2026 J.P. Morgan Healthcare Conference

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About Upstream Bio

Clinical-stage immunology company focused on severe respiratory diseases

Developing only known clinical-stage antagonist of the TSLP receptor

- Verekitug's pharmacology is unique and characterized by rapid, complete and sustained occupancy of the TSLP receptor, for up to 24 weeks after the last dose

Studying verekitug across multiple indications with high unmet need

- VIBRANT, our phase 2 trial in CRSwNP, now complete and reported top-line results in September 2025
- VALIANT, our phase 2 trial in severe asthma, on track to report top-line results in Q1 2026
  - VALOUR, our open-label extension study, is currently enrolling eligible participants who have completed VALIANT
- VENTURE, our phase 2 trial in COPD, currently enrolling
- All trials randomized and placebo-controlled, with registrational endpoints
- TSLP biology supports expansion into other therapeutic areas, including dermatology and GI

Addressing significant commercial opportunities

- Asthma and COPD markets are expanding and expected to drive a $35B+ global biologics market by mid-2030s

Existing capital expected to fund planned operations through 2027

TSLP - thymic stromal lymphopoietin; CRSwNP - chronic rhinosinusitis with nasal polyps; COPD - chronic obstructive pulmonary disease.

Leadership team

Deep experience and complementary areas of expertise

EXECUTIVE TEAM

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Chief Medical Officer & Head of R&D
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Founding Member, Mass General Brigham

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Chief Financial Officer & Chief Operating Officer
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Adam Houghton, PhD
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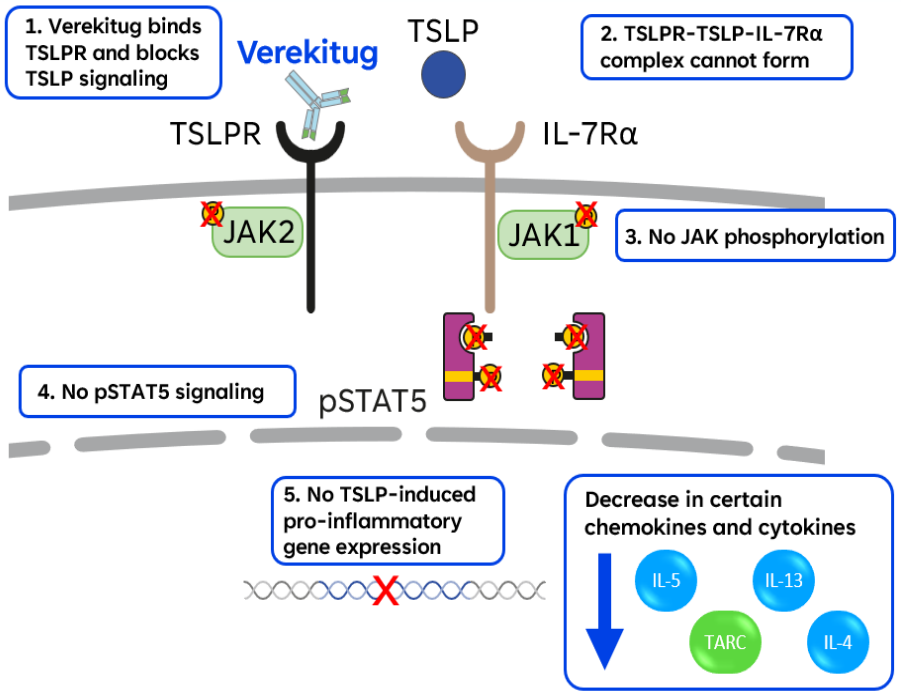
Lilly · abbvie

Stacy Price
Chief Technology Officer
INVIVYD · AKOUOS

About verekitug

- Verekitug is the only known clinical-stage antagonist targeting the TSLP receptor
  - Fully-human IgG1 antibody, discovered by Astellas/Regeneron and acquired by Upstream Bio
- Phase 1 clinical trials have demonstrated a differentiated profile
  - Complete and sustained occupancy of the TSLP receptor, for up to 24 weeks after last dose
  - High-potency antagonism of TSLP signaling as reflected by differentiated suppression of disease-associated biomarkers exhaled nitric oxide (FENO) and eosinophils in patients with asthma
- Pharmacology enables:
  - Extended interval dosing with evaluation of every 12-week and every 24-week dosing in ongoing Phase 2 trials
  - Potential for enhanced efficacy relative to TSLP ligand-targeting approaches
- Phase 2 trial of verekitug in CRSwNP delivered clinical activity meeting or exceeding that of other approved biologics at 24 weeks, with less-frequent Q12W dosing

Mechanism of verekitug inhibition of TSLP signaling[1,2,3]

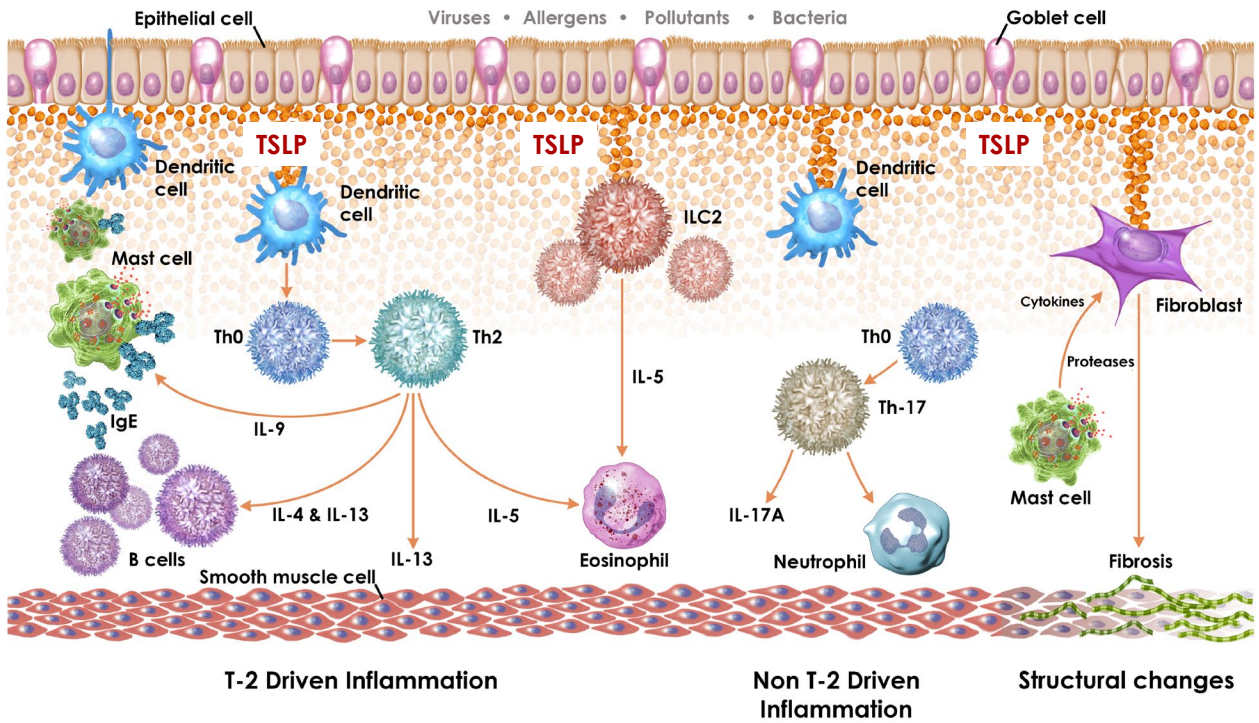


FENO – fractional exhaled nitric oxide

1. Verstraete et al, *Nat Commun,* (2017). 2. Numazaki et al, *J Pharmacol Exp Ther,* (2022). 3. Chowdhury et al, *ERS presentation, (2025).*

