Nektar Therapeutics Corporate Presentation



November 2026

Bold immune science.
Transformative immune health.

Forward-looking statements

This presentation includes forward-looking statements regarding Nektar's proprietary drug candidates, the timing of the start and conclusion of ongoing or planned clinical trials, the timing and outcome of regulatory decisions, unaudited year-end cash and investments and sufficiency of working capital and future availability of clinical trial data.

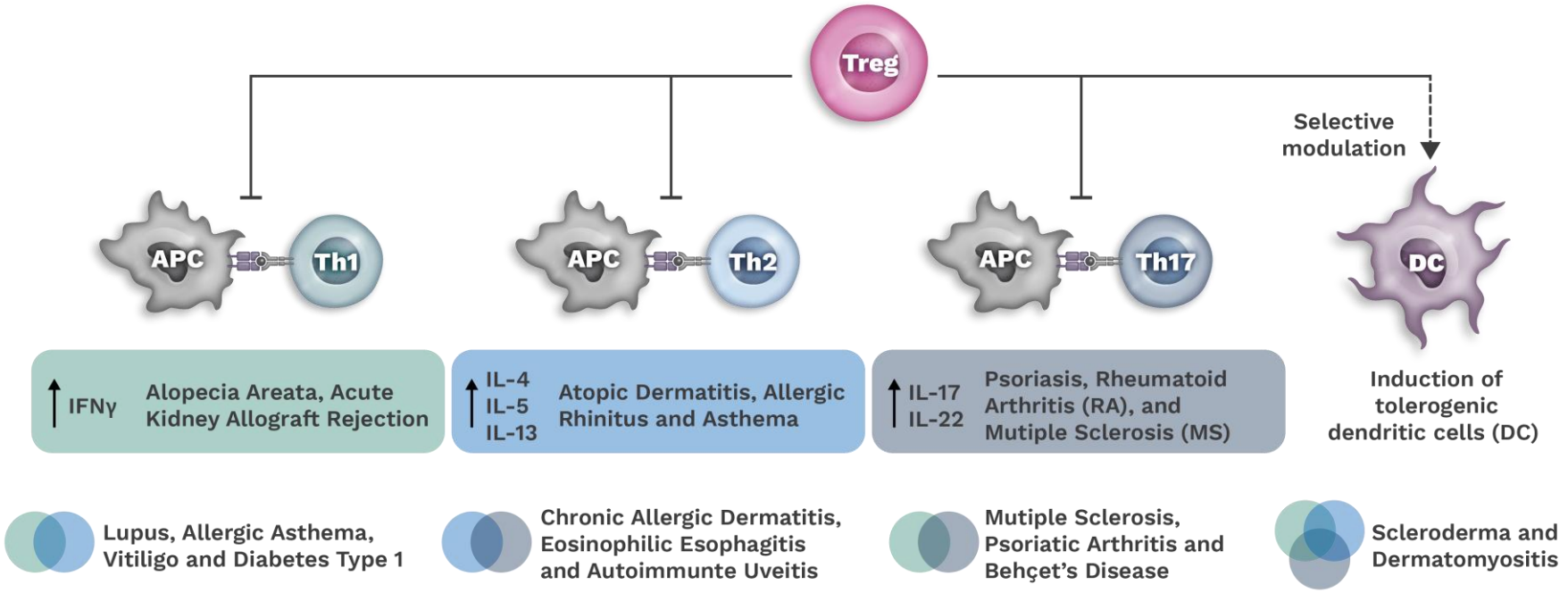
Actual results could differ materially and these statements are subject to important risks detailed in Nektar's filings with the SEC including the Form 10-Q filed on November 12, 2026.

Nektar undertakes no obligation to update forward-looking statements as a result of new information or otherwise.

Nektar pipeline

Program	Indication	Stage	Preclinical	Phase 1	Phase 2	Phase 3	Partner
Rezpegaldesleukin *(IL-2 T Regulatory Cell Stimulator)*	**Moderate-to-Severe Atopic Dermatitis**	**Completed Enrollment in Phase 2b Study (REZOLVE-AD)**			***Phase 2; Fast Track Designation***		***Off-treatment Data Q1 2027***
	Severe-to-Very-Severe Alopecia Areata	**Enrollment Completion in March 2025 (REZOLVE-AA)**			***Phase 2; Fast Track Designation***		
	New Onset Stage 3 Type 1 Diabetes (Stage 3)	**TrialNet P2 Study**			***Phase 2***		Type 1 Diabetes TrialNet ***Initial Data from the First Cohort in 2027***
NKTR-0165 *(TNFR2 Agonist Antibody)*	**Multiple Sclerosis & Other I&I Indications**	**Preclinical**		***Preclinical***	BiolojicDesign		
NKTR-0166 *(Bispecific Antibody)*	**I&I Indications**	**Preclinical**		***Preclinical***			
NKTR-422 *(PEG-CSF)*	**Fibrotic Diseases & Other Indications**	**Preclinical**		***Preclinical***			

The central role of regulatory T cells in immune homeostasis



APC=Antigen-presenting cell; Th1 = Mature helper T cell (Th1); Th2 = Mature helper T cell (Th2); Th17 = Mature helper T cell (Th17)

Tregs are crucial for immune homoeostasis and the prevention of autoimmune conditions[1]

- ***IL-2 pathway agonism***
- ***TNFR2 agonism***

Sources: 1 Lykhopiy V, et al. Genes Immun. (2023)



