APOGEE THERAPEUTICS®

APG333 Phase 1 Interim Results

November 10th, 2025

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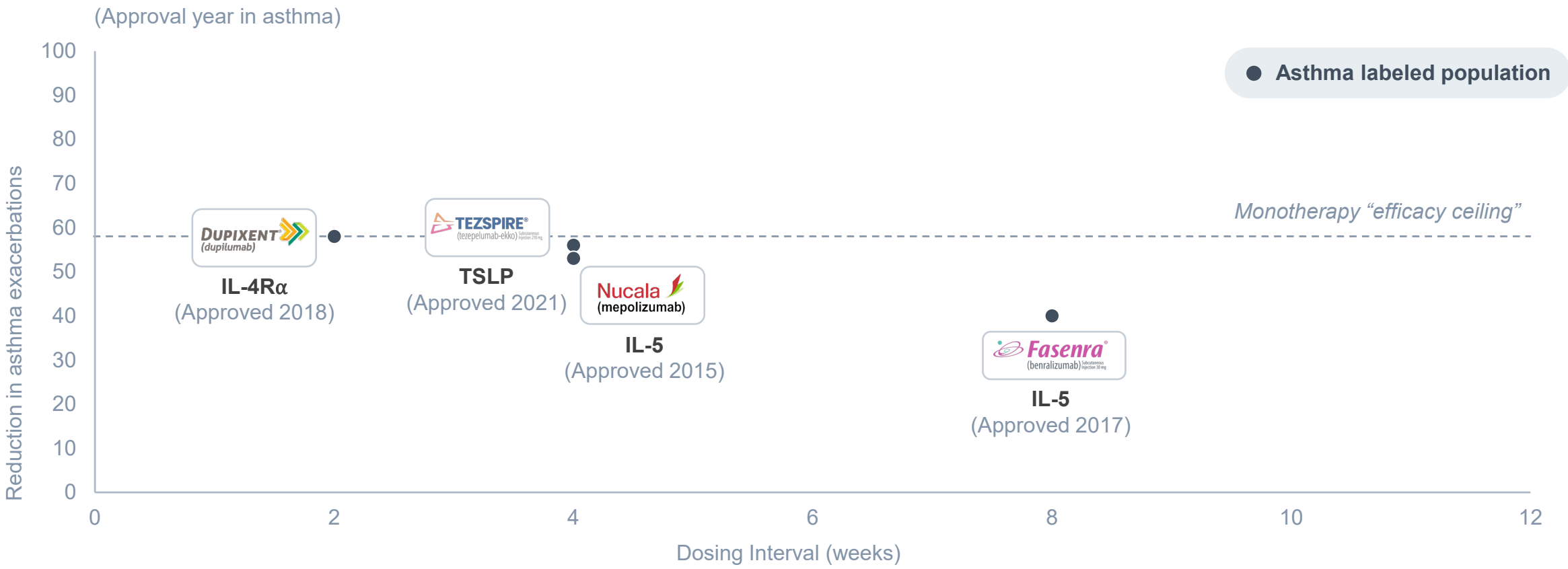
This presentation contains data based on cross-study comparisons and not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences. The values shown in cross-study comparisons are directional and may not be directly comparable.

Monotherapies have hit an efficacy ceiling in asthma and COPD



DUPIXENT (Ph3), NUCALA (Ph3), and TEZSPIRE (Ph2) have shown lower AER reductions in COPD patients

NOTE: AER = Annualized Exacerbation Rate. These data are derived from different clinical trials conducted at different points in time, with differences in trial design, dosing regimen and patient populations. DUPIXENT label indicates reductions in exacerbations were significant in those with eos ≥150. TEZSPIRE data from population without a biomarker requirement. NUCALA data from population with eos ≥150 at screening or ≥300 in prior year. FASENRA data from two Phase 3 trials in patients with eos ≥300. DUPIXENT and NUCALA COPD data reflective of two Ph3 trials in patients with eos ≥300. TEZSPIRE COPD data for patients with eos ≥150.
SOURCE: EvaluatePharma, FDA labels.