Verekitug blocks the TSLP receptor and potently reduces the TSLP-driven inflammation that drives severe asthma, CRSwNP, and COPD

- Inhibition of TSLP signaling reduces type 2 and non-type 2 inflammation, as well as fibrotic responses
- Verekitug blocks the formation of the heterodimeric TSLP receptor and reduces key disease-associated biomarkers
- Verekitug's potency is approximately 300-fold greater than that of tezepelumab
- Upstream Bio's clinical programs are designed to evaluate the impact of verekitug's high potency on both dosing interval and efficacy in CRSwNP, severe asthma, and COPD



Large and growing commercial opportunity in core indications, with asthma and COPD alone expected to be a $35B+ global biologics market in 2033

Asthma

2023: $7.5B[2]
2032e: $12.6B[2]

- Currently, ~1.3M biologic eligible severe asthma patients in the US[1]; ~80% of biologic sales are in the US[2]
- 5 of 6 asthma biologics have each achieved or are projected to achieve greater than $1.0 billion in global annual sales by 2025[2]
- Tezspire is projected to reach peak global annual sales of over $3B for severe asthma alone in 2032,[2] and achieved more than 20% of new to brand share of prescriptions in the US in its first commercial year[3]

CRSwNP

2025: >$1.5B[4,5*]

- Biologics to treat CRSwNP have been available for only ~6 years, now with 4 approved treatment options
- Use of biologics is growing rapidly, with >20% increases in number of claims, prescribing HCPs, and patients receiving biologics to manage CRSwNP[4]
- Current global biologics sales in CRSwNP alone estimated to be $1.5B+ annually[4,5*]
- Significant potential for growth as the proportion of eligible patients taking a biologic increases and novel biologics enter the market

COPD

2033e: $23B[2]

- Currently ~1.1M severe COPD patients in the US, expected to be ~3.5M globally by 2033[2]; ~70% of 2033 biologic sales are expected to be in the US[2]
- Currently only 2 biologics are approved for the treatment of COPD
- If approved in this indication, Tezspire is projected to reach global annual sales of over $5B for COPD alone in 2033[2]

[1] Amgen Business Review Program Feb 2022 [2] Datamonitor [3] Amgen Investor Presentation May 2024 [4] Symphony Claims Data (June '24 – May '25) [5] Manufacturer Sales and Pricing Disclosures
* As of October 2025

Developing verekitug in multiple indications with unmet need

TARGET	DEVELOPMENT: PRECLINICAL	PHASE 1	PHASE 2†	PHASE 3	MILESTONE(S)
Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) (vibrant Rhinosinusitis study)					Positive Phase 2 Top-line Results Reported in Sept 2025
Severe Asthma (valiant Asthma study)					Phase 2 Top-line Data Expected 1Q 2026 Phase 2 LTE Initiated May 2025
Chronic Obstructive Pulmonary Disease (COPD) (VENTURE Study)					Phase 2 First Patient Dosed July 2025

† Phase 2 clinical trials in severe asthma completed enrollment in June 2025. The Phase 2 long-term extension trial (LTE) is a long-term safety and efficacy study of verekitug in eligible participants who completed the Phase 2 study.

UpstreamBIO™

Clinical Data Overview

Summary of verekitug development activity

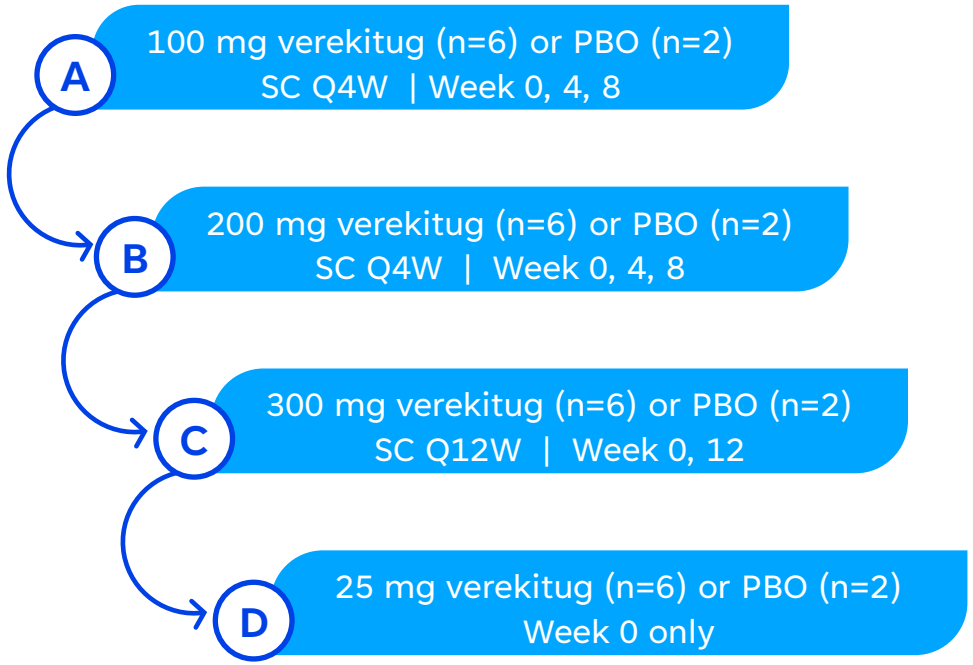
Preclinical (Astellas)	*In vitro* pharmacology	Verekitug produced potent suppression of TSLP/TSLPR-mediated responses in cell assays with clear differences in potency demonstrated compared to tezepelumab
	In vivo pharmacology	TSLPR mAb demonstrated superior biological effects to a TSLP mAb in preclinical mouse allergy models
	Toxicology	No toxicology concerns observed
Clinical	Phase 1 SAD study in healthy volunteers (HV) (Astellas)	Supported tolerability and potential for extended dosing intervals with subcutaneous (SC) administration
	Phase 1 MAD study in asthma patients	Showed full receptor occupancy and substantial suppression of disease biomarkers (blood eos and FeNO) for up to 24 weeks after last dose. PK/PD modeling indicated greater potency as compared to published data for tezepelumab
	Japanese bridging study	Demonstrated comparable PK between Japanese and non-Japanese HV
	Phase 2 study in CRSwNP	Top-line results met primary and key secondary endpoints and was generally well-tolerated at 100 mg administered Q12W
CMC	Novel formulation	200 mg/mL formulation developed – allows a Q24W dose in a single 2mL injection

MAD study designed to evaluate PD effects in asthma patients and inform Phase 2 dose selection

Study results presented at American Thoracic Society International Conference in May 2024

Key eligibility criteria

- Adults with asthma, aged 18-60 years
- Blood eosinophils ≥200 cell/µL or ≥150 cell/µL with FENO >25 ppb
- Participants on stable nonbiologic asthma medications with no dose adjustments, who experience no exacerbations, and with no new prescribed drugs within 8 weeks prior to screening



Primary objective:

To assess safety and tolerability of verekitug administered in MAD

Secondary objective:

- To assess PD effect of verekitug on FENO and blood eosinophils
- To assess the degree and duration of TSLPR occupancy in peripheral monoctyes
- To assess immunogenicity and PK of verekitug

