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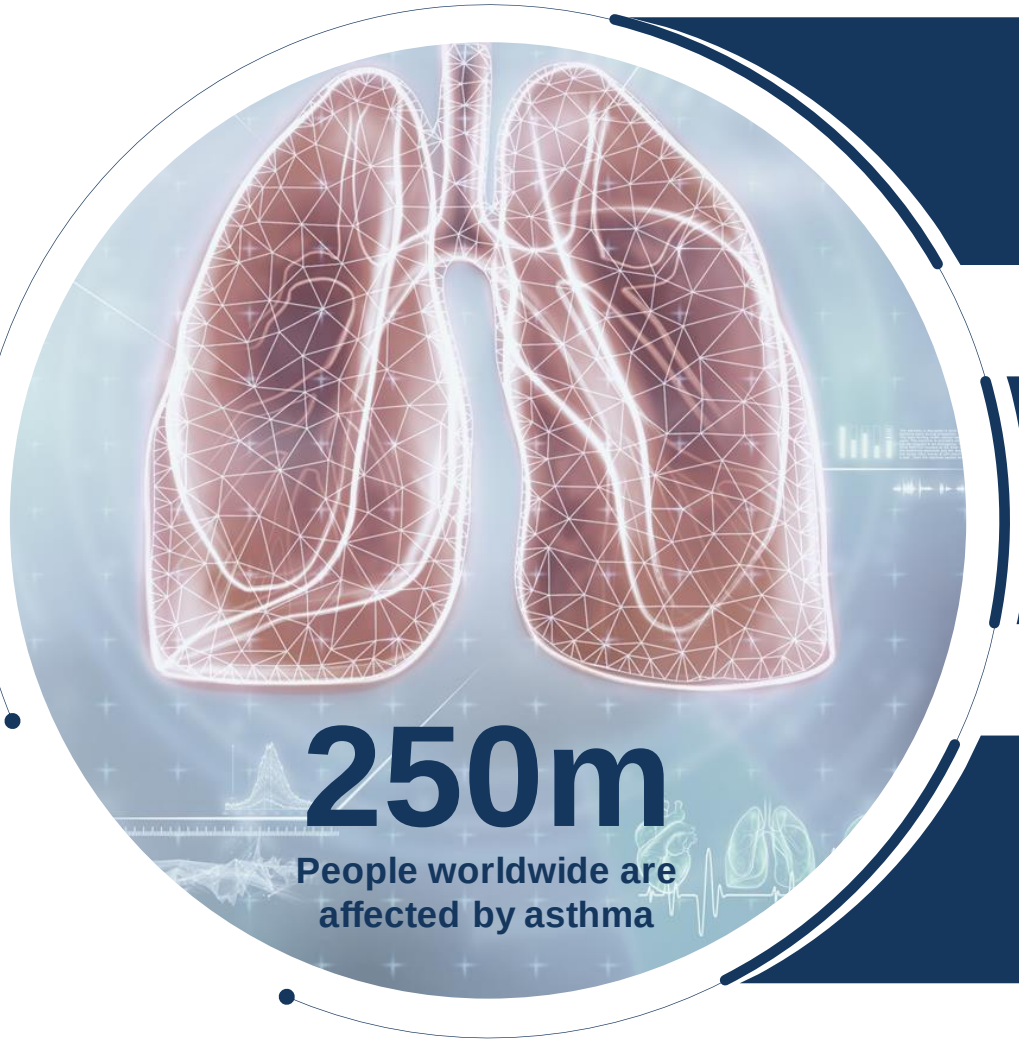
Areteia Therapeutics: Advancing the first-ever oral therapy for eosinophilic airway disease

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

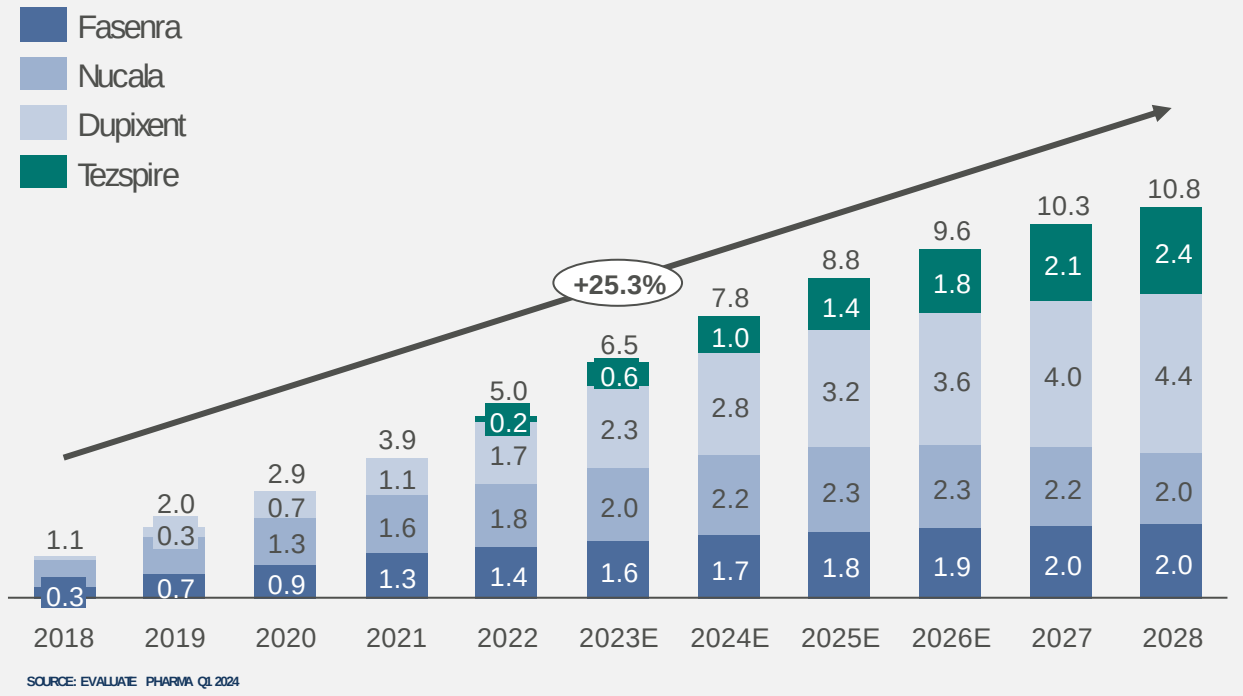
Market growing to $11B by 2028, driven by IL-5's and Dupixent

