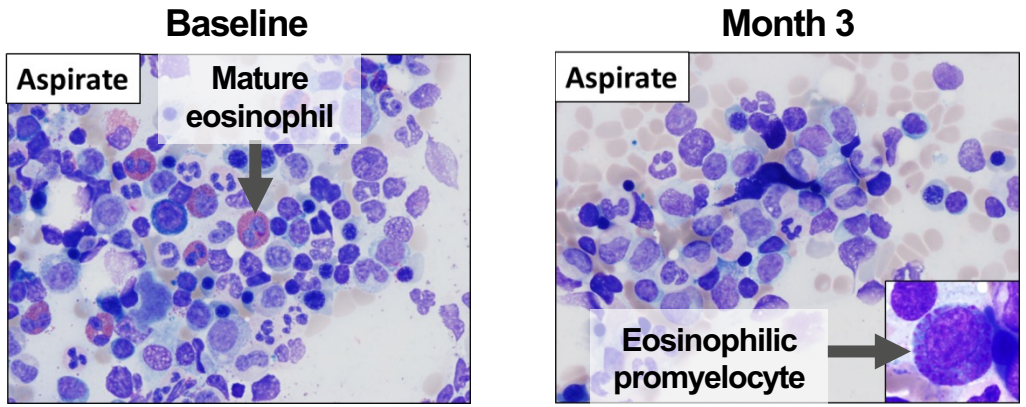
# MoA: Lowers Eosinophils in blood and tissue

## Dexpramipexole Inhibits Eosinophil Maturation prior to myelocyte stage

*Less differentiated* → *More differentiated*




- Effect limited to the eosinophil and basophil lineages
- Eosinophil-lowering kinetics consistent with eosinophil maturation inhibition
- Eosinophil maturation inhibition has been confirmed in CD34 derived eos culture system




**Bone marrow aspirate from NIH HES trial showing effect of dexpramipexole on eosinopoiesis**

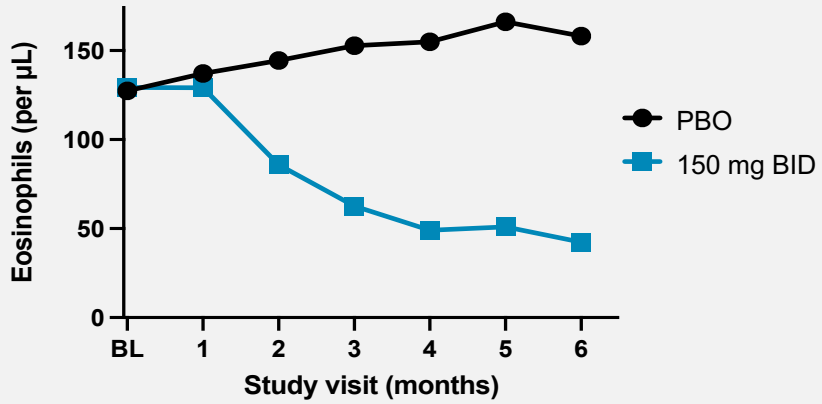
Source: Panch, Blood (2018).

# Consistent efficacy

## Potent and selective blood eosinophil lowering across multiple populations

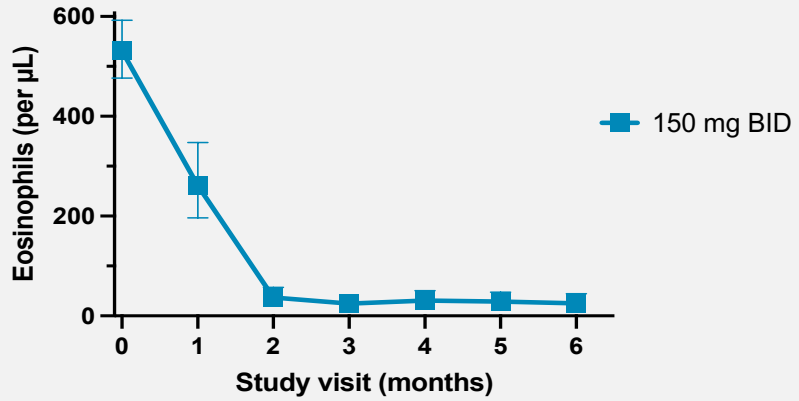
**Phase 3 ALS** (N=942)