Targeting both IL-13 and TSLP could more broadly address the key drivers of obstructive airway disease

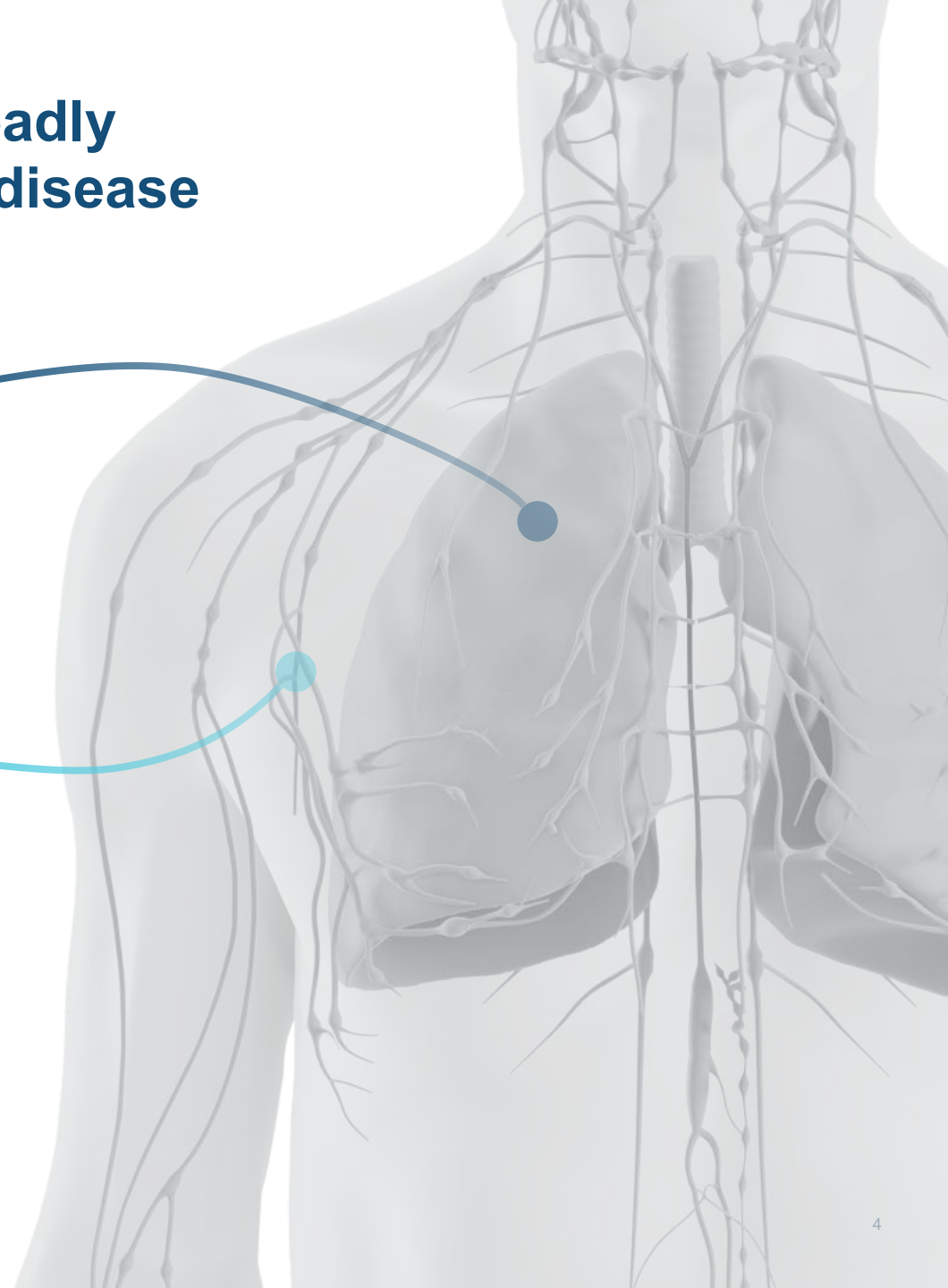
APG777 targets IL-13:
addresses local airway responses
(e.g., airway remodeling, mucus production)