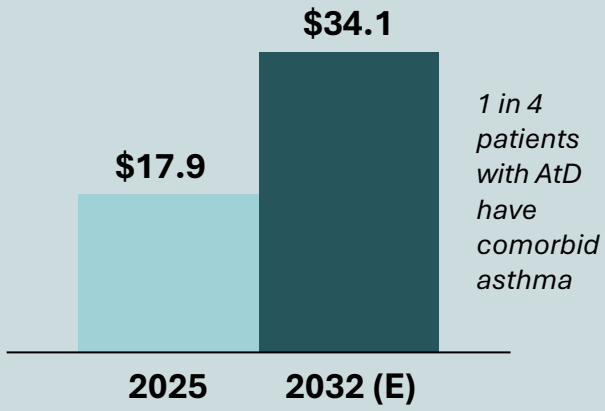
Rezpegaldesleukin in Atopic Dermatitis

Rezpegaldesleukin (REZPEG) Phase 2 Program Spans Immune-Mediated Diseases to Evaluate the Causal Biology of Tregs

Atopic Dermatitis (REZOLVE-AD) Inflammatory Skin Disease

- Achieved TPP with data indicating strong clinical efficacy and safety profile with differentiation to IL-13, IL-31, JAKi and OX-40 MoAs[1,2]
- Only biologic in development to demonstrate positive efficacy data in comorbid asthma[3]

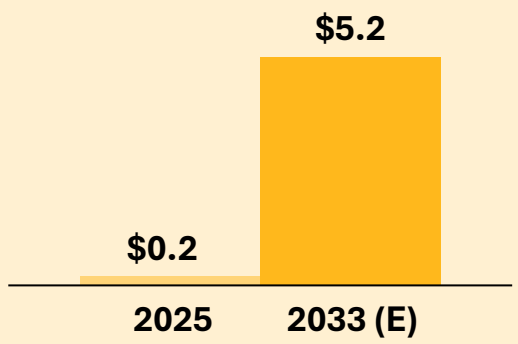
G7 Market Size ($B)[4]



Alopecia Areata (REZOLVE-AA) Inflammatory Skin Disease

- Achieved TPP with data indicating clinical efficacy similar to low-dose Olumiant® (JAK inhibitor) and a superior differentiated safety profile
- First biologic to demonstrate clear proof-of concept in severe-to-very-severe AA

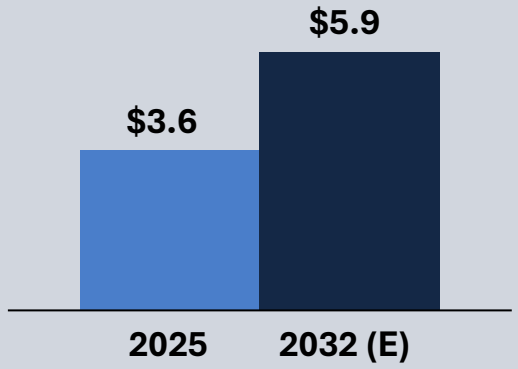
G7 Market Size ($B)[5]



Type 1 Diabetes (T1D) Metabolic Disease

- Ongoing phase 2 placebo-controlled clinical trial in patients with new onset Stage 3 T1D
- Sponsored and funded by TrialNet (NIH/NIDDK) Type 1 Diabetes Consortium
- Initial data expected in 2027

G7 Market Size ($B)[4]



Sources: 1. Silverberg J, et al. Nature Communications (2025); 2. Silverberg J, et al. EADV (2025); 3. Corren J, et al. ACAAI (2025); 4. Evaluate Pharma WW Market Size Estimates; 5. Decision Resources Group
TPP: Target Product Profile; (E): Estimate; Olumiant® is a registered trademark owned or licensed by Eli Lilly and Company, its subsidiaries, or affiliates.