p<0.001




**Phase 2 CRSwNP*** (N=20)

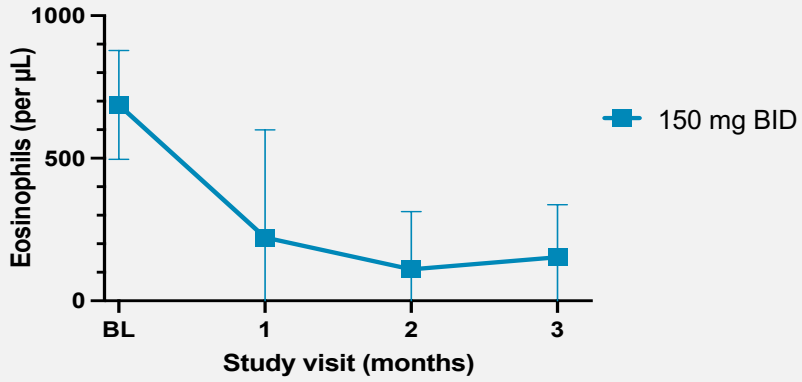
p<0.001




Chronic rhinosinusitis with nasal polyps (CRSwNP)

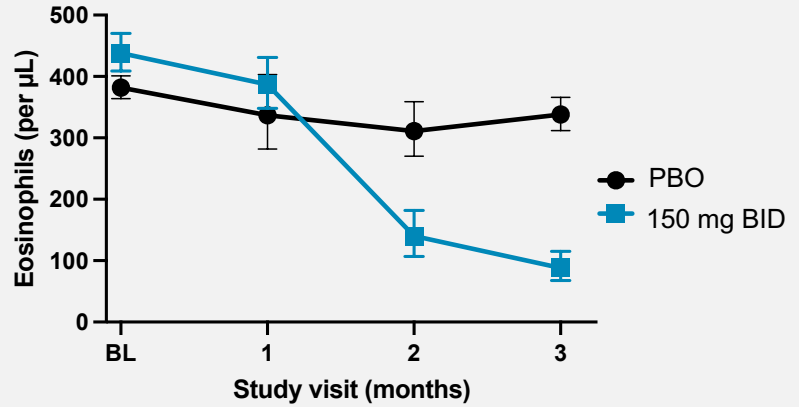
**Phase 2 HES*** (N=10)