+

APG333 targets TSLP:
blocks immune cell recruitment / activation
(e.g., eosinophils)

↓

Potential to **break through the monotherapy efficacy ceiling** in obstructive airway disease



APG333 Phase 1 Interim Results

Interim APG333 Phase 1 data achieved or exceeded trial objectives

GOAL

Confirm tolerable **safety profile to enable future combination trials**

RESULT

All tested doses well-tolerated, supporting continued development

✓ **ACHIEVED**

GOAL

Establish **optimized PK profile** supporting every **3-month dosing or better**

RESULT

APG333 demonstrated an interim **half life of ~55 days**

Modeled exposures support potential **APG333 every 3- and 6-month dosing**

✓ **ACHIEVED**

GOAL

Demonstrate **pharmacodynamic response** comparable to tezepelumab

RESULT

APG333 demonstrated **suppression of biomarkers through 6-months** for pathways **orthogonal to IL-13 inhibition**

✓ **EXCEEDED**

APG333 Phase 1 in healthy volunteers is fully enrolled with interim data from all cohorts

Trial design elements

Double-blind, placebo-controlled, first-in-human trial
Single ascending dose in healthy volunteers

N = 32

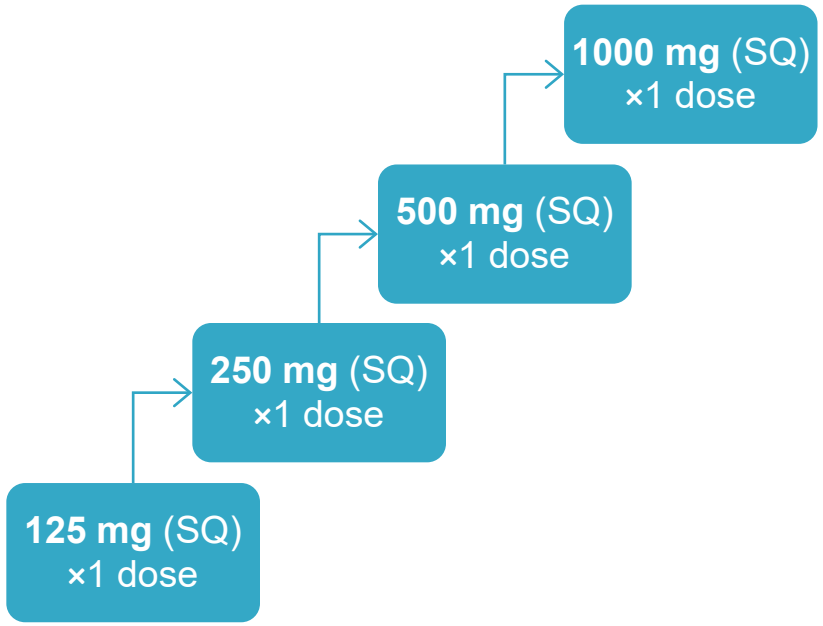
8 per cohort (6:2 active:placebo)

Key inclusion criteria: healthy adult volunteers

Primary endpoint: safety

Secondary endpoints: PK, PD

Single ascending dose



Interim data available from all cohorts

NOTE: SQ = subcutaneous. PK = pharmacokinetics. PD = pharmacodynamics.

Baseline characteristics were in line with expectations

	Single dose				
	Placebo N=8	**APG333 Cohort 1** 125 mg N=6	**APG333 Cohort 2** 250 mg N=6	**APG333 Cohort 3** 500 mg N=6	**APG333 Cohort 4** 1000 mg N=6
Age (yrs), mean (SD)	40.5 (12.9)	31.5 (15.6)	37.8 (14.1)	31.5 (6.6)	28.0 (7.3)
Female	62.5%	50.0%	50.0%	83.3%	50.0%
Caucasian	100.0%	66.7%	50.0%	66.7%	50.0%
Weight (kg), mean (SD)	72.8 (10.1)	75.0 (18.0)	70.8 (12.0)	67.0 (11.9)	68.9 (14.5)

Demographics were generally well-balanced across cohorts

APG333 was well-tolerated and exhibited a safety profile consistent with the TSLP class