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)

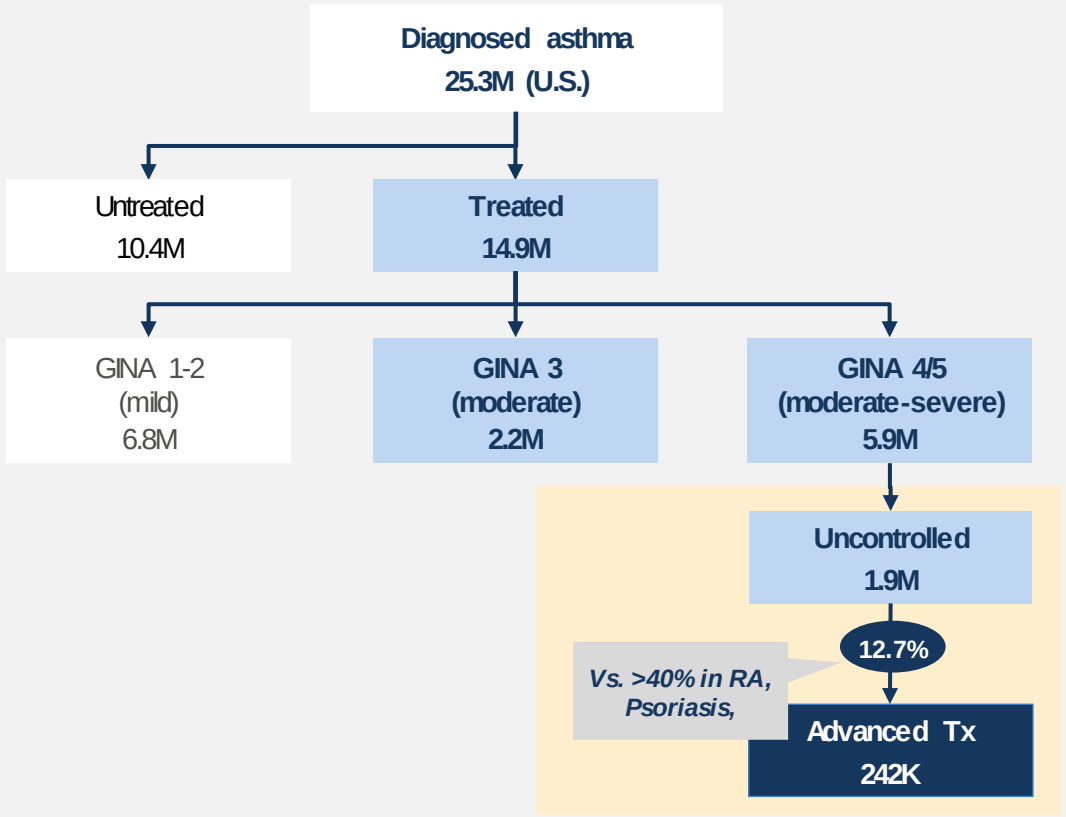


SOURCE: EVALUATE PHARMA Q1 2024

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

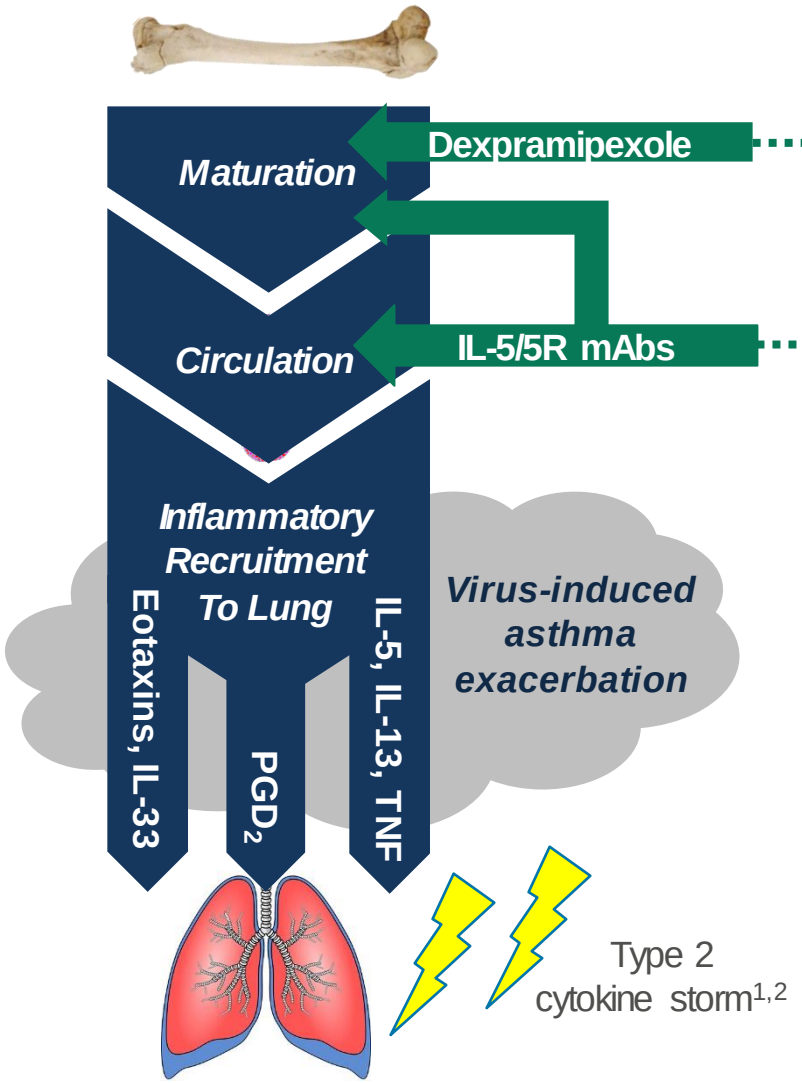
Favorable safety profile from 1,300+ patients over 10+ years of large-scale clinical research

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



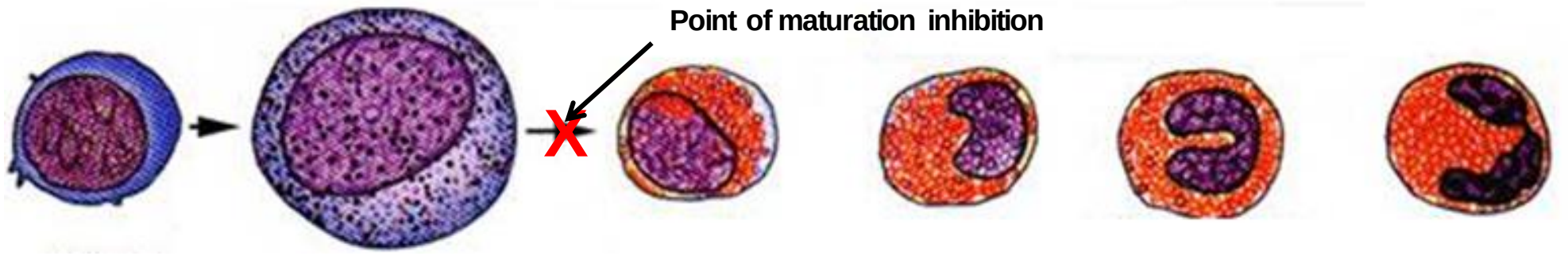
MoA	Molecule	↓ Blood Eos	↓ Exacerbations