p<0.03




**Phase 2 asthma** (N=103)

p<0.001

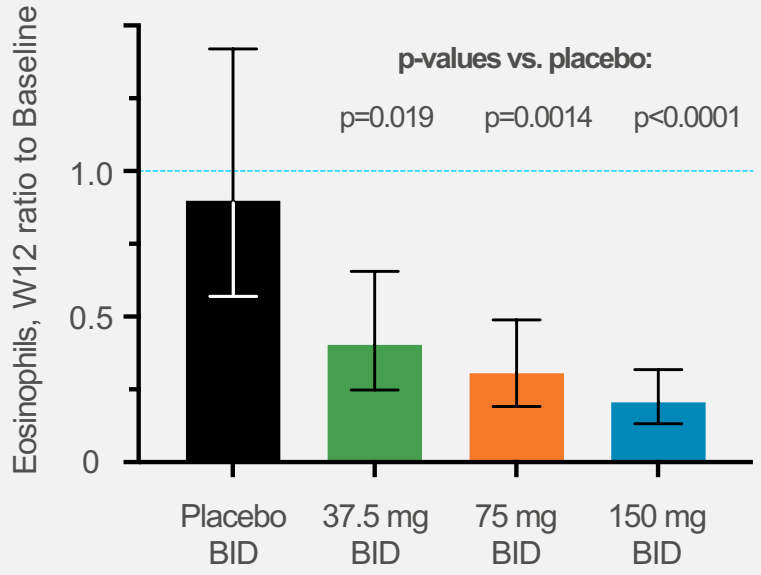



(1) *Open-label

# EXHALE-1 Primary Outcome: Blood eosinophil reduction highly significant

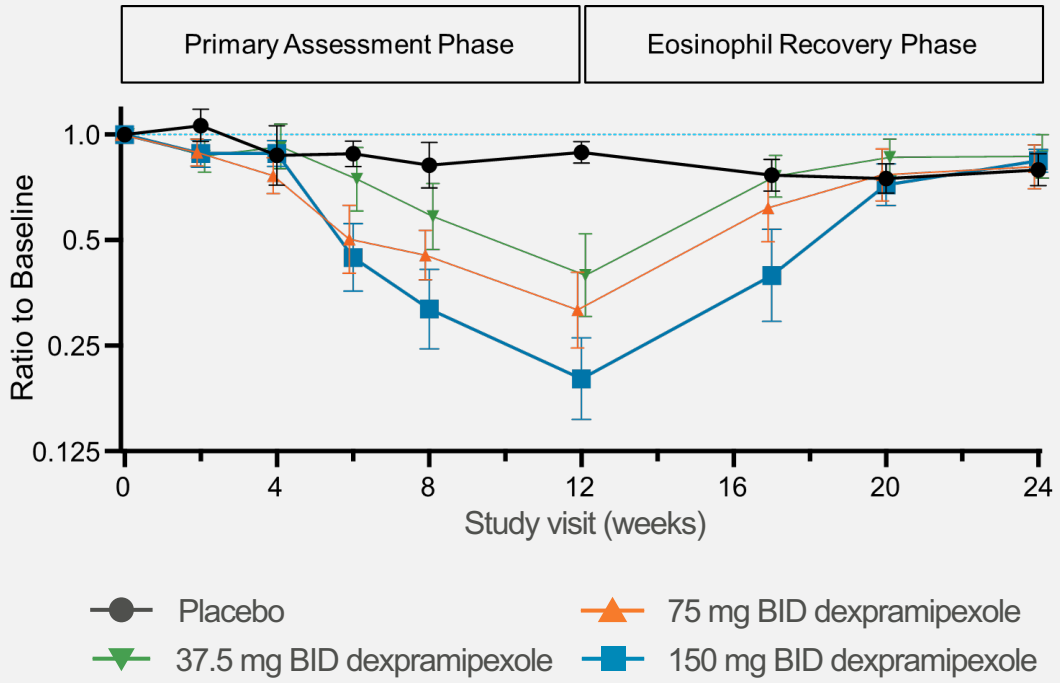
Clear dose response, with mepolizumab-like efficacy in 150 mg BID dose

## Highly significant, ~80% eosinophil reduction vs. placebo with 150 mg BID dose




Week 12 log-linear dose response trend: p<0.0001

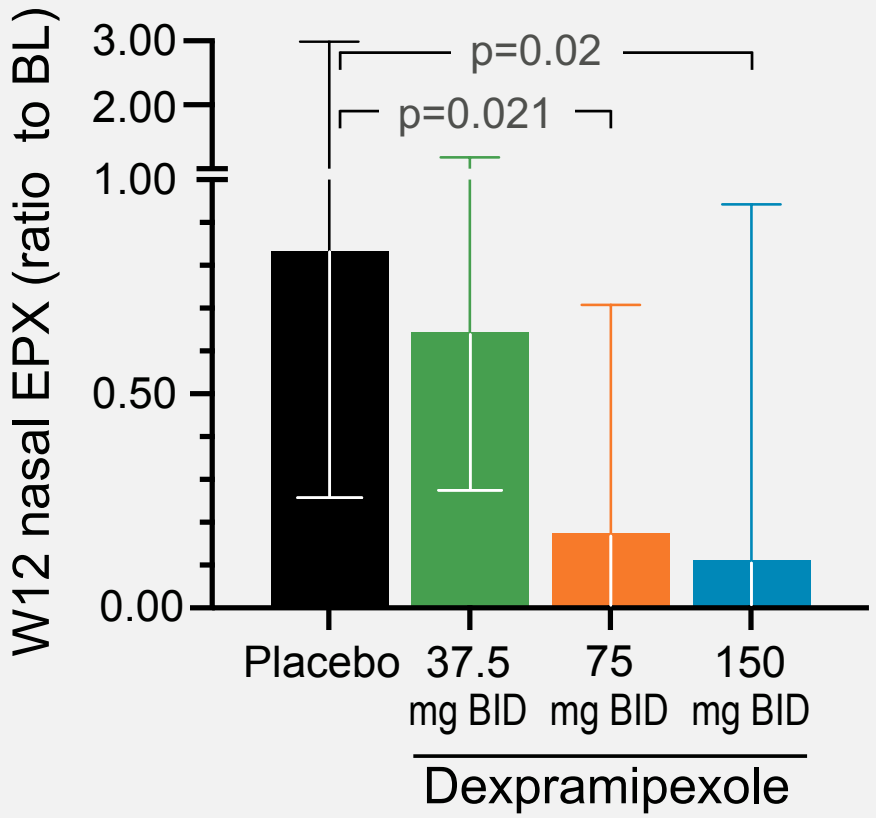
## Recovery to baseline across all doses