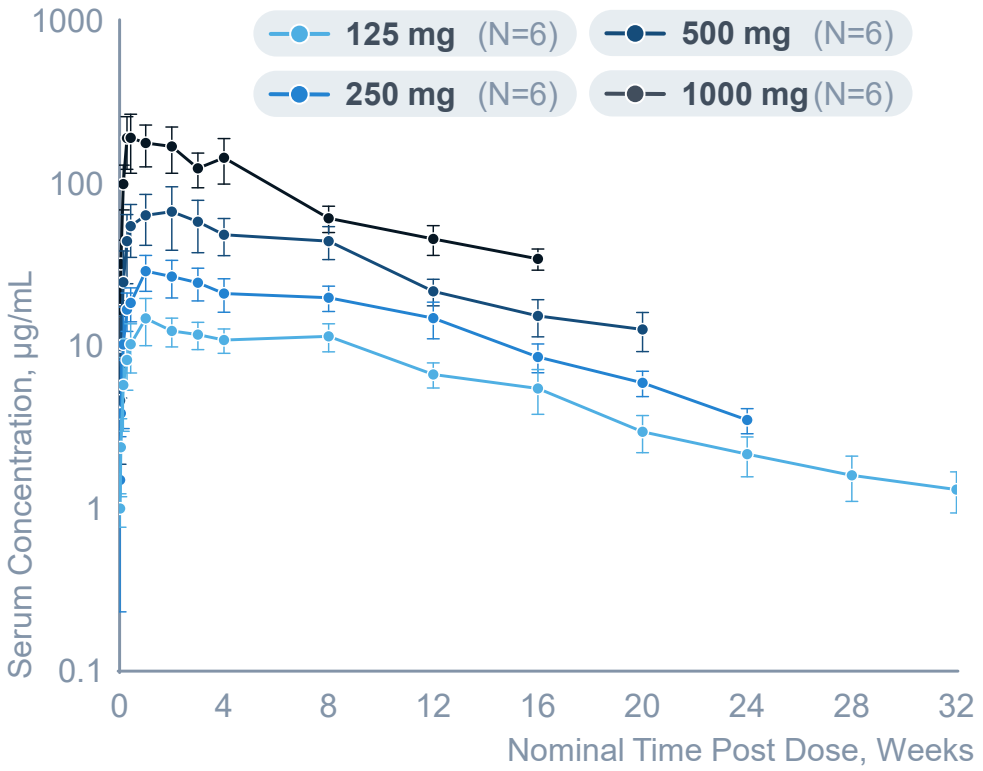
	Single dose					Overall trial	
	Placebo N=8	APG333 Cohort 1 125 mg N=6	APG333 Cohort 2 250 mg N=6	APG333 Cohort 3 500 mg N=6	APG333 Cohort 4 1000 mg N=6	Placebo N=8	APG333 N=24
≥1 TEAE	3 (37.5)	4 (66.7)	6 (100)	4 (66.7)	4 (66.7)	3 (37.5)	18 (75.0)
≥1 serious TEAE	0	0	0	0	0	0	0
≥1 drug-related TEAE	0	1 (16.7)	1 (16.7)	1 (16.7)	1 (16.7)	0	4 (16.7)[1]
≥1 Grade 3 TEAE	0	0	1 (16.7)	0	0	0	1 (4.2)[2]
Discontinued study due to TEAE	0	0	0	0	0	0	0

APG333 safety profile supports continued development in combination studies with APG777