MAD study showed a generally favorable tolerability profile

Treatment emergent adverse events were mild or moderate

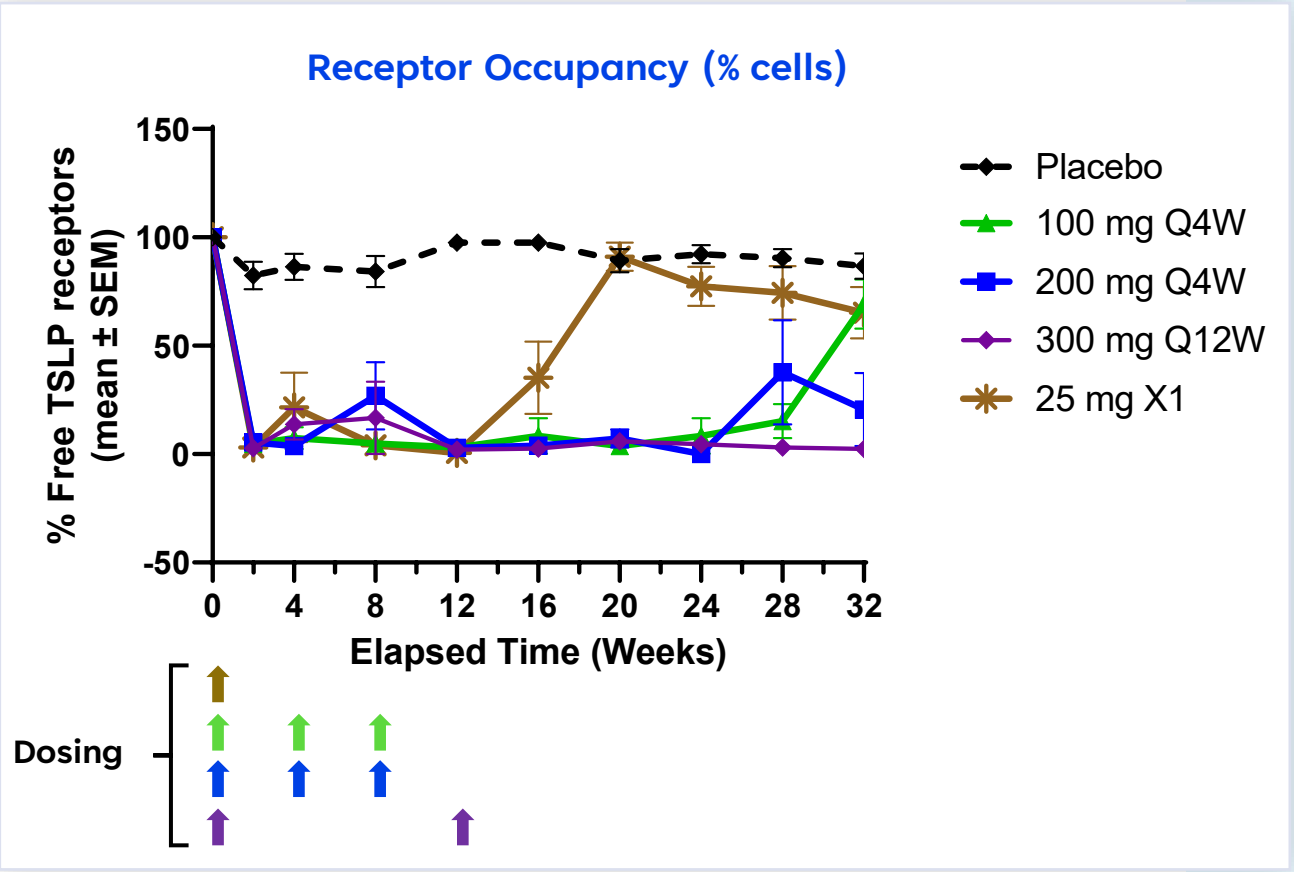
>90% of TEAEs were deemed unrelated to study drug

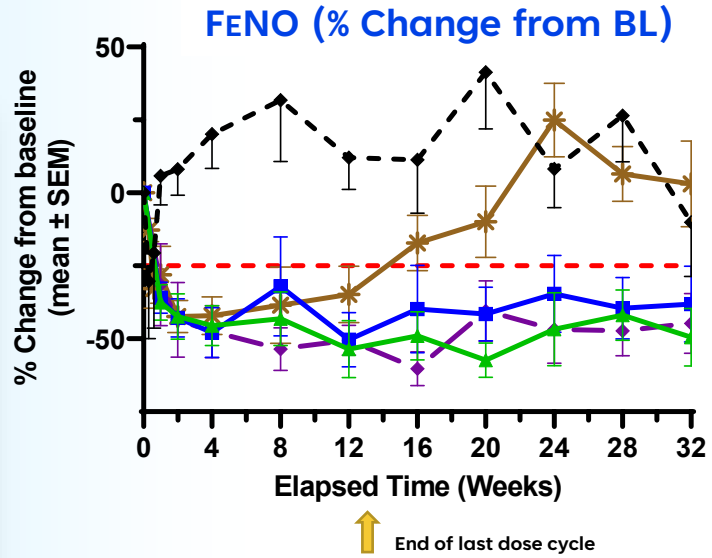
	100 mg Q4W (N=6)	200 mg Q4W (N=6)	300 mg Q12W (N=6)	25 mg X 1 (N=6)	Placebo (N=8)	Overall (N=32)
Number of TEAE	19	17	12	9	25	82
Number of Related TEAE	2	1	3	0	1	7
Subjects with any TEAE, n (%)	5 (83.3)	6 (100)	6 (100)	4 (66.7)	7 (87.5)	28 (87.5)
Mild, n (%)	1 (16.7)	4 (66.7)	5 (83.3)	0	3 (37.5)	13 (40.6)
Moderate, n (%)	4 (66.7)	2 (33.3)	1 (16.7)	4 (66.7)	4 (50.0)	15 (46.9)
Severe, n (%)	0	0	0	0	0	0
Subjects with any Related TEAE, n (%)	1 (16.7)	1 (16.7)	2 (33.3)	0	1 (12.5)	5 (15.6)
Subjects with any Serious TEAE, n	0	0	0	0	0	0
Subjects with any TEAE Leading to Withdrawal, n	0	0	0	0	0	0
Subjects with any TEAE Leading to Discontinuation of IMP, n	0	0	0	0	0	0

Most Common TEAE: Headache
Several participants had mild, short-lived, and self-limited injection site reactions; none were reported as an adverse event
No withdrawals from the trial or treatment discontinuation due to TEAEs

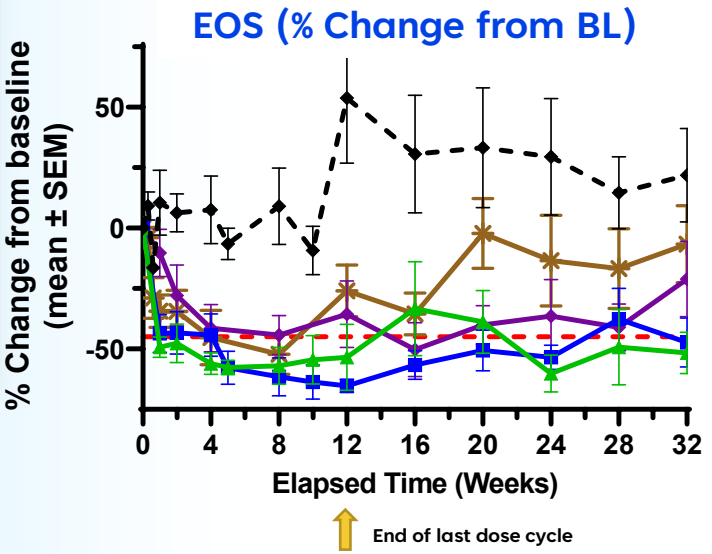
TEAE - treatment emergent adverse event; Q4W - every 4 weeks.