(1) N=103

# EXHALE: Tissue eosinophil reduction confirmed in asthma

Nasal eosinophil peroxidase (EPX) is a biomarker for airway eosinophils in the lungs




**EPX is a biomarker for airway eosinophil lowering**

**EPX has been identified as a potential mediator of mucus plugging and asthma exacerbations**

**Significant 90% reduction in nasal EPX @ 150 mg BID dose**

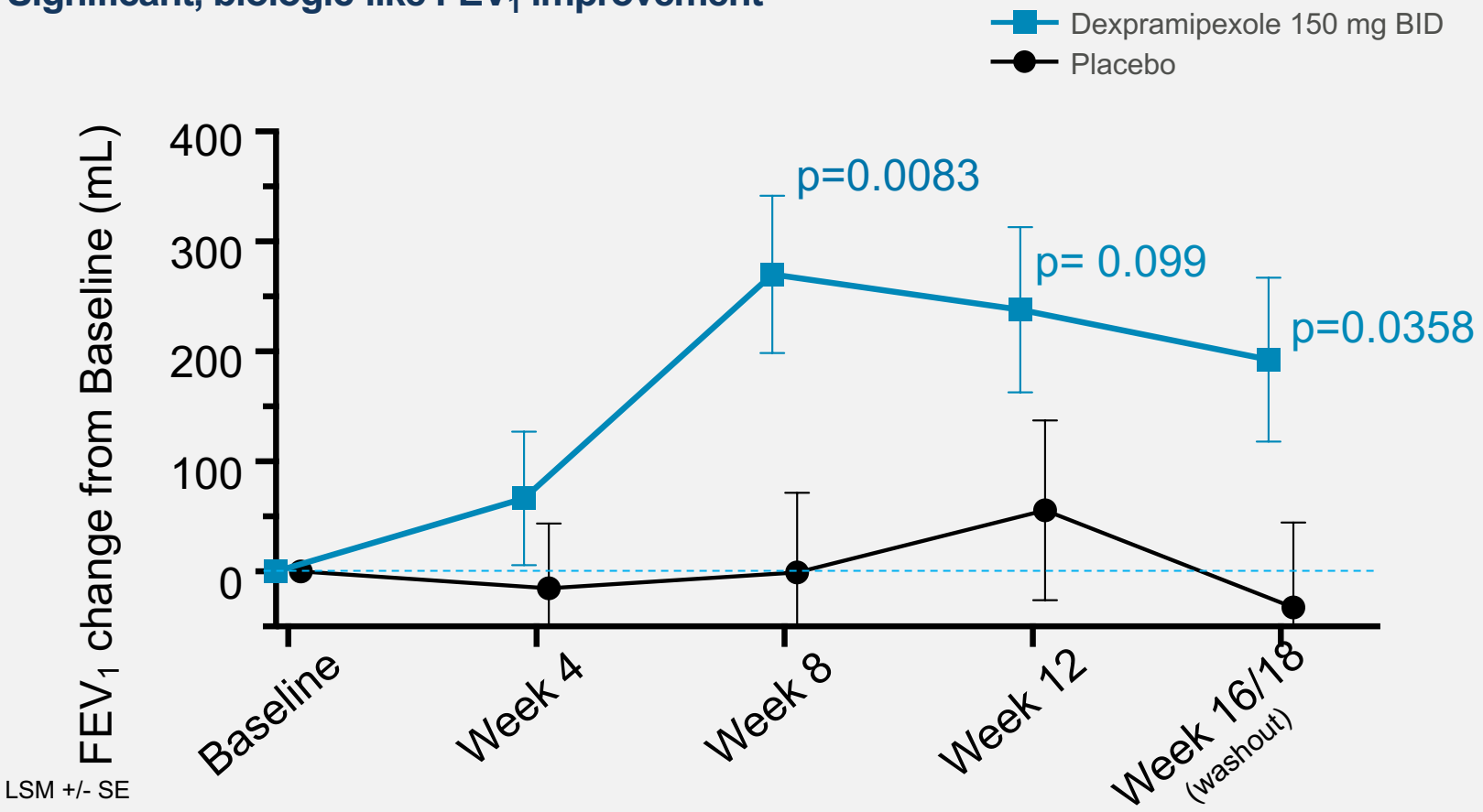
**90% reduction competitive with current biologic impact on sputum EOS**