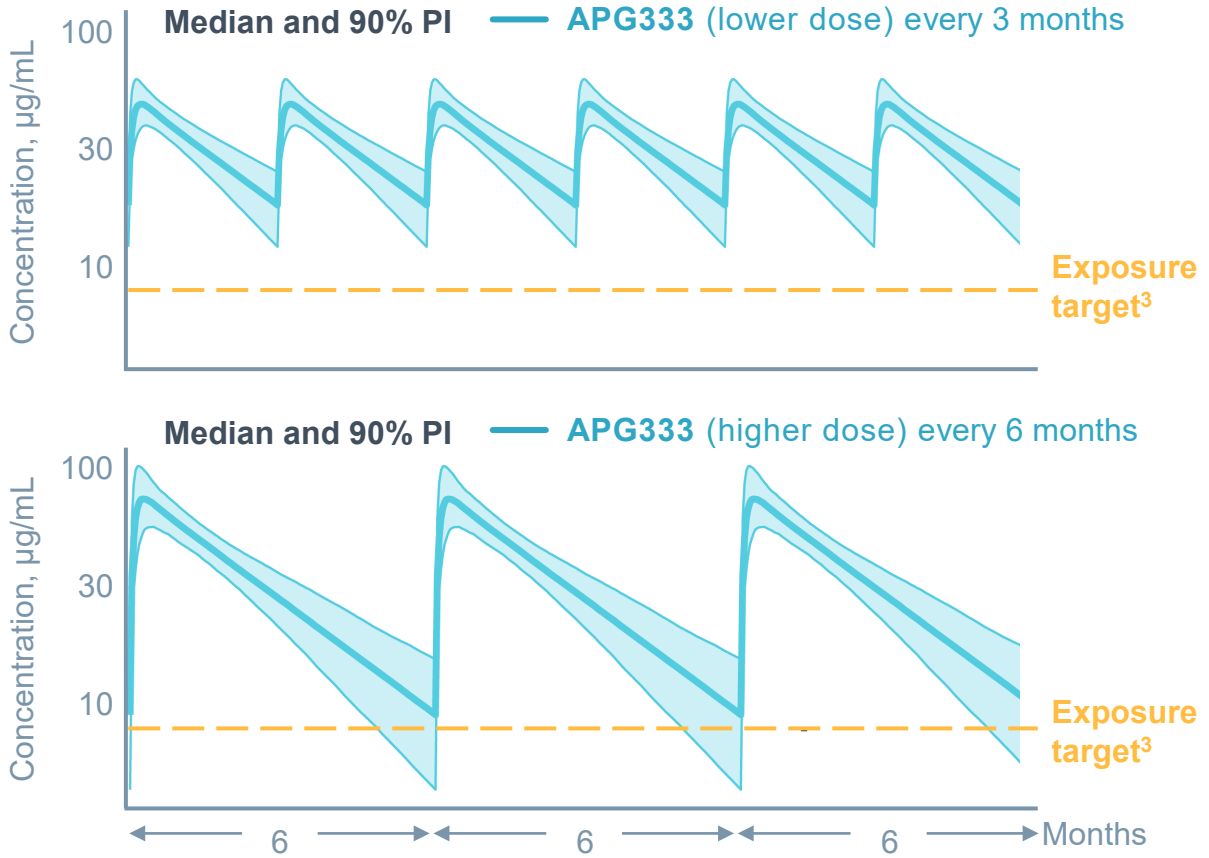
NOTE: TEAE = Treatment-Emergent Adverse Event. Interim data includes AEs reported as of 21 August 2025 data cut. The trial is ongoing.
[1] Drug-related TEAEs were headache (1 subject); neutropenia (1 subject); injection site erythema, nausea & vomiting (1 subject); and nausea (1 subject). All resolved by the data cut off.
[2] Gastritis: assessed as unrelated to study drug. Patient presented to the emergency department with bilateral upper quadrant abdominal pain and left flank pain, treated with analgesics, and discharged on oral anti-reflux medication.

APG333 demonstrated an interim half-life of ~55 days

APG333 single-dose concentration-time profile[1]



Modeled exposures based on APG333 Phase 1 PK[2]