EMI	Dexpramipexole[6]	-80%, -94%	Ph. 3
IL-5/5R mAbs	Mepolizumab[3] (Nucala)	-86%	- 53%
	Benralizumab[4] (Fasenra)	-99%	- 51%
	Reslizumab[5] (Cinqair)	-92%	- 54%

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 CRSw NP

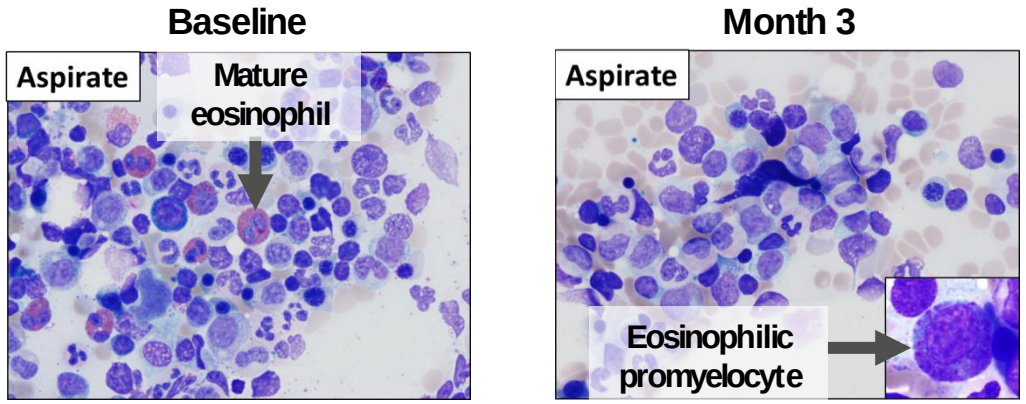
MoA: Lowers Eosinophils in blood and tissue

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

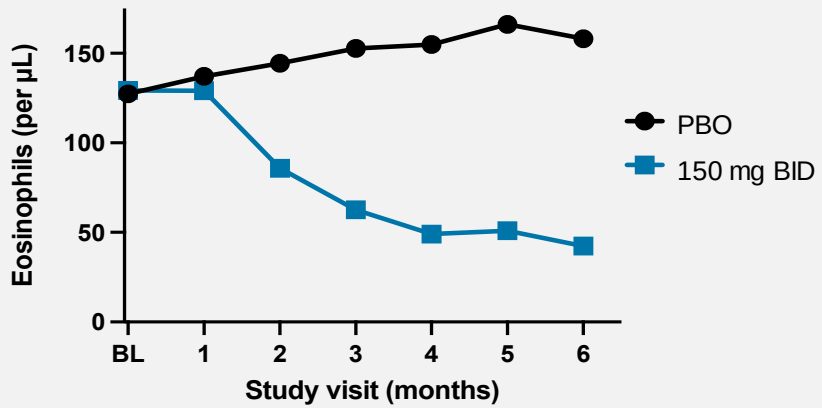
Source: Panch, Blood (2018).