32-week MAD data showed substantial PD effects for up to 24 weeks after last dose





-54% at W12
-51% at W12
-51% at W12



-54% at W12
-65% at W12
-36% at W12

*Note: Data from per protocol dosing shown

- Dashed red line = Teze data with Q4W dosing up to 52-weeks. Corren et al, *Allergy*, (2022).
- Low titer ADA observed in 33-83% of subjects in each cohort without clinically meaningful impact on PK or PD.

Singh et al, *Clin Pharm Ther*, (2025).

Asthma MAD data provide proof of concept, support differentiated profile

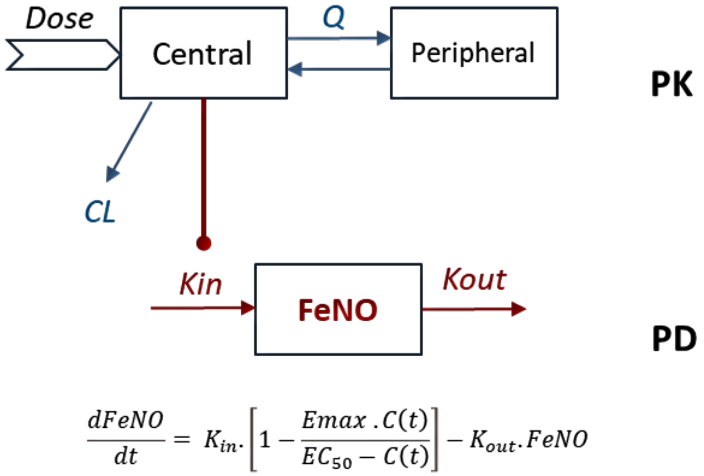
Attribute	Verekitug	Tezepelumab	Dupilumab	Mepolizumab
Target	TSLP Receptor	TSLP Ligand	IL-4/-13 Receptor	IL-5 Ligand
Dosing Interval	12, 24 weeks	4 weeks[2]	2 weeks[3]	4 weeks[5]
Injection Volume	0.5 mL (100 mg) 2.0 mL (400 mg)	1.91 mL[2]	2 mL[3]	1 mL[5]
Effect on FeNO	↓54%[1]	↓~25%[2]	↓~27%[4]	No effect[6]
Effect on Eosinophils	↓54%[1]	↓~45%[2]	↑~30%[4]	↓84%[5]
Biomarker – restricted population	Not anticipated	No[2]	Yes; eosinophilic phenotype or CS resistant asthma[3]	Yes; eosinophilic phenotype[5]

FeNO - Fractional Exhaled Nitric Oxide.
[1] 100 mg dose data from MAD study; [2] Astrazeneca AB, Tezspire (tezepelumab-ekko) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761224s003lbl.pdf; [3] Regeneron Pharmaceuticals, Dupixent (dupilumab) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761055s059lbl.pdf; [4] Multidisciplinary review of Dupixent in moderate-to-severe eosinophilic asthma. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/761055Orig1s007.pdf; [5] Glaxosmithkline LLC, Nucala (mepolizumab) [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125526Orig1s021,761122Orig1s011Corrected_lbl.pdf; [6] Ramonelle et al, *Ann Allergy Asthma Immunol*, (2021).

Information for approved products based on FDA-approved labeling and publicly available data; head-to-head clinical studies have not been conducted. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.

Verekitug has shown high potency in asthma patients

Modeled effect of verekitug on FeNO is substantially greater than that published for tezepelumab



$$\frac{dFeNO}{dt} = K_{in} \cdot \left[1 - \frac{Emax \cdot C(t)}{EC_{50} - C(t)}\right] - K_{out} \cdot FeNO$$

Verekitug FeNO PK/PD Model Parameters with Tezepelumab

Verekitug			Tezepelumab[1]		
E_{MAX} (reduction from BL)	EC_{50} (µg/ml)	EC_{90} (µg/ml)	E_{MAX} (reduction from BL)	EC_{50} (µg/ml)	EC_{90} (µg/ml)
43.4 %; 95% CI (36.6-50.4)	0.008	0.07	27.8 %; 95% CI (23.1-32.2)	2.5	22.5

→ ~1.5 times greater maximal reduction in PD (FeNO)

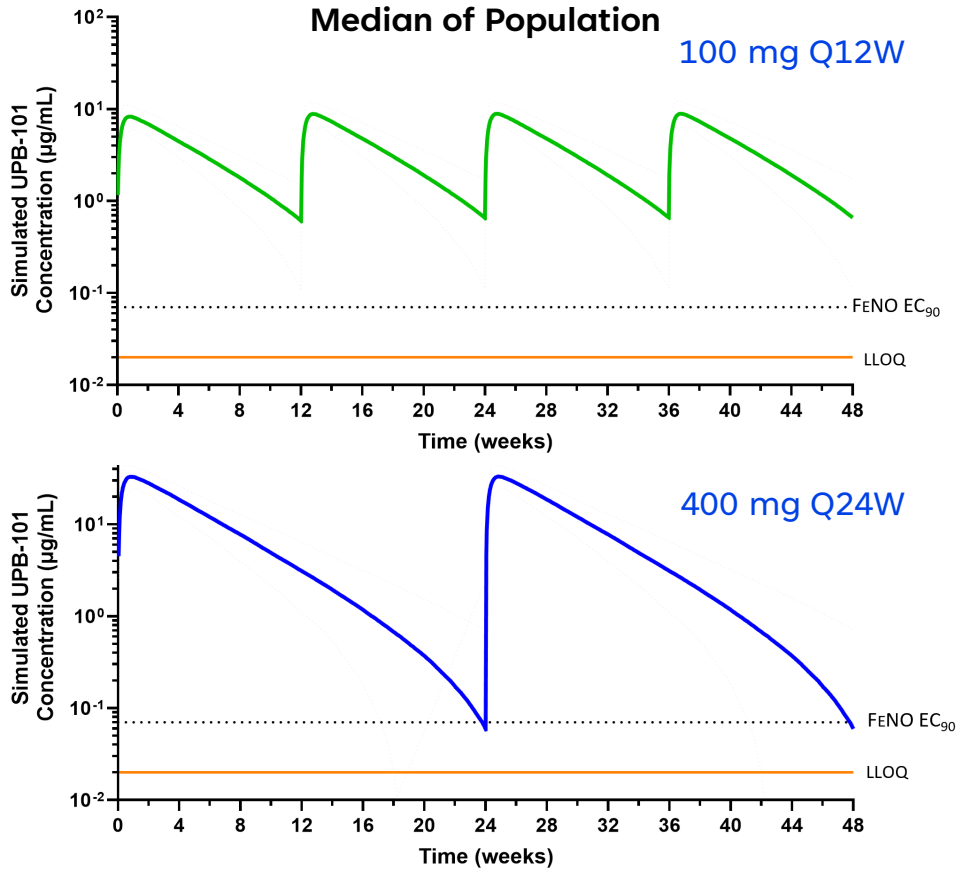
→ >300-fold lower EC_{50} /EC_{90} compared to tezepelumab

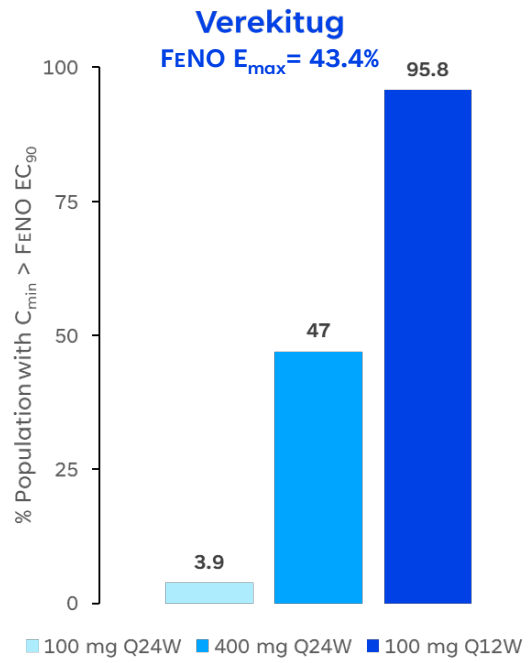
[1]Ly et al, *J Clin Pharm*, (2021).