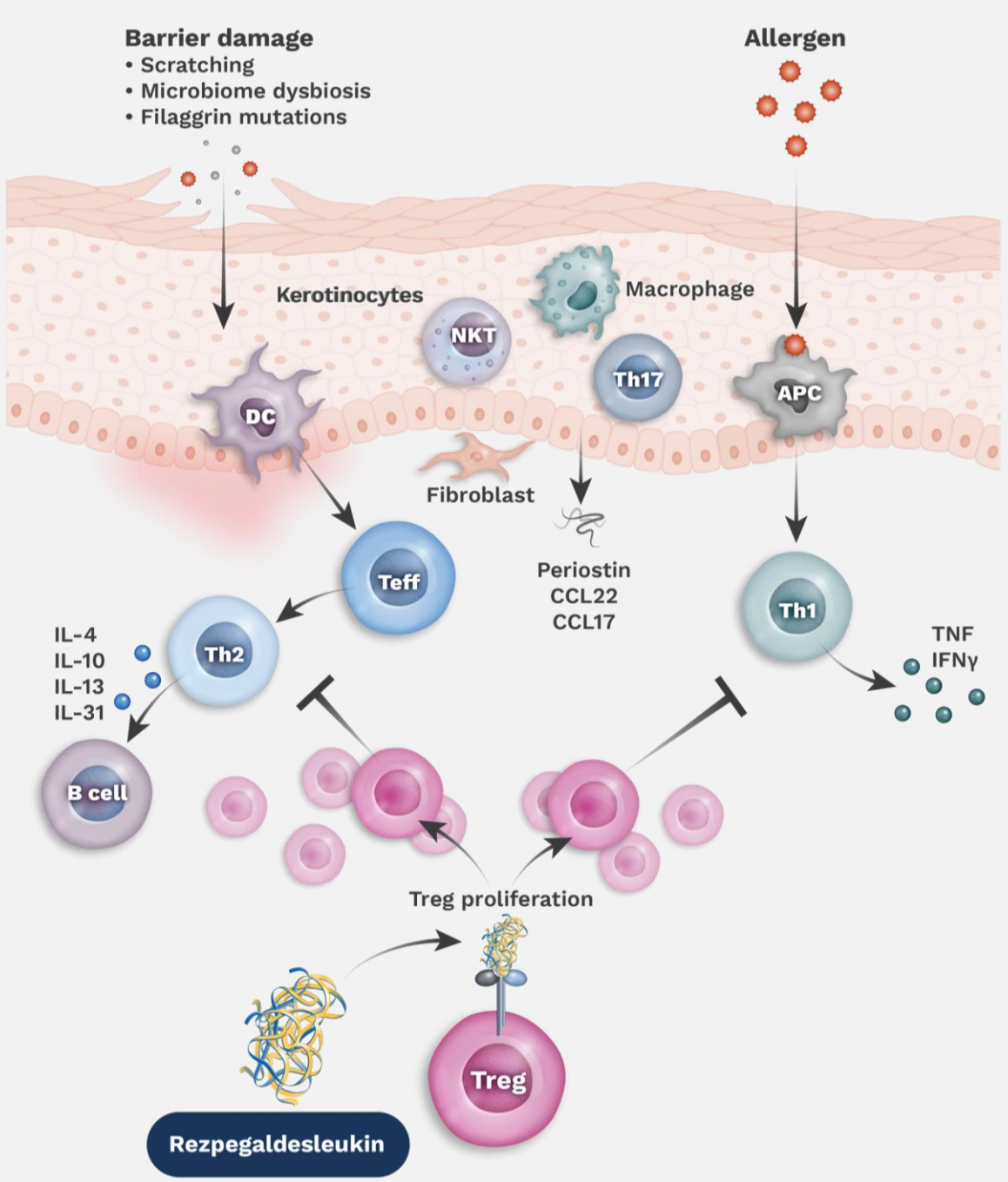
Rezpegaldesleukin
Atopic Dermatitis MOA

Scientific rationale

- By targeting receptors on regulatory T cells (Tregs), rezpegaldesleukin stimulates the proliferation of these cells, including FOX-P3+ Tregs

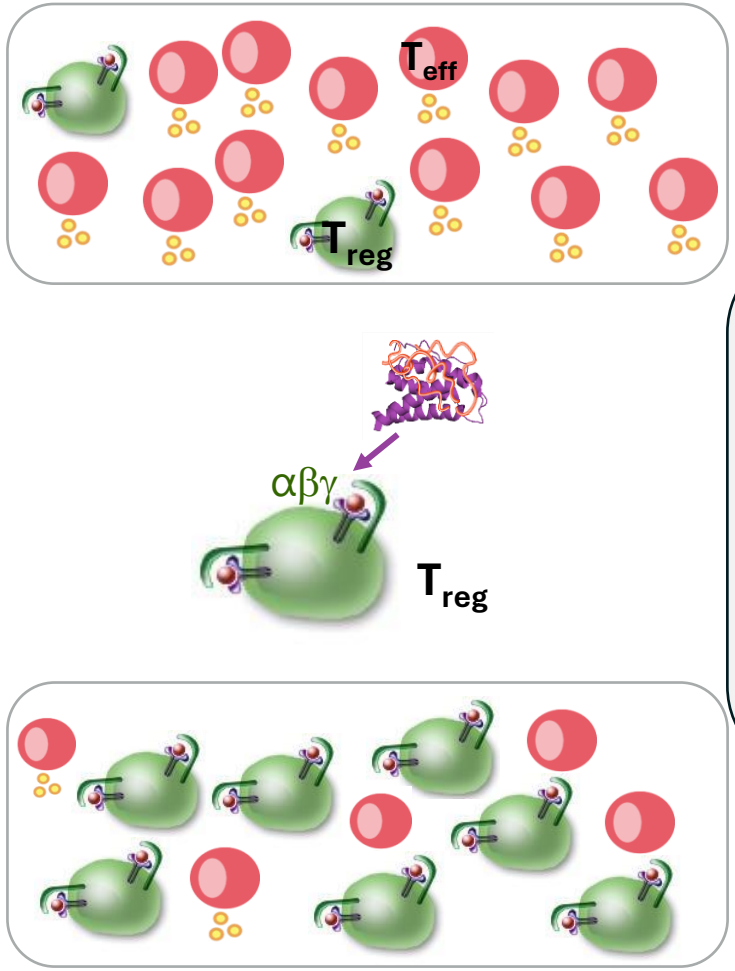
- Regulatory T cells act as a master immune-modulator upstream of the pro-inflammatory cytokine pathways, which drive Th1, Th2, Th17-mediated inflammatory disorders, such as atopic dermatitis

- By increasing the number and functionality of regulatory T cells, this investigational therapy aims to reduce inflammation more effectively than specific antagonist mechanisms that may target only one pathway



Rezpegaldesleukin is a potential first-in-class regulatory T cell mechanism to restore balance in immune system

- Many patients with moderate-to-severe atopic dermatitis (AD) **do not adequately achieve disease control** or have safety/tolerability issues with current therapies
- **Tregs play a central role in controlling AD** by dampening inflammatory cytokines and overactive T cells[1]
- **Granted Fast Track designation in Feb 2025** for treatment of adult and pediatric patients ≥12 years of age with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable



Increased activity and number of T effector cells shift the balance toward inflammation

Rezpegaldesleukin is a potential T-cell balancing therapy that acts on IL2 receptors and has been shown to[2,3]:

- **Proliferate** regulatory T cells
- **Restore** their functionality, reducing proinflammatory cytokines
- **Offer potential long-term control** of overactive immune responses

Treg expansion and activation restores the immunoregulatory balance

Sources: 1. Silverberg et al. 2024 Nature Communications, 15:9230; 2. Fanton et al. 2022 J. Translational Autoimmunity, 5:100152; 3. Dixit et al. 2021 J Translational Autoimmunity, 4:100103

Atopic dermatitis presents a multi-billion dollar market opportunity

Still high unmet need, especially for new therapies with potential for remittive effect

Atopic dermatitis (AD) is a chronic autoimmune condition that causes inflammation, redness and irritation of the skin. Moderate-to-severe AD is associated with unbearable itching that can result in significant negative impact to quality of life.



~30 million[1]

Adults with AD in U.S.