Consistent efficacy

Potent and selective blood eosinophil lowering across multiple populations

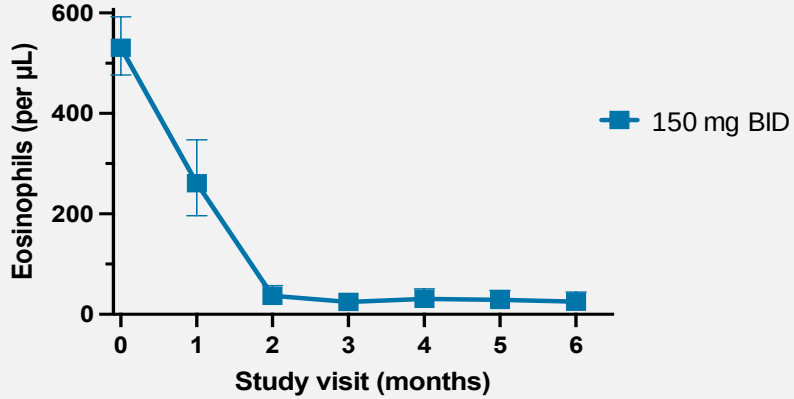
Phase 3 ALS (N=942)

p<0.001



Phase 2 CRSwNP* (N=20)

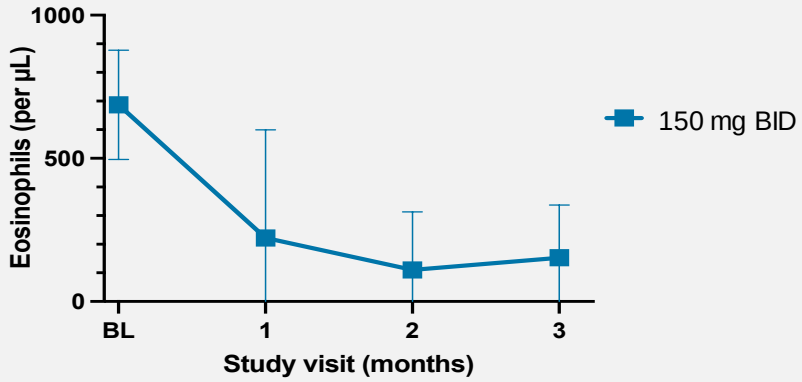
p<0.001



Chronic rhinosinusitis with nasal polyps (CRSwNP)

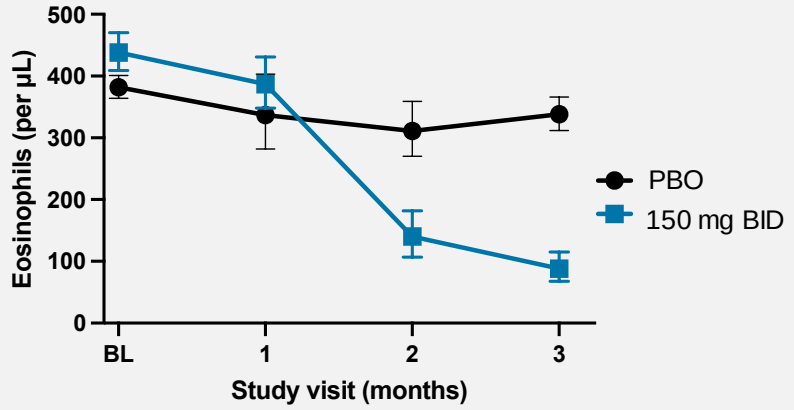
Phase 2 HES* (N=10)

p<0.03



Phase 2 asthma (N=103)