No head-to-head clinical studies have been conducted. Differences exist between modeled data and trial design, and caution should be exercised when comparing data across studies.

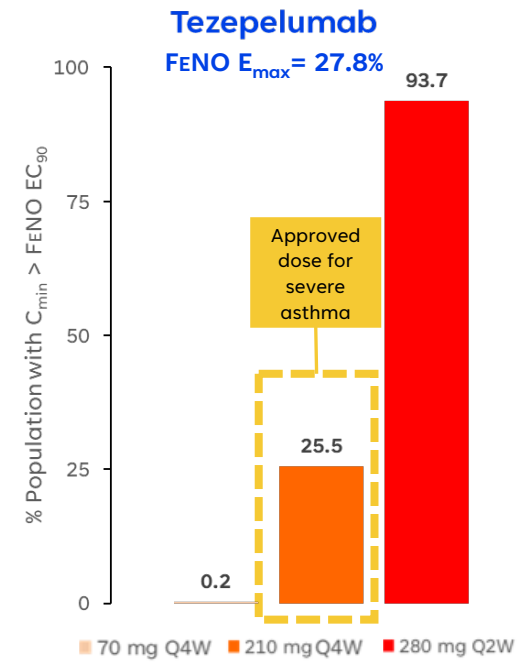
Phase 1 PK/PD model used to select Phase 2 doses predicted to maintain verekitug concentrations ≥FENO EC_{90} for 12 or 24 weeks

Exposure also predicted to be greater than that of approved tezepelumab dose





Phase 1 PK/PD model prediction



Tezepelumab values modeled from parameters in Ly et al, *J Clin Pharm,* (2021).

Solid line: median
LLOQ - lower limit of PK quantification

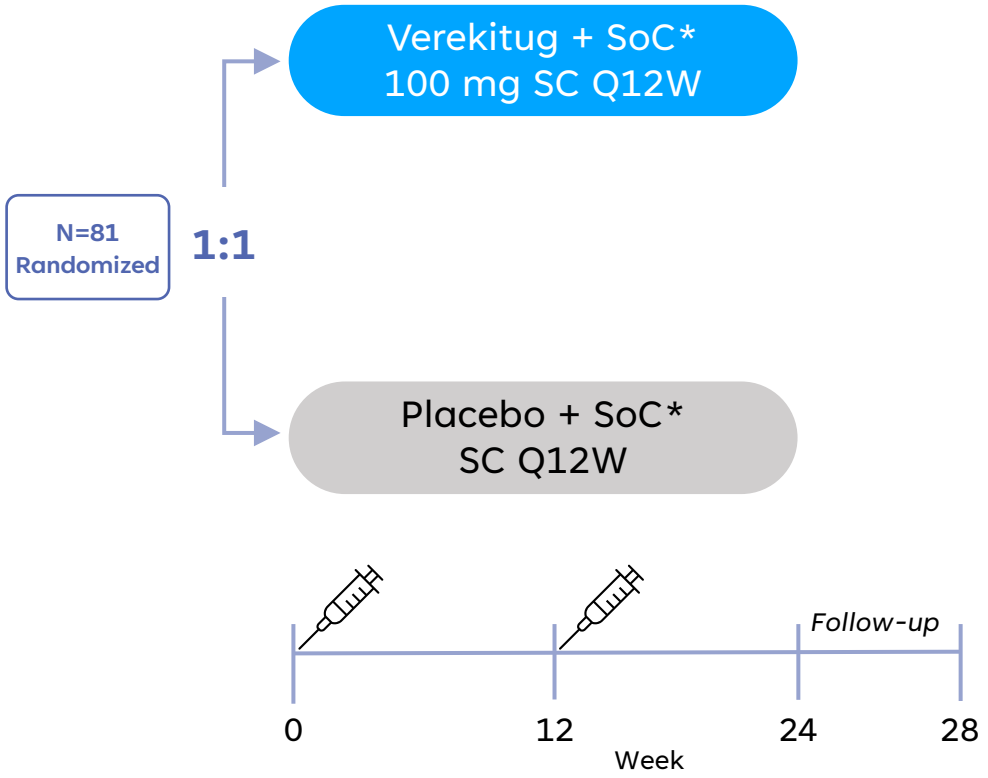
VIBRANT Phase 2 trial design

Enrolled 81 patients with CRSwNP in the US and Europe

Randomized, double-blind, placebo-controlled Phase 2 study with a 24-week treatment period (NCT06164704)

Key inclusion criteria:

- History of nasal polyp (NP) surgery OR NP exacerbation requiring systemic steroids in past 24 months
- Endoscopic nasal polyp score (NPS) ≥5
- Nasal congestion score (NCS) ≥2 over 14 days
- CRSwNP symptoms for ≥8 weeks
- Stable standard of care treatment for CRSwNP for ≥30 days



Primary endpoint:

Change in NPS

(from baseline to week 24)

Key secondary endpoints:

- Change from baseline to week 24
  - NCS
  - Sinus opacification (Lund-Mackay score)
  - Total Symptom Score (TSS)
  - Difficulty with sense of smell (DSS score)
- Proportion of patients requiring surgery or systemic corticosteroids over 24 weeks

*SoC issued is an inhaled corticosteroid; SC - subcutaneous; SoC - standard of care.

Top-line results for Phase 2 VIBRANT study of verekitug in CRSwNP

Study drug dosed every 12 weeks, treatment period 24 weeks

Phase 2 VIBRANT

100 mg Q12W vs placebo

- Met primary endpoint, with NPS reduction of -1.8 ($p<0.0001$)
- Met key secondary endpoints, including NCS reduction of -0.8 ($p=0.0003$*) and 76% reduction in need for surgery/steroids ($p=0.03$*)
- Generally well tolerated, no SAEs observed
- Observed clinical benefit at 12-week dosing interval supports potential utility in severe asthma and other Type 2 inflammatory diseases

*Nominal p values

NPS - Nasal Polyp Score; NCS - Nasal Congestion Score; Q12W - every 12 weeks; SAEs - serious adverse events.