~220 million[2]

Adults with AD globally



~30%[3]

Adults with AD have moderate-to-severe disease



~8%[4]

Patients with moderate/severe AD are treated with a biologic

There is a high unmet need for a novel mechanism of action to:

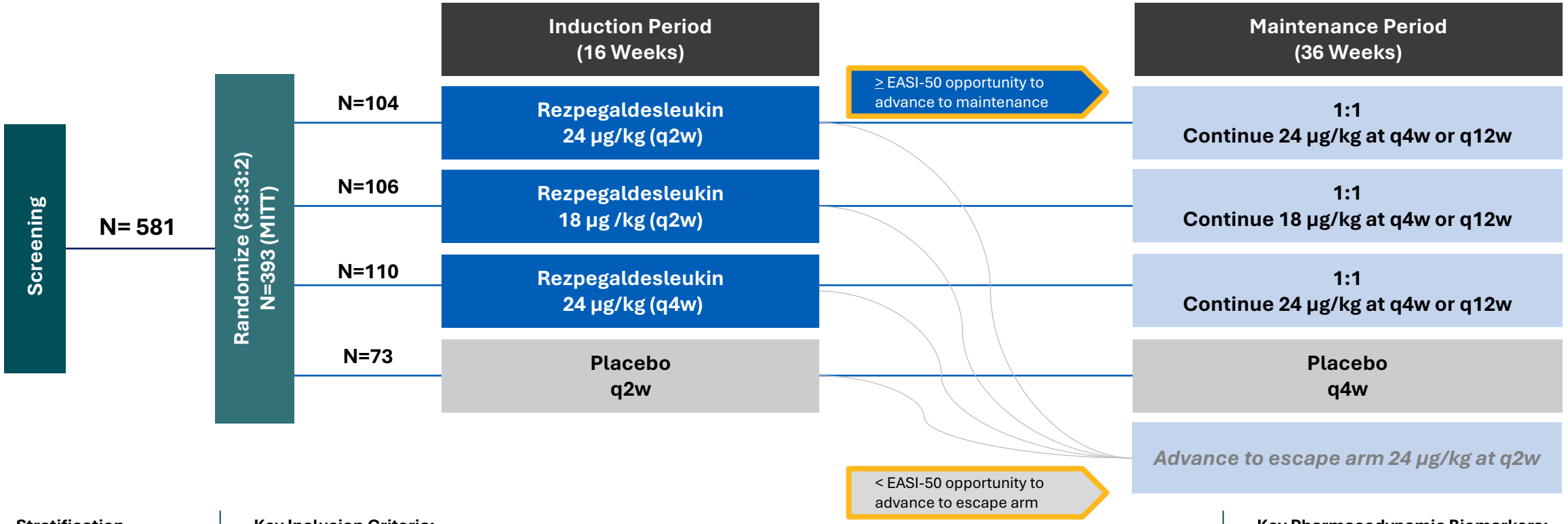
- **Offer dosing schedules without rebound effect**
- **Induce deep and potentially therapy-free remission**
- **Favorable safety and tolerability profile as compared to standard-of-care**

Dupixent: current market leader in atopic dermatitis exceeding $10.5 B in annual sales, **but 50% of patients fail on therapy**[5, 6]

Sources: 1. Eczema stats. National Eczema Association. (September 2022). https://nationaleczema.org/research/eczema-facts/; 2. Eczema council. (n.d.). https://www.eczemacouncil.org/assets/docs/global-report-on-atopic-dermatitis-2022.pdf; 3. ClarivateTM DRG Mature Markets Data 2023.; 4. DRG Epidemiology; 5. N Engl J Med 2016; 375:2335-2348 DOI: 10.1056/NEJMoa1610020; 6. EvaluatePharma, accessed January 2025

REZOLVE-AD: Phase 2b trial design

Patients with Moderate-to-Severe Atopic Dermatitis



Stratification

- ✓ Geographic region
- ✓ Disease severity by vIGA-AD

Key Inclusion Criteria:

- ✓ Age: ≥18 years
- ✓ Moderate/severe AD diagnosis for ≥ 12 months
  - EASI ≥ 16
  - vIGA-AD of 3 or 4
  - BSA ≥ 10%
- ✓ Biologic-naive (no prior biologic systemic therapy) and systemic JAKi-naïve
- ✓ Failure of prior therapy, including TCS of medium or higher potency, within last 6 months