p<0.001

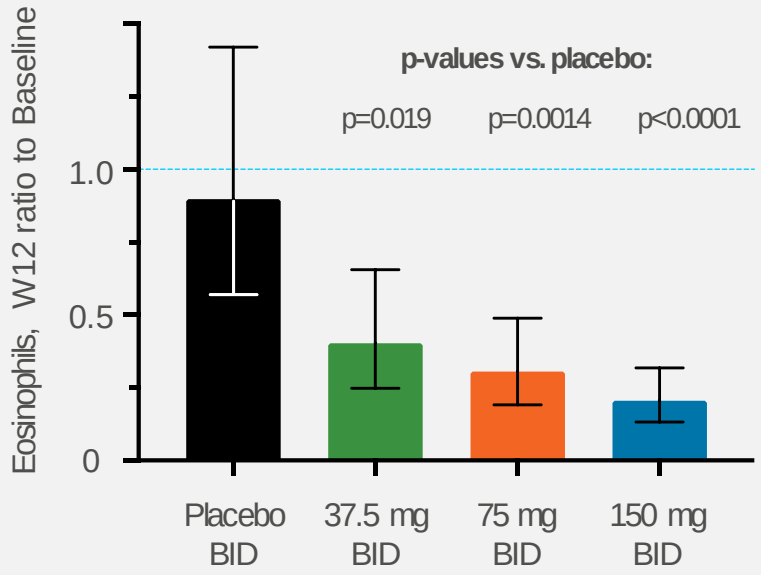


(1) *Open-label

EXHALE-1 Primary Outcome: Blood eosinophil reduction highly significant

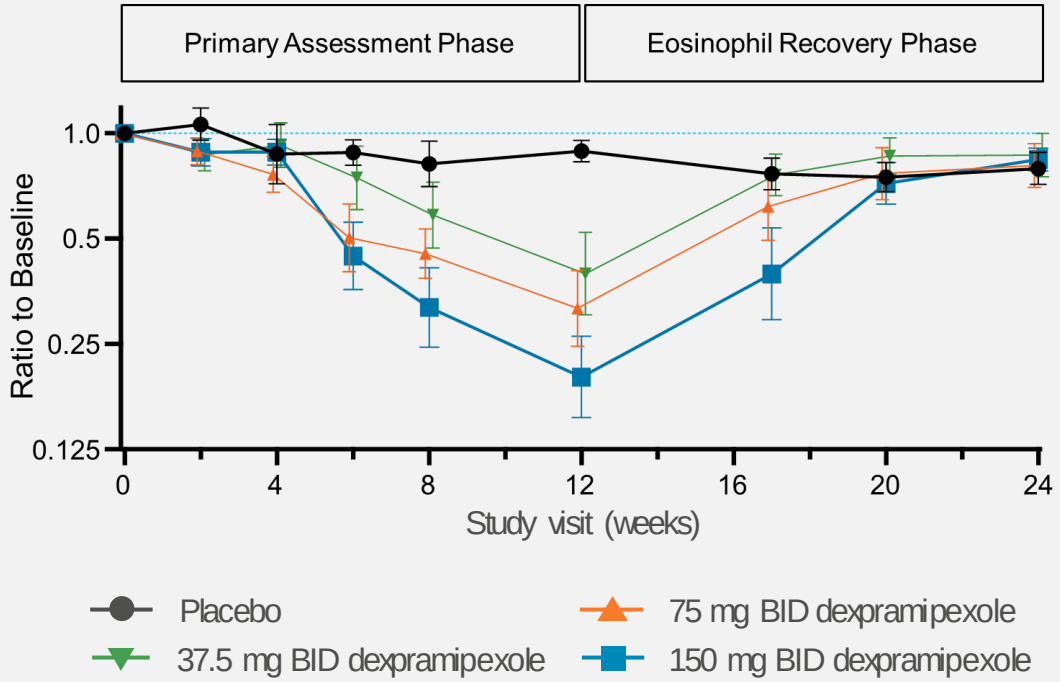
Clear dose response, with mepolizumab-like efficacy in 150 mg BID dose