Baseline characteristics were balanced across treatment groups

Slightly higher blood eosinophils observed in placebo group

	Verekitug	Placebo
Age (years), mean (SD)	49.8 (13.26)	49.6 (13.42)
CRSwNP duration (years), mean (SD)	13.7 (9.92)	11.7 (6.78)
Patients with systemic corticosteroid use in the preceding 2 years, n (%)	17 (41.5)	15 (37.5)
Patients with ≥1 prior NP surgery, n (%)	26 (63.4)	26 (65.0)
Patients with comorbid asthma, n (%)*	24 (58.5)	23 (57.5)
Bilateral endoscopic NPS (mean)	5.9 (1.6)	6.1 (1.32)
Baseline NCS (mean)	2.6 (0.43)	2.6 (0.44)
Baseline DSS (mean)	2.85 (0.33)	2.75 (0.57)
Baseline LMK (mean)	17.1 (4.84)	16.9 (4.92)
Blood eosinophil count (mean, cells/µL)	404 (260)	496 (378)
% < 150 cells/µL	7.3	7.5
% ≥ 150 cells/µL	92.7	90.0
% < 300 cells/µL	36.6	32.5
% ≥ 300 cells/µL	63.4	65.0

*Includes participants with AERD. AERD - aspirin-exacerbated respiratory disease; SD - standard deviation.

vibrant Rhinosinusitis study

Verekitug was generally well tolerated

Adverse Event Category, n, subjects (%)	Verekitug (n=40)	Placebo (n=40)
Any treatment-emergent adverse events (TEAE)	27 (67.5)	26 (65.0)
Any TEAEs related to study treatment	1 (2.5)	3 (7.5)
Any serious TEAEs	0	0
Any serious TEAEs related to study treatment	0	0
Any TEAEs with outcome of death	0	0
Any TEAEs leading to study drug discontinuation	0 (0.0)	1 (2.5)

Most Common TEAEs consistent with disease symptoms:
Upper respiratory tract infections, sinusitis, nasopharyngitis, nasal polyps, headache

- Overall, incidence of AEs was similar across treatment groups
- TEAEs related to study treatment occurred more frequently in placebo
- No serious adverse events reported

Verekitug led to significant and clinically meaningful improvements in NPS and key secondary endpoints, including reduction in need for surgery or systemic corticosteroids

		Verekitug	Placebo	Treatment difference
Primary Endpoint	**NPS change from baseline***	-2.1 (0.26)	-0.3 (0.27)	-1.8 (-2.51, -1.03) p<0.0001
Key Secondary Endpoints	**NCS change from baseline***	-1.5 (0.14)	-0.8 (0.14)	-0.8 (-1.17, -0.37) p=0.0003†
	LMK change from baseline*	-9.0 (0.8)	-1.0 (0.8)	-8.0 (-10.2, -5.9) p<0.0001†
	TSS change from baseline*	-10.1 (0.94)	-5.8 (0.95)	-4.3 (-6.94, -1.65) p=0.0018†
	DSS change from baseline*	-1.5 (0.15)	-0.6 (0.16)	-0.9 (-1.29, -0.42) p=0.0002†
	% requiring sinus surgery and/or SCS	7.3%	25.0%	76% reduction** p=0.03†

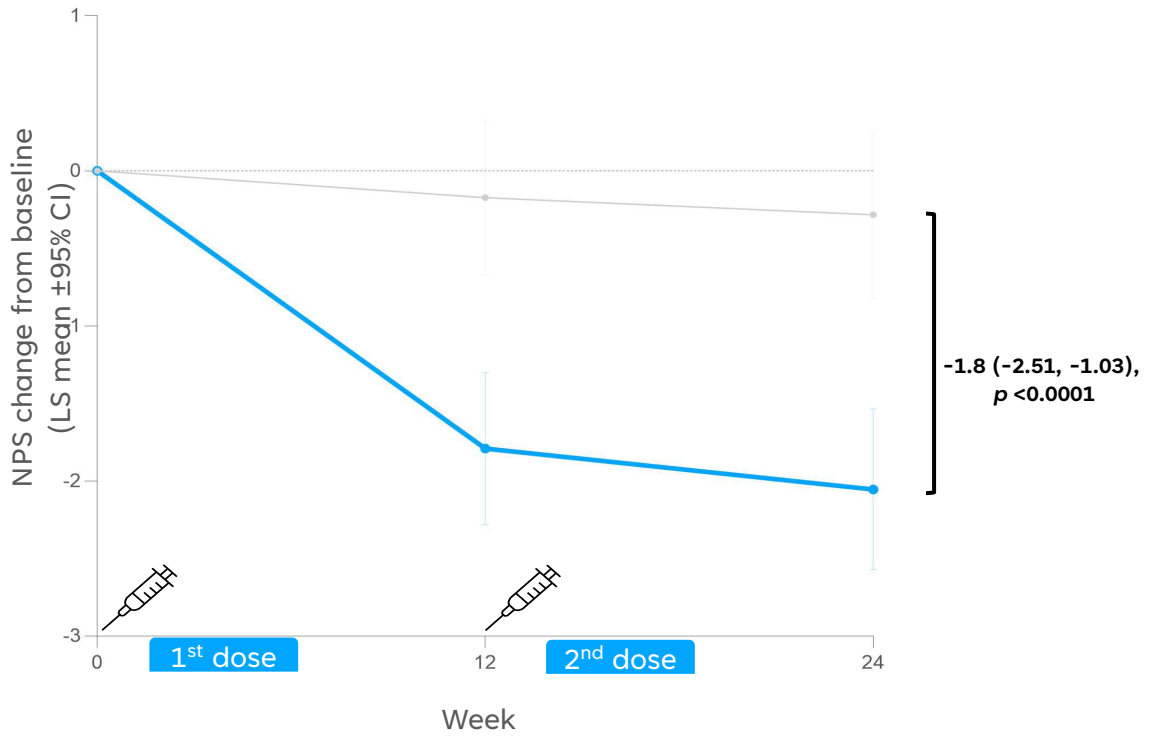
*Change from baseline is least square (LS) mean (standard error) and treatment difference is LS mean difference vs placebo (95% confidence interval)
**Risk reduction vs placebo
†p values for secondary endpoints are nominal and not adjusted for multiple comparisons.
LMK - Lund-Mackay; TSS - total symptom score; DSS - difficulty with smell score; SCS - systemic corticosteroids.
NPS range: 0–8; NCS range: 0–3 over 2 weeks; LMK CT score (0-24); TSS range: 0–24; 8 symptoms over 2 weeks; DSS range: 0–3 over 2 weeks.

Upstream BIO™

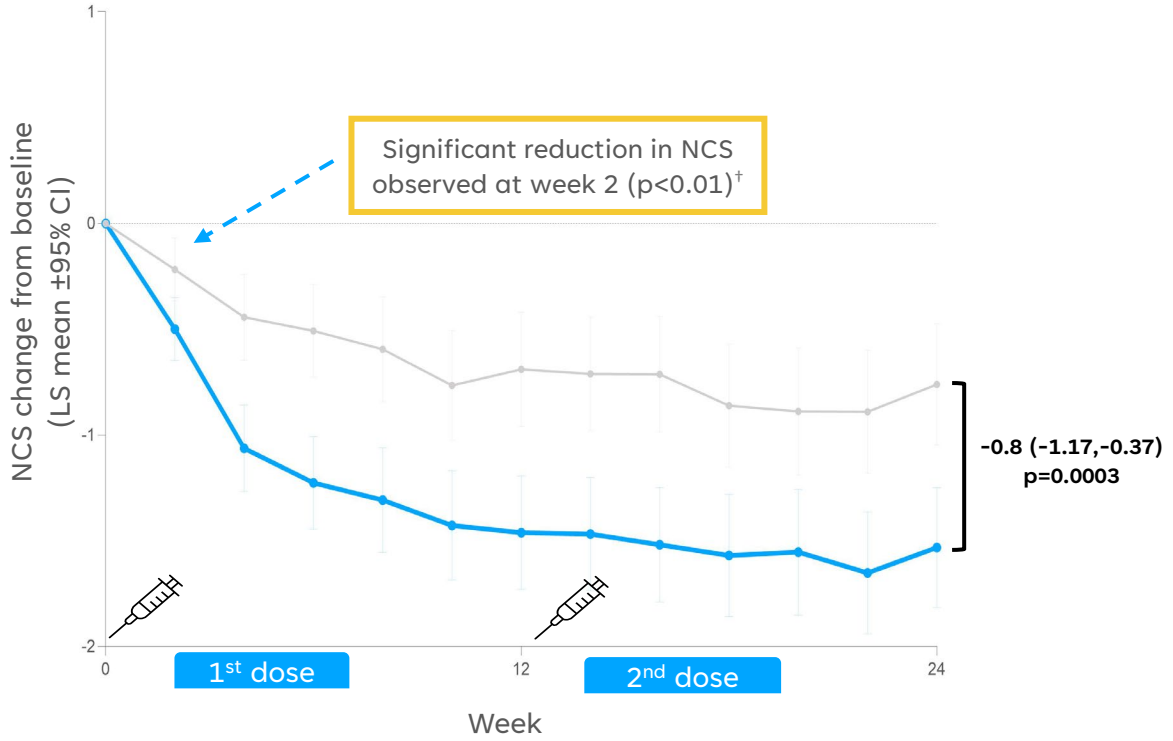
vibrant Rhinosinusitis study

Verekitug dosed every 12 weeks led to significant reductions in NPS and NCS over 24 weeks