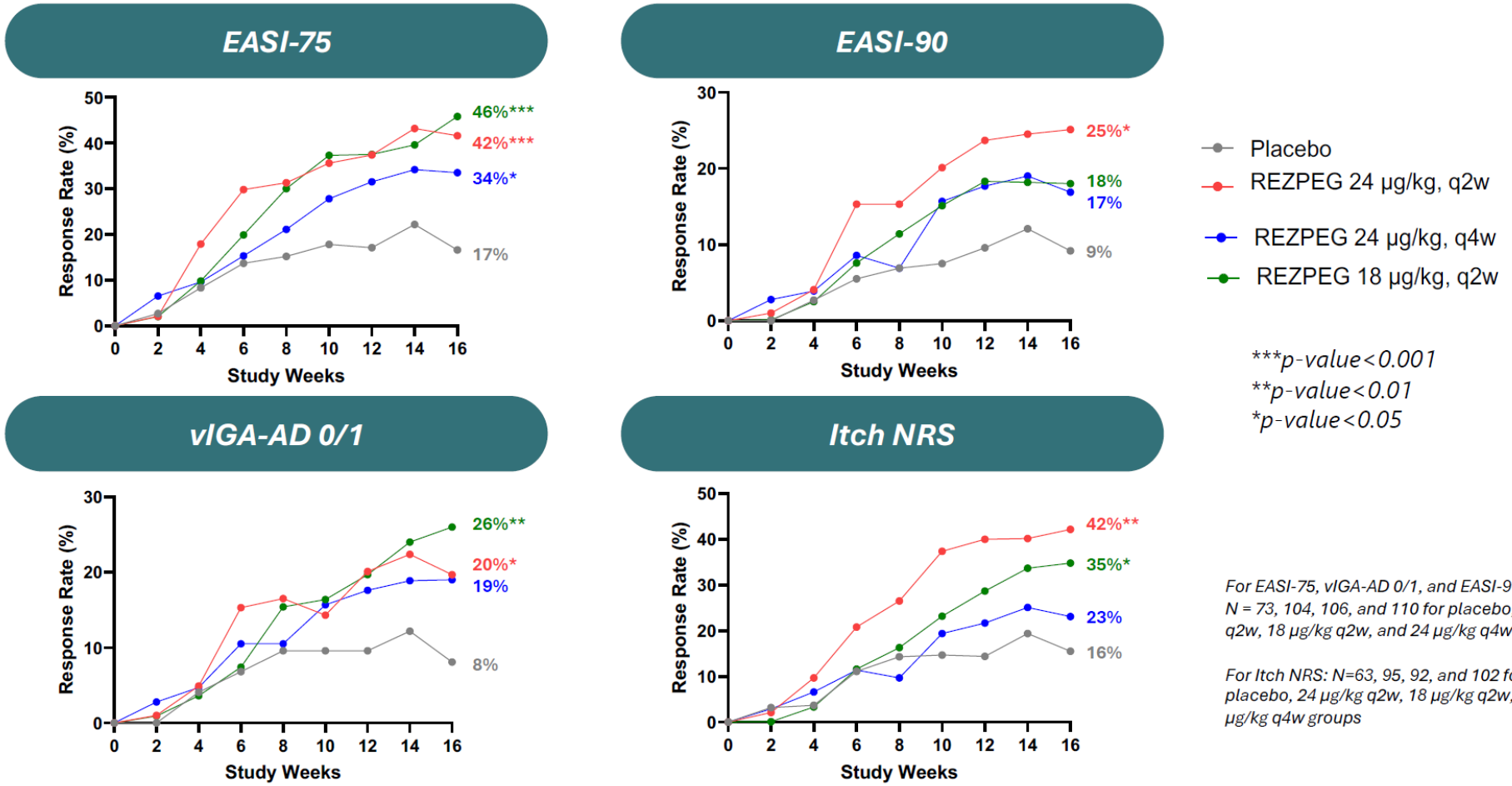
Key Pharmacodynamic Biomarkers:

- T regulatory cell
- TARC/CC17
- Periostin
- MDC/CCL22
- IL-19

MITT is defined as patients who were randomized and received at least one dose of study treatment or placebo.

Fast Onset of Action Across All Key Secondary Endpoints

EASI-75, EASI-90, vIGA-AD 0/1, and Itch NRS (≥ 4-point Reduction) Responses Seen Early and Sustained Throughout

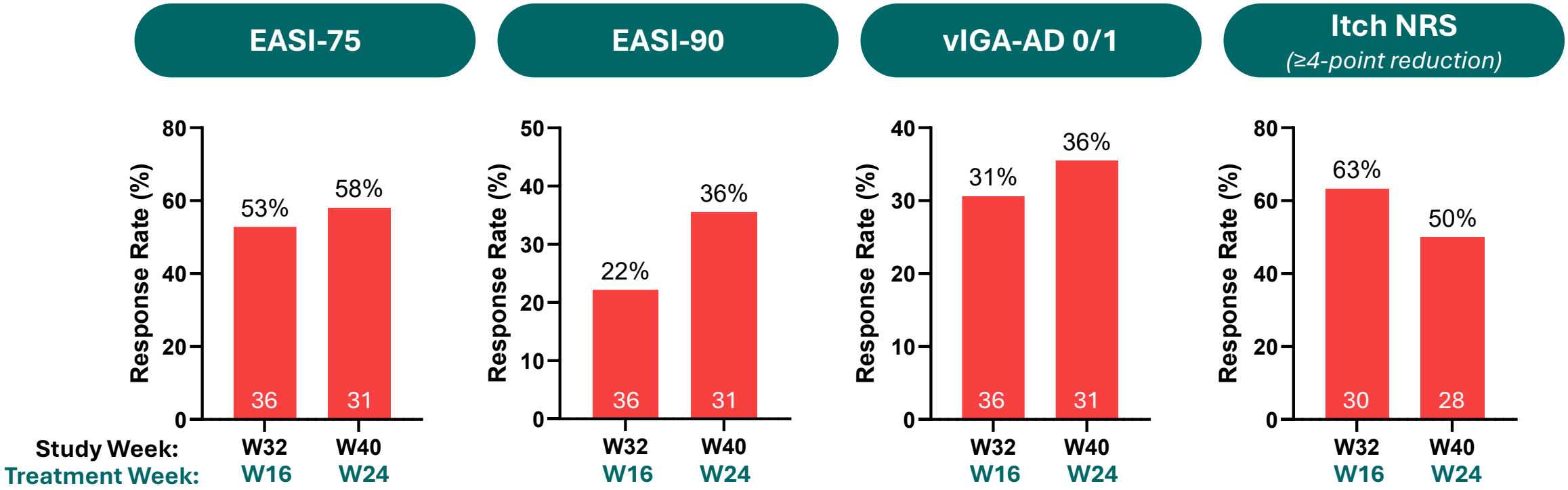


For EASI-75, vIGA-AD 0/1, and EASI-90: N = 73, 104, 106, and 110 for placebo, 24 µg/kg q2w, 18 µg/kg q2w, and 24 µg/kg q4w

For Itch NRS: N=63, 95, 92, and 102 for the placebo, 24 µg/kg q2w, 18 µg/kg q2w, and 24 µg/kg q4w groups