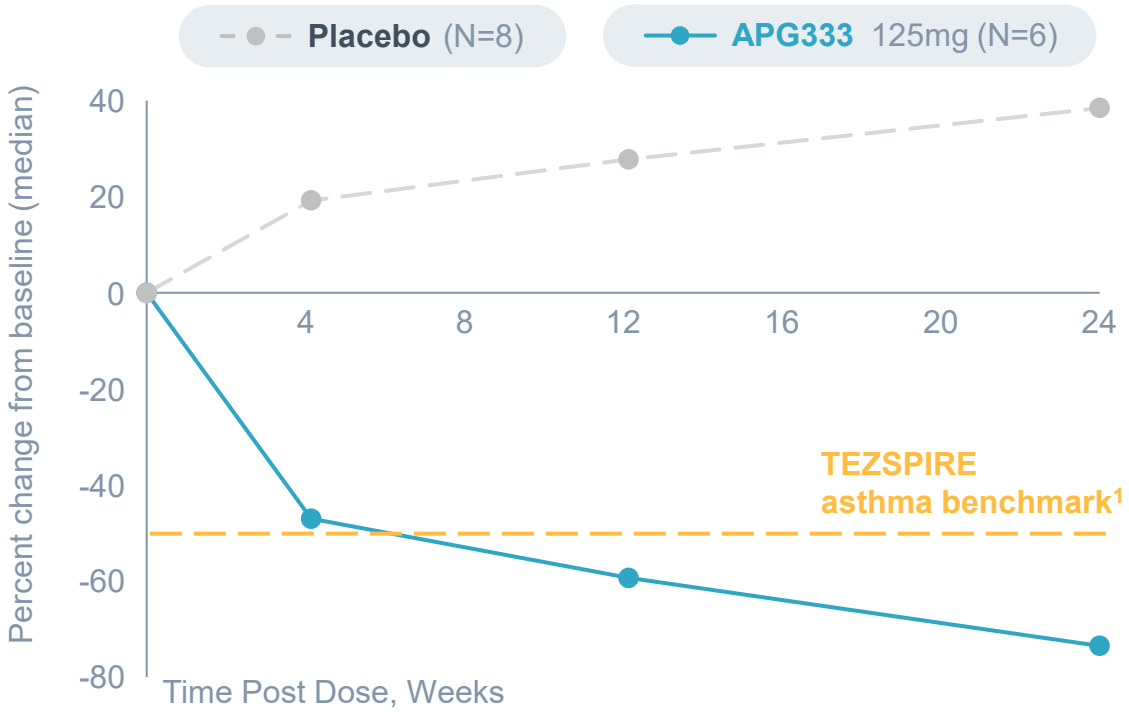


Modeled exposures support potential for APG333 every 3- and 6-month dosing

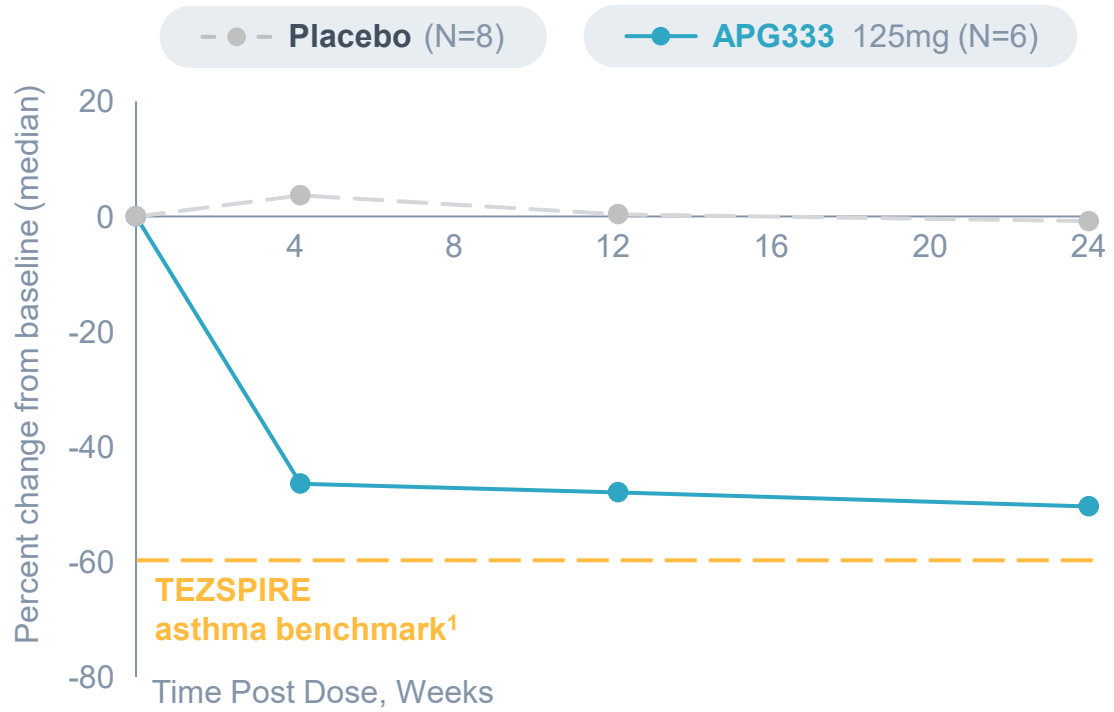
NOTE: The above graphs are illustrative only with respect to plans for dosing of APG333 and does not present comparative data.
[1] Mean (SD) profiles. [2] Solid blue line represents population PK (PPK) model predicted median concentrations of APG333 for Q3M or Q6M dosing regimen, shaded blue area represents 90% prediction interval (PI).
[3] Based on Apogee modeled exposures for tezepelumab 70mg Q4W dosing in PATHWAY Phase 2b trial (Ctrough,ss = ~8 µg/mL).