Source: Siddiqui, JACI (2023)
TLF: Table 14.2.1-7.1
EPX measured as ng EPX/mg protein
Kruskal-Wallis test, median values shown

# EXHALE-1: Biologic-like efficacy in lung function improvement

IL-5-like $FEV_1$ improvement reinforces clinical benefit

## Significant, biologic-like $FEV_1$ improvement




**Eosinophil reduction and $FEV_1$ results competitive with IL-5 mAbs**

**Eosinophil reduction predictive of exacerbation success in Ph. 3**

**Reinforces a differentiated target product profile**

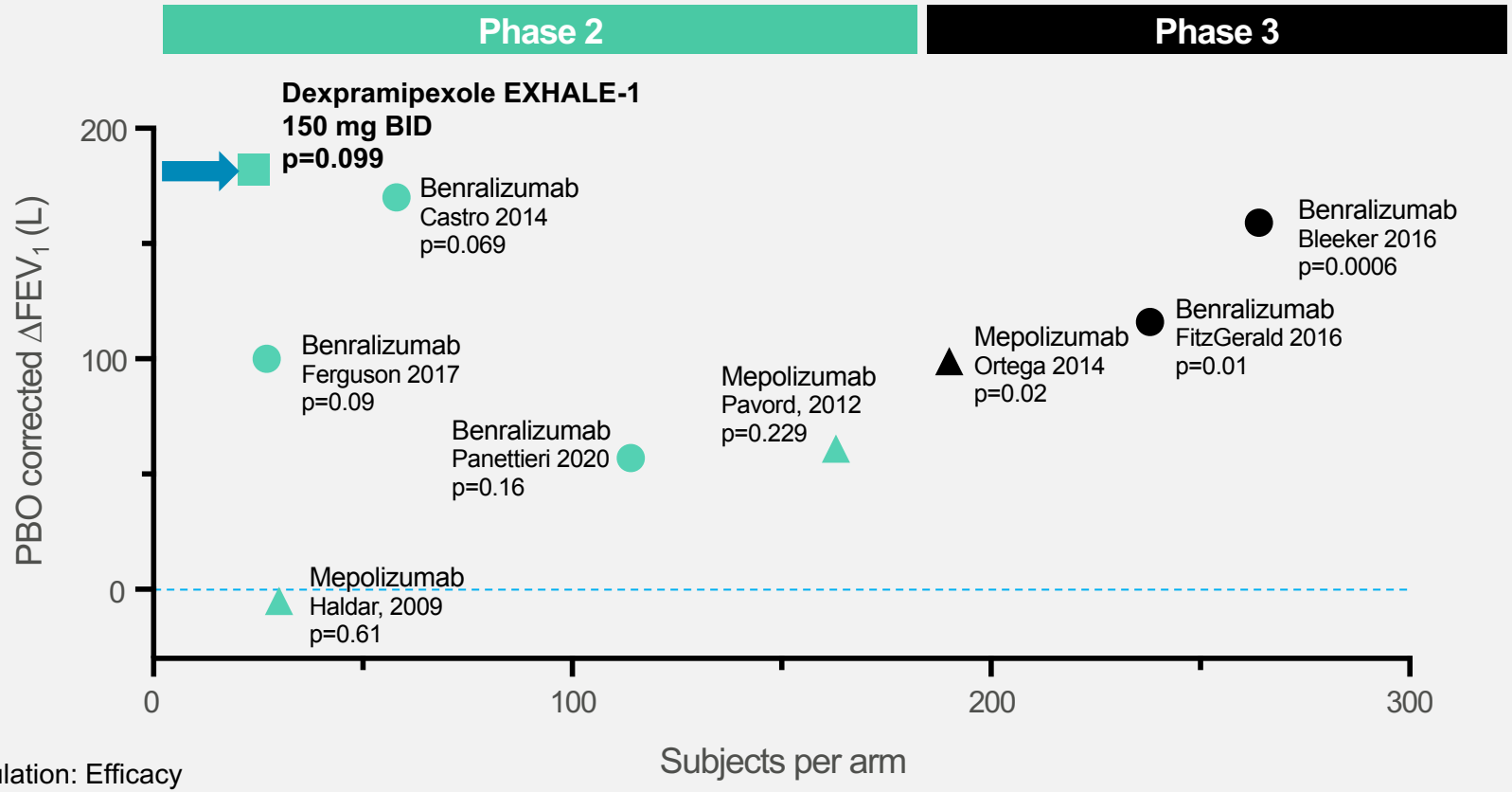
- Biologic-like efficacy
- First-to-market oral
- Well-tolerated (>1,300 Dex patients)