The Primary Estimand analysis for binary endpoints use logistic regressions. Data after use of rescue therapy outside protocol specifications or discontinued treatment due to lack of efficacy were imputed as non-responders; data after patients who discontinued due to other reasons were set to missing and all missing data are imputed using the multiple imputation method.
Source: Nektar Investor and Analyst Event (June 2025)

Rezpegaldesleukin 24 µg/kg Q2W for 24 Weeks Compared to 16 Weeks Achieved Superior Response Rates in Placebo Crossover Arm

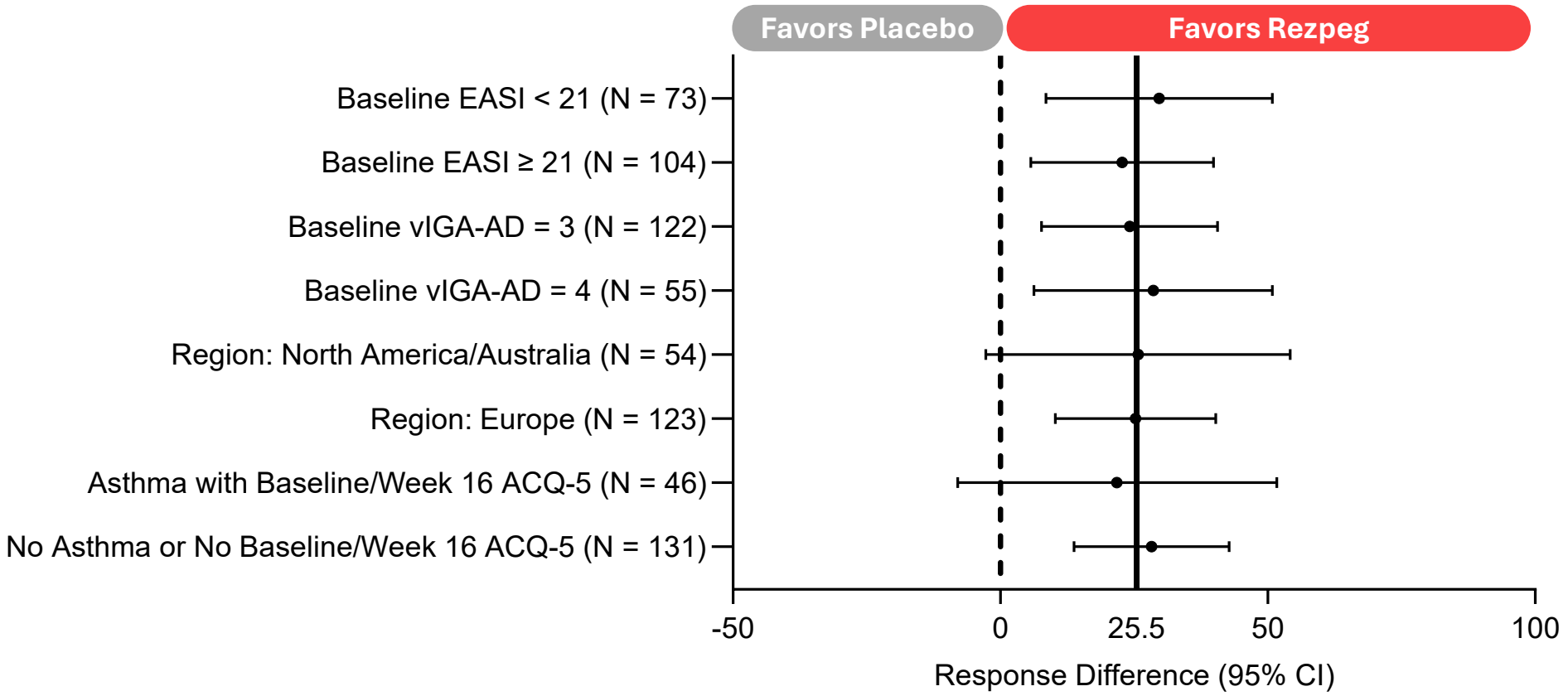


Data Support Induction Dose of 24 µg/kg Q2W for 24 Weeks in Phase 3 Program

The analysis of binary endpoints (EASI-75, EASI-90, vIGA-AD 0/1, and Itch NRS response) for the crossover patients uses descriptive summaries and number of patients with observed data as denominator.

EASI-75 Response for Rezpegaldesleukin 24 µg/kg q2w vs. Placebo

Consistent Treatment Effect Observed Across Baseline Severity of Disease, Geographical Region and Comorbidity of Asthma



The Primary Estimand analysis for binary endpoints use logistic regressions. Data after use of rescue therapy outside protocol specifications or discontinued treatment due to lack of efficacy were imputed as non-responders; data after patients who discontinued due to other reasons were set to missing and all missing data are imputed using the multiple imputation method.

Asthma in Atopic Dermatitis

Asthma commonly co-occurs with Atopic Dermatitis, reflecting substantial overlap in type 2 inflammatory disease

Patients with Atopic Dermatitis, particularly those with impaired skin-barrier function and a genetic predisposition toward IgE-mediated sensitization, are at increased risk of progressing to asthma as part of the "atopic march"