Endoscopic NPS change



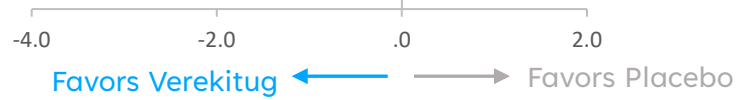
NCS change*



*NCS was calculated as the 14-day average of the daily scores. †Nominal p-value. Changes are shown as least-squares means. I bars indicate 95% confidence intervals (CI).

Verekitug demonstrated clinical effect in NPS across all subgroups

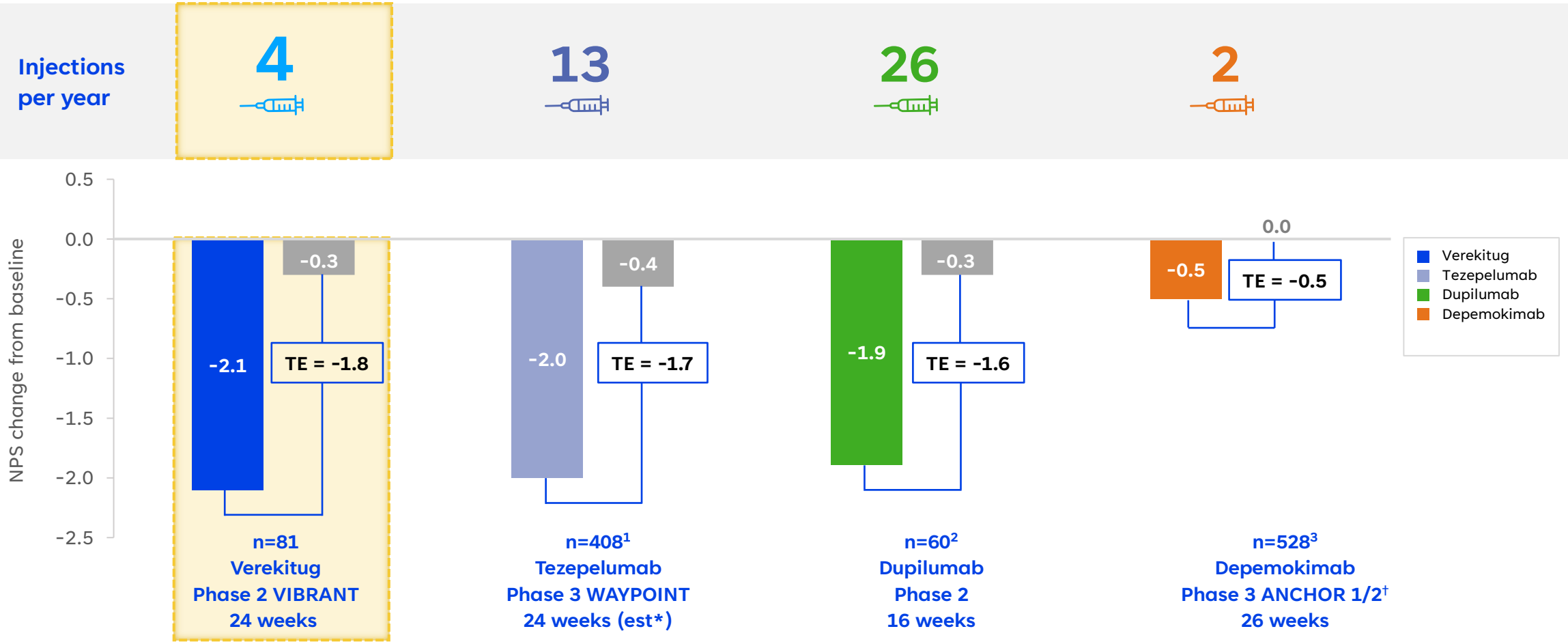
Subgroups		Verekitug n	Placebo n	Least Squares Mean Difference (95% CI)
Overall		**41**	**40**	-1.8 (-2.51 to -1.03)
Age (years)	<65	36	34	-1.8 (-2.68 to -0.98)
	≥65	5	6	-0.7 (-2.91 to 1.44)
Sex	Male	26	26	-2.1 (-3.08 to -1.19)
	Female	15	14	-0.9 (-2.36 to 0.59)
Region	USA and Western Europe	23	24	-1.9 (-2.81 to -0.99)
	Eastern Europe	18	16	-1.6 (-2.84 to -0.32)
Weight	<90 kg	22	27	-1.7 (-2.63 to -0.84)
	≥90 kg	19	13	-1.8 (-3.33 to -0.27)
Blood eosinophil level (cells/µL)	<300	15	13	-1.3 (-2.65 to -0.01)
	≥300	26	26	-2.1 (-3.00 to -1.12)
Comorbid asthma	Yes	24	23	-1.9 (-2.80 to -0.92)
	No	17	17	-1.7 (-2.93 to -0.39)
Prior Nasal Polyp surgery	Yes	26	26	-1.7 (-2.63 to -0.73)
	No	15	14	-2.0 (-3.28 to -0.80)
Prior systemic corticosteroids	Yes	17	15	-1.1 (-2.43 to 0.21)
	No	24	25	-2.1 (-3.05 to -1.13)



CI - confidence interval

vibrant Rhinosinusitis study

Verekitug dosed every 12 weeks delivered clinical activity at week 24 similar to tezepelumab dosed every 4 weeks

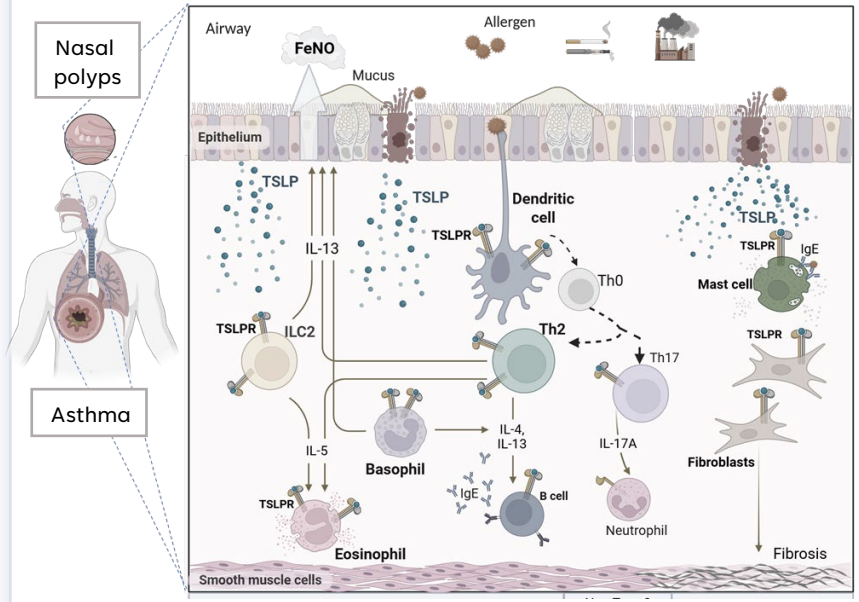


NOTE: For illustrative purposes only. Efficacy data are derived from different clinical trials conducted at different times with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted. All efficacy data shown based on statistical treatments of intercurrent events and missing data that varied across studies shown. Comparison to Phase 2 data[2] where possible. No Phase 2 studies were conducted for tezepelumab or depemokimab; *Data estimated from the Phase 3 trial[1]. †Integrated data, estimated. Only Dupilumab is FDA-approved for use in CRSwNP.
TE - placebo-adjusted treatment effect.
1. Lipworth et al, *N Engl J Med,* (2025). 2. Bachert et al, *JAMA,* (2016). 3. Gevaert et al, *Lancet,* (2025).