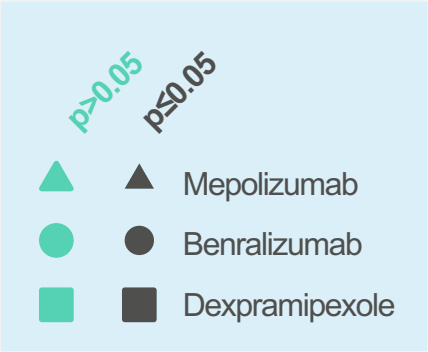
(1) N=103

# EXHALE-1: Biologic-like efficacy in lung function improvement

## Lung function improvement consistent with mepolizumab and benralizumab

### EXHALE-1 $FEV_1$ improvement in context of published IL-5 Ph. 2 and Ph. 3 results




*Data shown are for study arms corresponding to the approved dose**

Population: Efficacy
LSM +/- SE

*excluding Haldar, which used mepolizumab 750 mg I.V.

# EXHALE-1: Adverse events well balanced across treatment groups

## Summary of TEAEs during the Primary Assessment Phase

| | Placebo (N=27) | 37.5 mg BID dexpramipexole (N=22) | 75 mg BID dexpramipexole (N=26) | 150 mg BID dexpramipexole (N=28) |
|---|---|---|---|---|
| | Number of subjects (%) | Number of subjects (%) | Number of subjects (%) | Number of subjects (%) |
| **Overall** | 9 (33.3%) | 7 (31.8%) | 12 (46.2%) | 12 (42.9%) |
| **Serious (TESAE)** | --- | --- | --- | --- |
| **Leading to Discontinuation** | 1 (3.7%) | --- | --- | --- |
| **Leading to Death** | --- | --- | --- | --- |
| **Severity** | | | | |
| Mild | 7 (25.9%) | 4 (18.2%) | 6 (23.1%) | 8 (28.6%) |
| Moderate | 5 (18.5%) | 5 (22.7%) | 8 (30.8%) | 7 (25.0%) |
| Severe | | | 2 (7.7%) | 1 (3.6%) |

CSR Table 14.3.1-2

Note: N = number of subjects; % = percentage of subjects with an adverse event
Note: Severe AES were not treatment related as judged by study investigators
Note: TEAE = Treatment Emergent Adverse Events; TESAE = Treatment Emergent Serious Adverse Events

# Veteran Development Team

Proven team led by industry veterans and development experts, guided by leading Asthma KoLs

## Development team

**Peter Wijngaard**
**Chief Development Officer**

Led inclisiran global development program at MedCo

**Calman Prussin, MD**
**Chief Scientific Officer**

Led dexpramipexole Phase 2 asthma clinical trial, former senior investigator at NIH/NIAID and A&I expert

**Eric Bradford, MD**
**Chief Medical Officer**

Led GSK IIL-5 Development programs for GSK Respiratory franchise

**Steve Yancey**
**Development advisor**

Led GSK small molecule and biologic development programs at GSK, including IL-5 programs