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



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

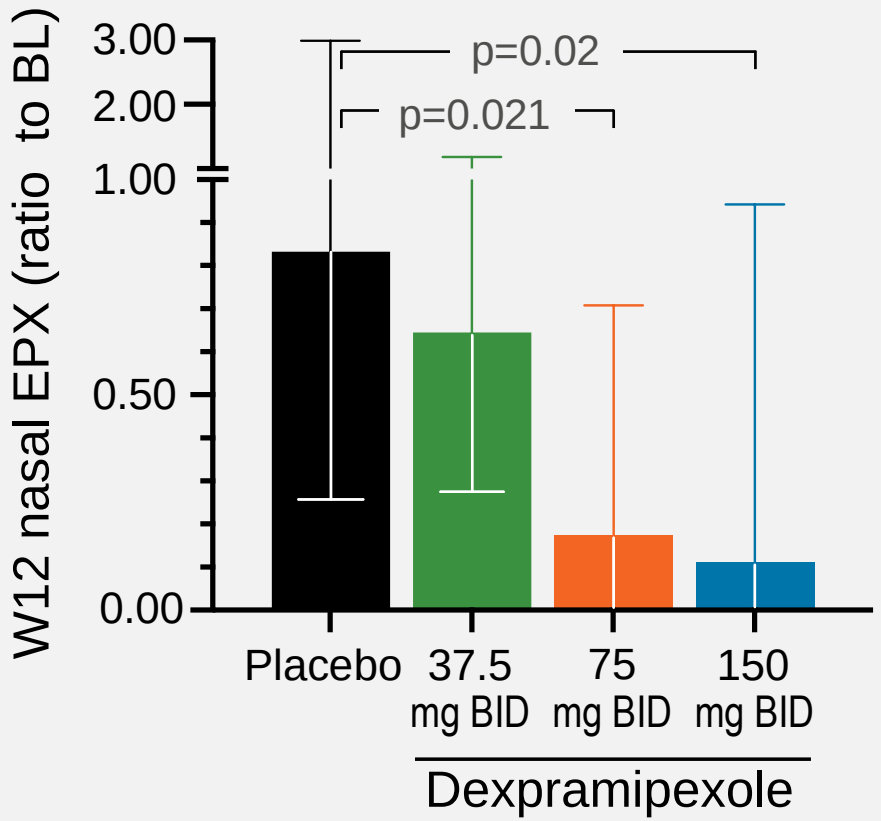
Recovery to baseline across all doses



(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

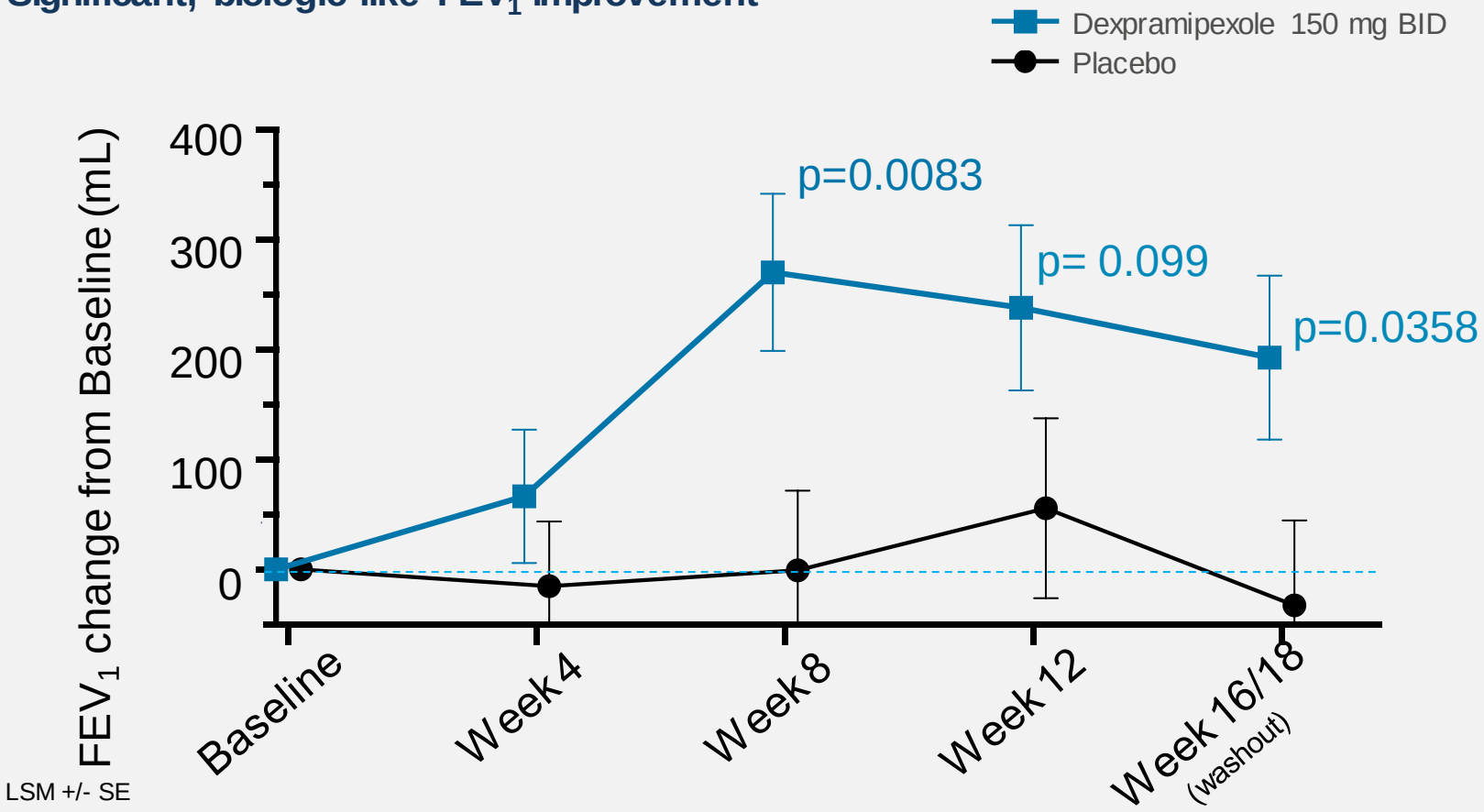
90% reduction competitive with current biologic impact on sputum EOS