US Prevalence

~21 M ***Diagnosed AtD pts.***

~34% moderate-severe

~7.1 M ***Mod.-severe patients***

~26% asthmatic

~1.9 M ***Mod.-severe AtD / asthma patients***

Treatment Approach & Biologic Use

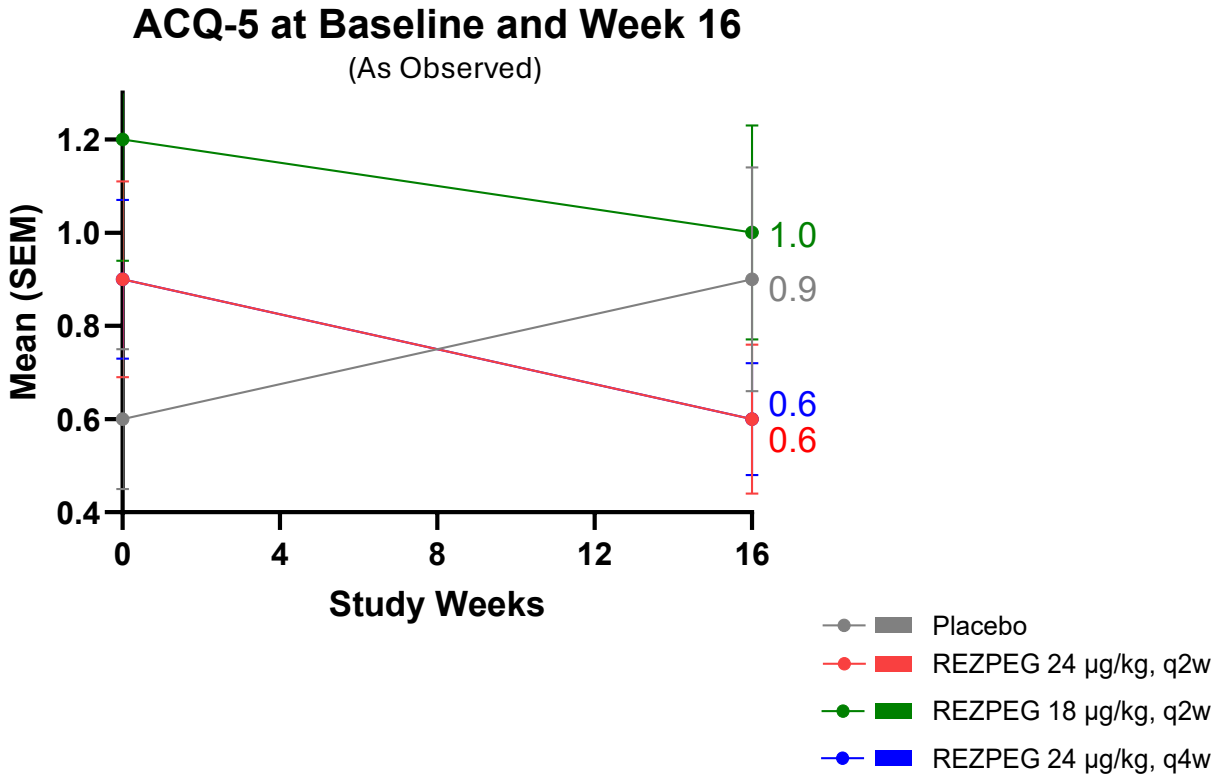
Dupilumab is the only biologic approved for both AtD and asthma; AtD guidelines highlight its benefits for patients with comorbid conditions such as asthma, and multiple peer-reviewed studies support its use as a first-line option in these patients

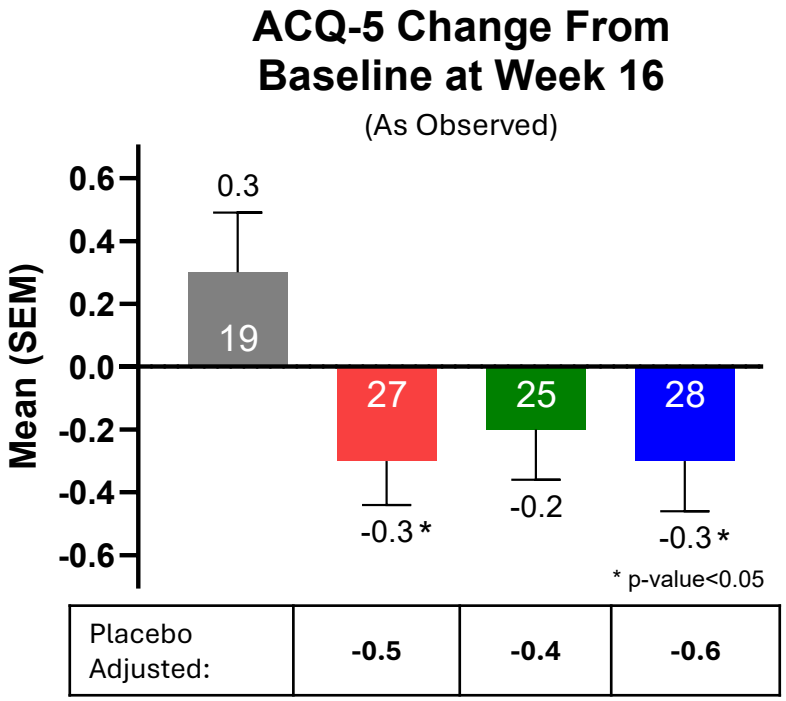
Indication	Treatment Landscape
Atopic Dermatitis	Approved biologics: **dupilumab**, tralokinumab, lebrikizumab, nemolizumab
	Guidelines recommend biologics for mod-severe patients who are refractory, intolerant, or unable to use topical treatments
Asthma	Approved biologics: **dupilumab**, omalizumab, tezepelumab, mepolizumab, benralizumab, reslizumab
	Biologics are recommended for mod-severe uncontrolled patients; several, including dupilumab, are indicated specifically for patients characterized by an eosinophilic phenotype

Sources: 1. Clarivate DRG Epidemiology (Diagnosed Population) 2. J Am Acad Dermatol 2025 DOI: 10.1016/j.jaad.2025.10.022 3. I Inv Dermatol 2019 DOI: 10.1016/j.jid.2018.08.028 4. Dermatitis 2014 DOI: 10.1097/DER.0000000000000034 5. J Am Acad Dermatol 2021; 84:471-478 DOI: 10.1016/j.jaad.2020.02.055 6. Ann Allergy Asthma Immunol 2023 DOI: 10.1016/j.anai.2023.11.009 7. Prim Care Respir Med 2023 DOI: 10.1038/s41533-023-00330-1 8. J Clin Med 2025 DOI: 10.3390/jcm14134749 9. UpToDate (Nov 2025)