Single dose of APG333 demonstrated durable biomarker suppression in HVs through 6-months; depth of suppression was comparable to TEZSPIRE

Blood Eosinophil Counts



IL-5



Durable biomarker suppression supports potential for APG333 every 3- and 6-month dosing

NOTE: HV = healthy volunteer. For illustrative purposes only. Biomarker data are derived from different clinical trials conducted at different times, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted. No data has been published showing TEZSPIRE impact on blood eosinophil counts or IL-5 in HVs.
SOURCE: [1] Corren JC, et al. Allergy, 2022 (median percent reduction for 210mg Q4W dose of tezepelumab at 52 weeks in PATHWAY Phase 2b asthma trial).

APG273

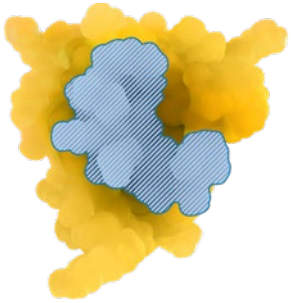
(APG777+APG333)

APG273 (APG777+APG333) combines validated mechanisms for potentially best-in-class efficacy and dosing in obstructive airway disease

OVERLAPPING EPITOPE

APG777

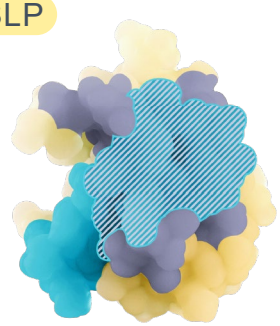
HUMAN IL-13



Overlapping region (vs. EBGLYSS)

APG333

HUMAN TSLP



Overlapping region (vs. TEZSPIRE)

OPTIMIZED PK AND FORMULATION

77-day human half-life

APG273

Potential for APG273 every 3-month dosing or better

~55-day human half-life

BROAD & ROBUST INHIBITION

Preclinical data

	Airway remodeling: Periostin[1]	Eosinophil recruitment: IL-5[2]
APG273 IL-13 + TSLP	23	7
Tezepelumab TSLP	65	7
Lebrikizumab IL-13	19	51

Clinical data: Durable biomarker suppression through 6 months after single dose
(e.g.,TARC for APG777; IL-5 for APG333)