CRSwNP and Severe Asthma

Biological, Epidemiological and Clinical Overlap

Shared biology with central role of TSLP driving activation of common cytokine pathways[1-4]



Shared Epidemiology[1]

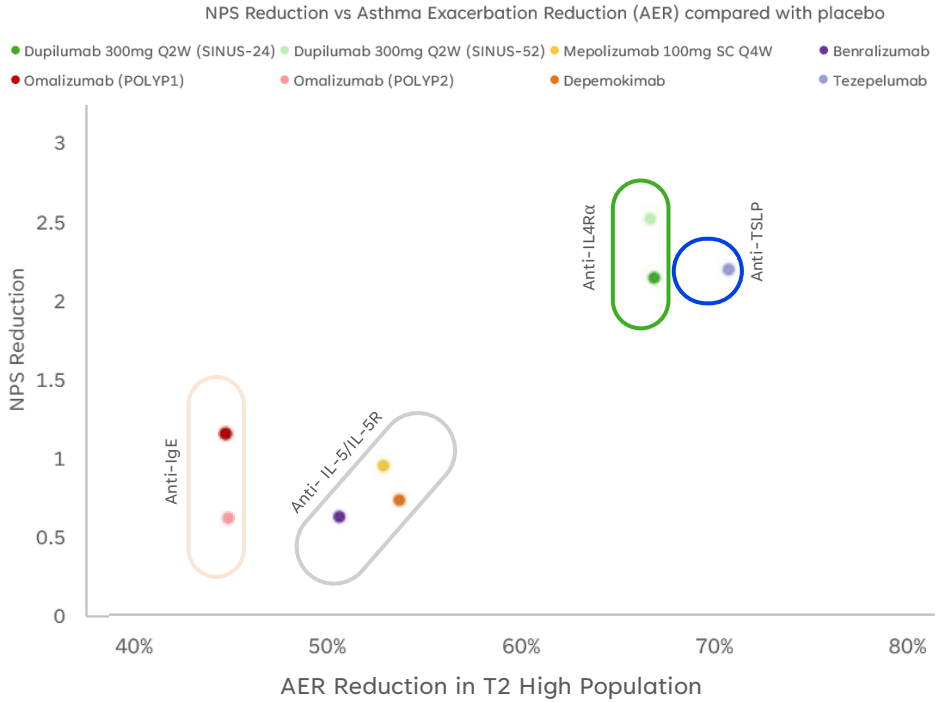
In patients with CRSwNP

Up to 70% have **comorbid asthma**

In patients with asthma

Over 40% have **comorbid CRSwNP**

Common biologic therapies and magnitude of response[5]



For illustrative purposes only. Efficacy 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. All efficacy data shown based on statistical treatments of intercurrent events and missing data that varied across studies shown. No trials simultaneously evaluating NPS/AER in same population have been conducted. AER - annualized exacerbation rate; BEC - blood eosinophil count; CRSwNP - chronic rhinosinusitis with nasal polyps; NPS - nasal polyp score; TSLP - thymic stromal lymphopoietin.

1. Bachert et al, *J Allergy Clin Immunol Pract,* (2023); 2. Castagnoli et al, *Exp Rev Respir Med,* (2020); 3. Giombi et al, *Int J Mol Sci,* (2024); 4. Pelaia et al *J Clin Med,* (2023); 5. Data derived: Dupilumab AER reduction based on BEC ≥300 (QUEST only); NPS based on SINUS-24 (Week 24) & SINUS-52 at (Week 52), Mepolizumab AER reduction based on USPI, 100 mg SC in MENSA trial only; NPS based on SYNAPSE at Week 52, Benralizumab AER reduction based on SIROCCO trial only in USPI, CALIMA was 37% reduction; NPS based on OSTRO at Week 40, Omalizumab AER reduction based on Normansell et al, *Cochrane Database Syst Rev,* (2014); NPS based on POLYP1/2 at Week 24, Depemokimab AER reduction based on Pooled SWIFT-1/2; NPS based on ANCHOR-1/2 at Week 52, Tezepelumab AER reduction based on Pooled Analysis of the PATHWAY and NAVIGATOR Clinical Trials, BEC≥300; NPS based on WAYPOINT at Week 52.

Phase 2 Clinical Trials

Summary of ongoing verekitug Phase 2 Clinical Trials

	VALIANT (Top-line data Q1 2026) Severe Asthma Phase 2 Study*	VENTURE Moderate-to-Severe COPD Phase 2 Study
Design Duration Doses	• 4 arm, randomized (1:1:1:1), parallel group • 24 week minimum→ 60 week maximum treatment • PBO, 100 mg Q24W, 400 mg Q24W, 100 mg Q12W	• 3 arm, randomized (1:1:1), parallel group • 60 week minimum→ 108 week maximum treatment • PBO, 400 mg Q24W, 100 mg Q12W
Target Population	• Age range: 18-80 years	• Age range: 40-85 years
Primary Endpoint	• Annualized Asthma Exacerbation Rate (AAER)	• Annualized rate of moderate or severe COPD exacerbation events

Secondary Endpoints	• Change from baseline:
	  • Pre–bronchodilator FEV_1
	  • FENO
	  • ACQ-6
	• Safety
		• Change from baseline:
		  • Pre–bronchodilator FEV_1
		  • FENO
		  • SGRQ
		• Safety

Sample Size	479 (actual)	666 (planned)

*A long-term safety and efficacy study (LTE) of verekitug in eligible participants who completed the Phase 2 study was initiated in May 2025.

NPS – Nasal Polyp Score; FEV_1 – forced expiratory volume in first second; ACQ-6 – six element asthma control questionnaire; NCS – Nasal Congestion Score; SGRQ – St. George's Respiratory Questionnaire; FeNO – Fractional Exhaled Nitric Oxide; CT – computed tomography, PBO – placebo

About Upstream Bio

Clinical-stage immunology company focused on severe respiratory diseases

Developing only known clinical-stage antagonist of the TSLP receptor

- Verekitug's pharmacology is unique and characterized by rapid, complete and sustained occupancy of the TSLP receptor, for up to 24 weeks after the last dose

Studying verekitug across multiple indications with high unmet need

- VIBRANT, our phase 2 trial in CRSwNP, now complete and reported top-line results in September 2025
- VALIANT, our phase 2 trial in severe asthma, on track to report top-line results in Q1 2026
  - VALOUR, our open-label extension study, is currently enrolling eligible participants who have completed VALIANT
- VENTURE, our phase 2 trial in COPD, currently enrolling
- All trials randomized and placebo-controlled, with registrational endpoints
- TSLP biology supports expansion into other therapeutic areas, including dermatology and GI

Addressing significant commercial opportunities

- Asthma and COPD markets are expanding and expected to drive a $35B+ global biologics market by mid-2030s

Existing capital expected to fund planned operations through 2027