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

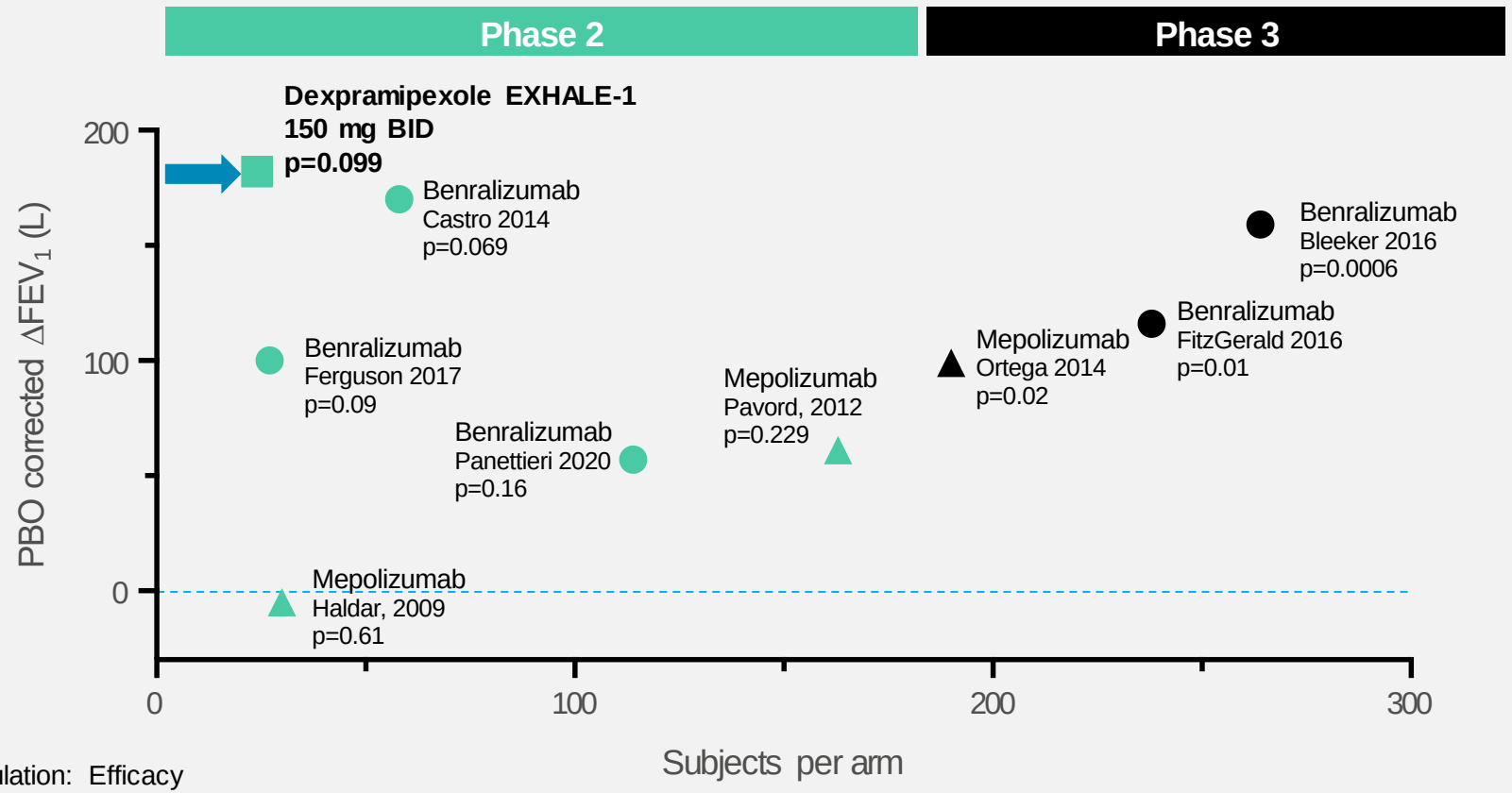
- Biologic-like efficacy
- First-to-market oral
- Well-tolerated (>1,300 Dex patients)

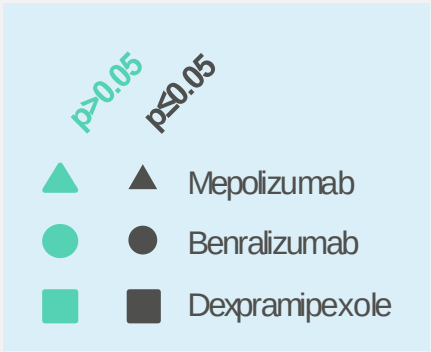
(1) N=103

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 IL-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

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University of Oxford, UK

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Chair Respiratory Medicine
Kings College London, UK

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Head Pulmonary Dept.
Mainz University, Germany

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

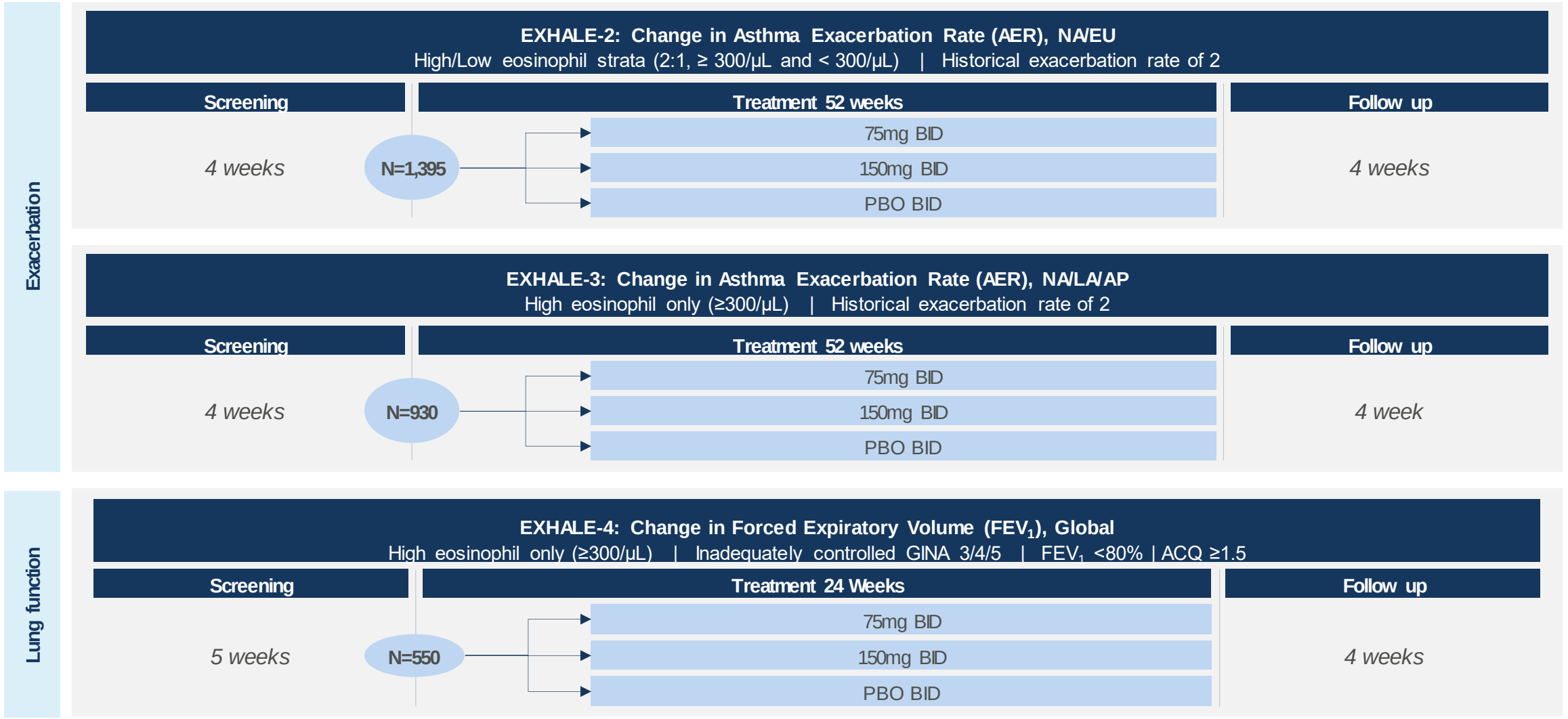
Michael Wechsler
Professor of Medicine
National Jewish Health, US