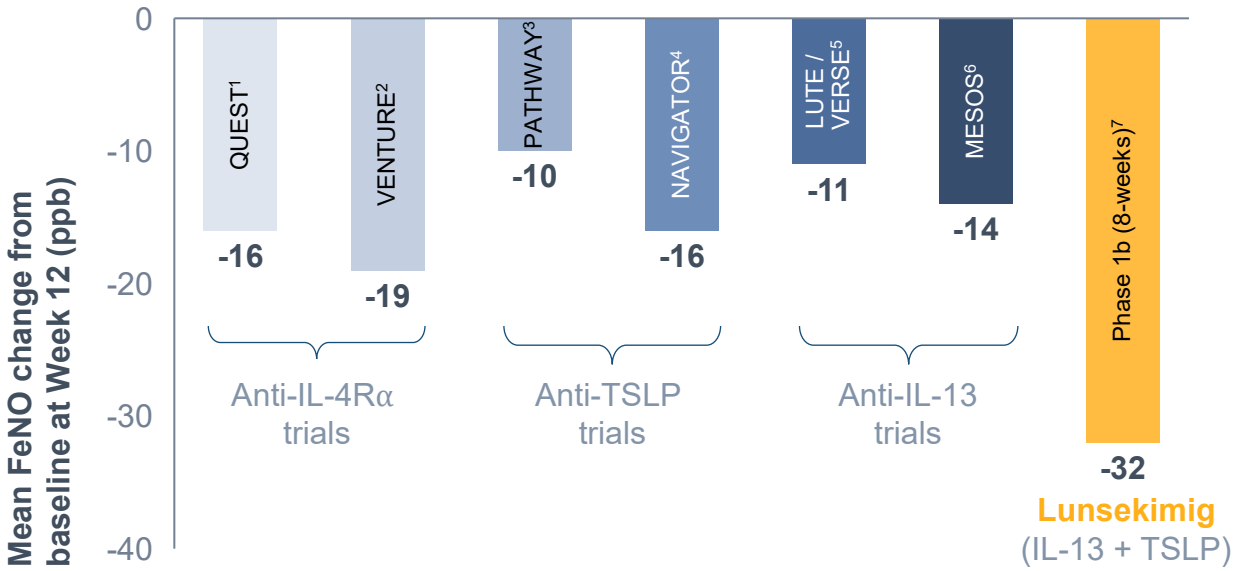
Cytokine level (% of untreated)[3]

0 20 40 60 80 100

NOTE: [1] Human airway epithelial cells from one COPD donor were cultured at the air-liquid interface and treated with TSLP+IL-13. After 7 days, cytokines were measured in the basal supernatants. [2] ALR performed using four donor pairs of TSLP-primed mDCs plus allogeneic CD4 cells for 5 days. [3] Responses are reported as mean percent of control across all donors.

Clinical POC for combining IL-13 + TSLP inhibition exists with lunsekimig

FeNO data from lunsekimig asthma Ph1b demonstrates potential for combos to break through the monotherapy efficacy ceiling



Lunsekimig has multiple readouts in next ~18 months, including Ph2b asthma data in 1H 2026

- **Moderate-severe asthma data in 1H 2026**
- **Mild-moderate asthma data in 2H 2026**
- **COPD Ph2/3 study launching**
- **CRSwNP data in 1H 2027**

- **APG273 potential every 3-month dosing or better** could improve on lunsekimig's dosing (9-11 day half-life; testing monthly dosing[8-10])
- **Potential for greater efficacy with APG273's optimized stoichiometry** vs. fixed 1:1 target ratio for lunsekimig, which clinical evidence suggests is not optimal

SOURCE: [1] Castro M, et al. NEJM, 2018. [2] Rabe KF et al. NEJM, 2018. [3] Corren JC, et al. NEJM, 2017. [4] Menzies-Gow A, et al. NEJM, 2021. [5] Hanania NA, et al. Thorax, 2015. [6] Russell RJ, et al. Lancet Respir Med, 2018. [7] Deiteren A, et al. ATS, 2023. Week 12 not available. [8] Lunsekimig clinical trial design for Chronic Rhinosinusitis With Nasal Polyps (NCT06454240). [9] Deiteren et al. (2024) Clin Transl Sci. DOI: 10.1111/cts.13864. [10] Deiteren A et al Eur Respir J 2025 DOI 10.1183/13993003.01461-2024.
NOTE: FeNO = fractional exhaled nitric oxide. ppb = parts per billion. COPD: chronic obstructive pulmonary disease. CRSwNP: chronic rhinosinusitis with nasal polyps.


Apogee /ˈapəjē/ noun
The highest point in the development of something; a climax or culmination