## Scientific Advisory Board

**Ian Pavord**
Professor,
Respiratory Medicine
University of Oxford, UK

**Mona Bafadhel**
Professor,
Chair Respiratory Medicine
Kings College London, UK

**Roland Buhl**
Professor,
Head Pulmonary Dept.
Mainz University, Germany

**Dan Jackson**
Professor, Allergy
Immunology & Rheumatology
University of Wisconsin, US

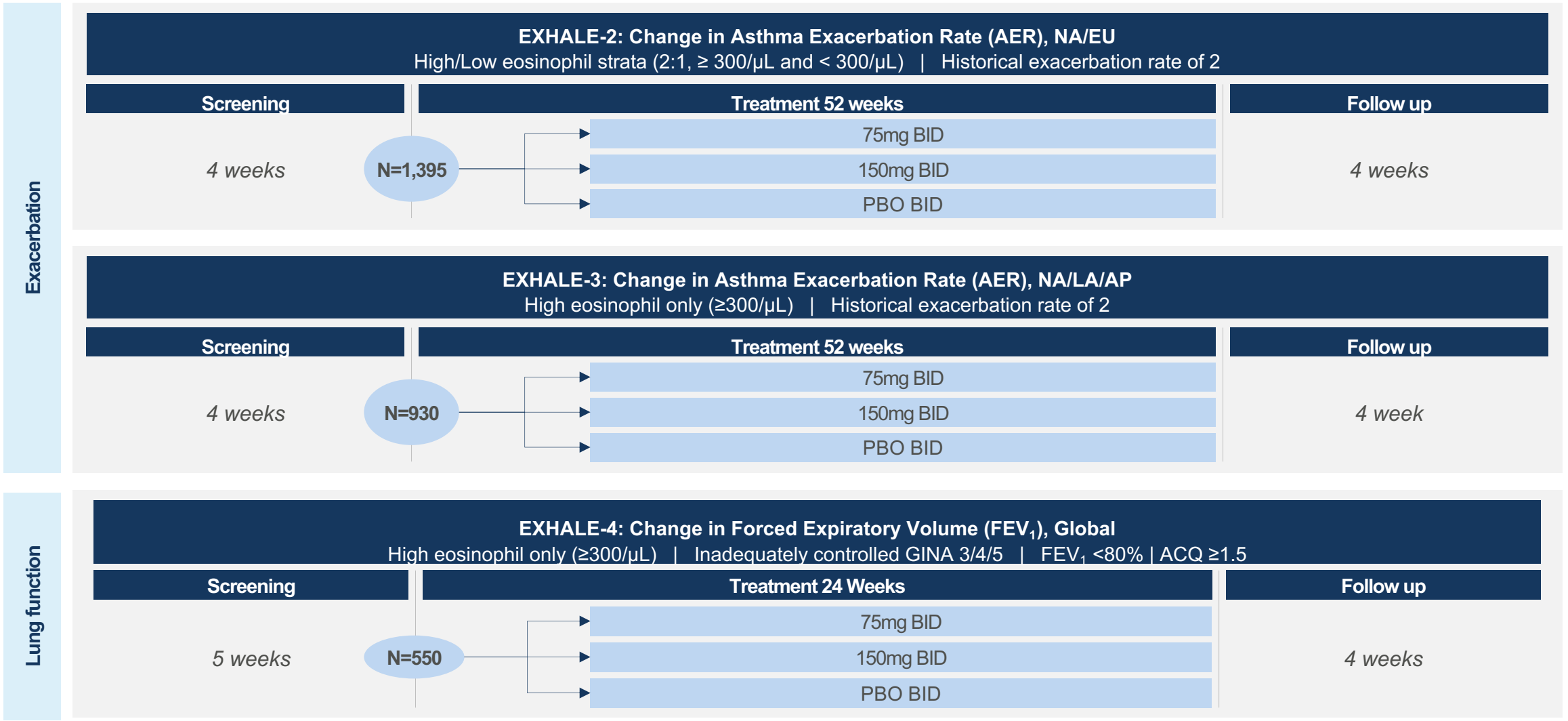
**Michael Wechsler**
Professor of Medicine
National Jewish Health, US

**Salman Siddiqui**
Professor, Respiratory Medicine
Imperial College London, UK
Via Imperial Consultants

**Chris Brightling**
Professor,
Respiratory Medicine
Univ. of Leicester, UK

# Phase 3 Program: Asthma exacerbation (EXHALE-2/3) and lung function (EXHALE-4) studies

3 trials, 2,875 patients




(1) Adolescents and Adults age 12 and up
(2) EXHALE – Dexpramipexole Research to Assess Lung function and Exacerbations