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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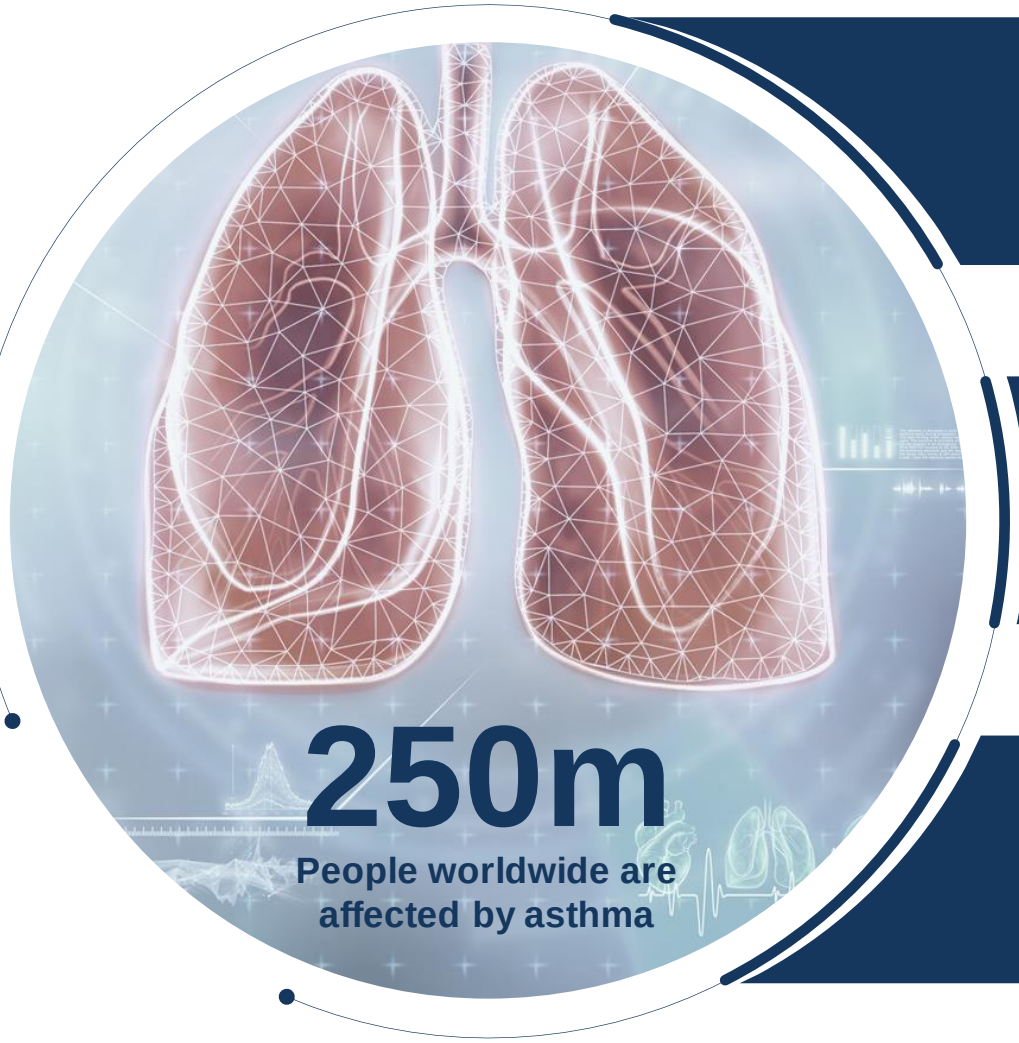
Key takeaways



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