# Phase 3 program progressing as planned

Achieved and upcoming key milestones

## ACHIEVED

- ✓ FDA, EMA, PMDA, global regulatory alignment
- ✓ EXHALE-4 First Participant dosed **Q1’23**
- ✓ EXHALE-2/3 First Participant dosed **Q1/2’23**

## UPCOMING

- EXHALE-4 Full Enrollment
- EXHALE-4 TLR
- EXHALE-2/3 Full Enrollment
- EXHALE-2/3 TLR

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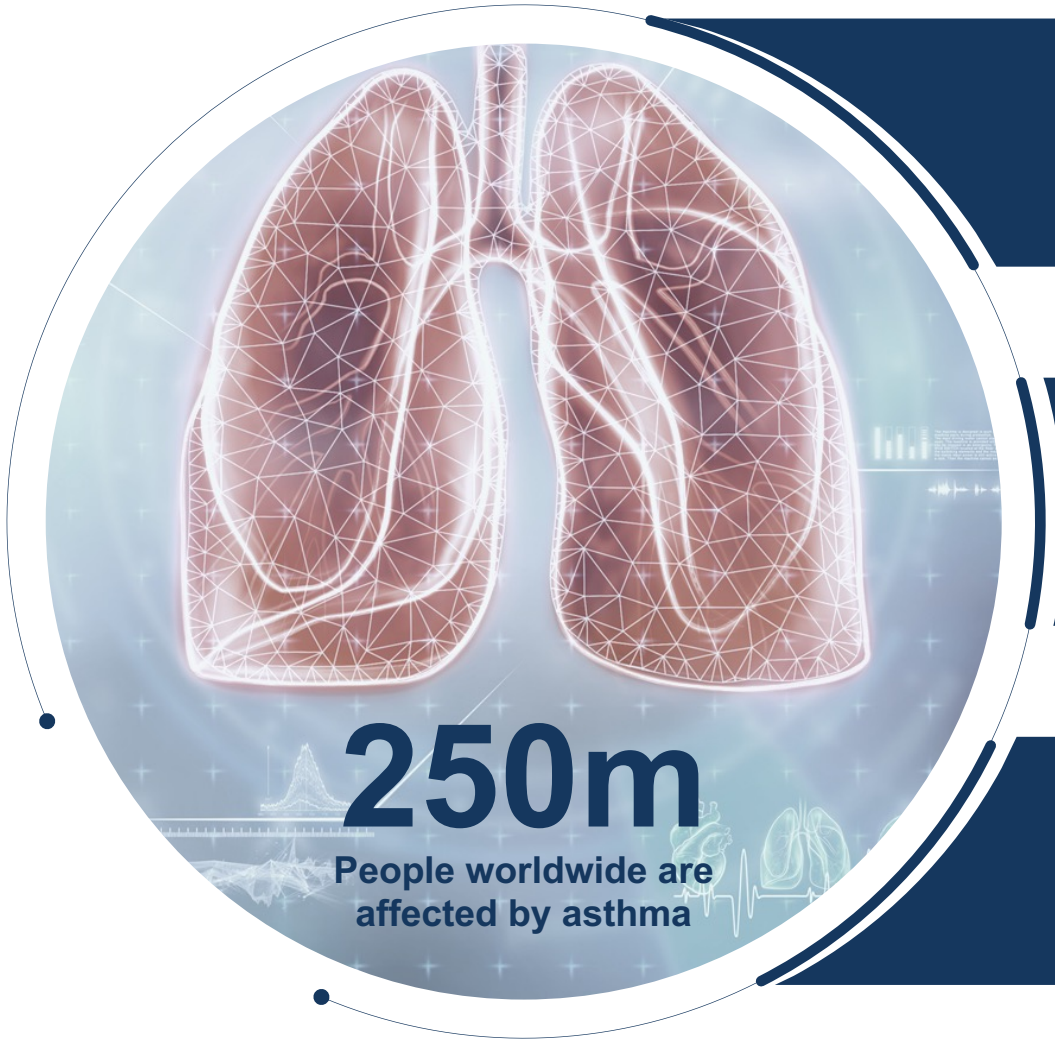
Key takeaways

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Experienced, well financed team **executing on FDA and EMA aligned development path**