ACQ-5 Response in Patients with Self-Reported Asthma History

Improvement in ACQ-5 Scores From Baseline to Week 16 in Rezpegaldesleukin Treated Patients with Asthma Comorbidity





Placebo Adjusted:	**-0.5**	**-0.4**	**-0.6**

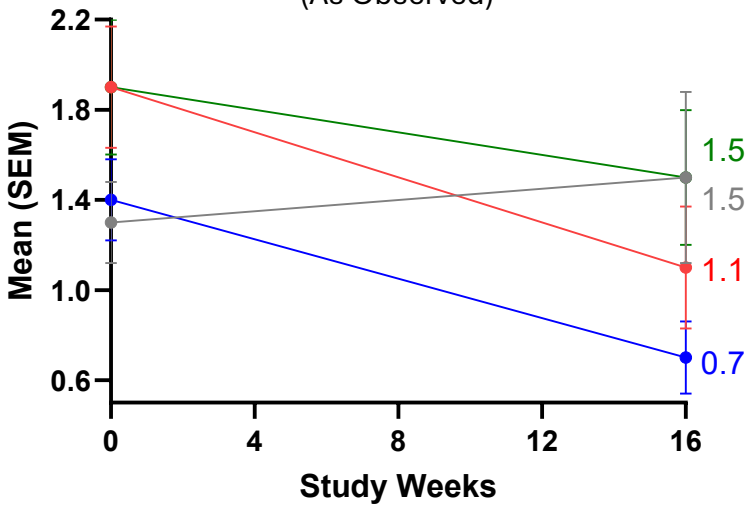
Only patients with both Baseline and Week 16 ACQ-5 data are included. The analysis for ACQ-5 data uses descriptive summary measures on observed data. P-value for change from baseline is from two-sample t-test.

Patients with Self-Reported Asthma History and Baseline ACQ-5 ≥0.5

Improvement in ACQ-5 From Baseline to Week 16 in Rezpegaldesleukin Treated Patients with Baseline ACQ-5 Score ≥ 0.5

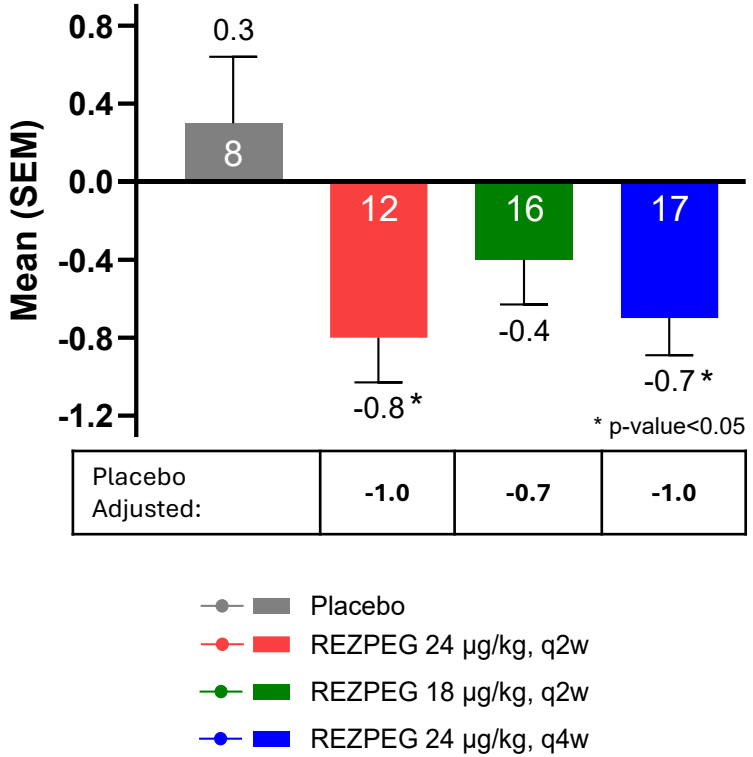
ACQ-5 at Baseline and Week 16

(As Observed)



ACQ-5 Change From Baseline at Week 16

(As Observed)

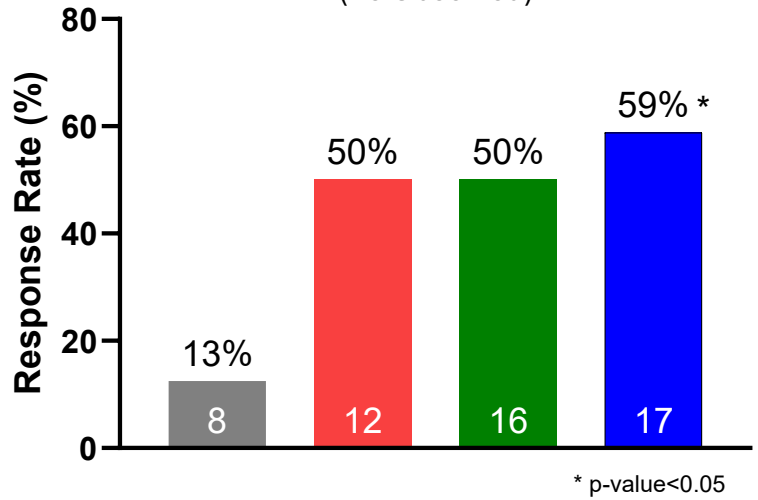


Placebo Adjusted:	-1.0	-0.7	-1.0

Placebo
REZPEG 24 µg/kg, q2w
REZPEG 18 µg/kg, q2w
REZPEG 24 µg/kg, q4w

Proportion of Patients with ACQ-5 Improvement of ≥ 0.5 at Week 16

(As Observed)



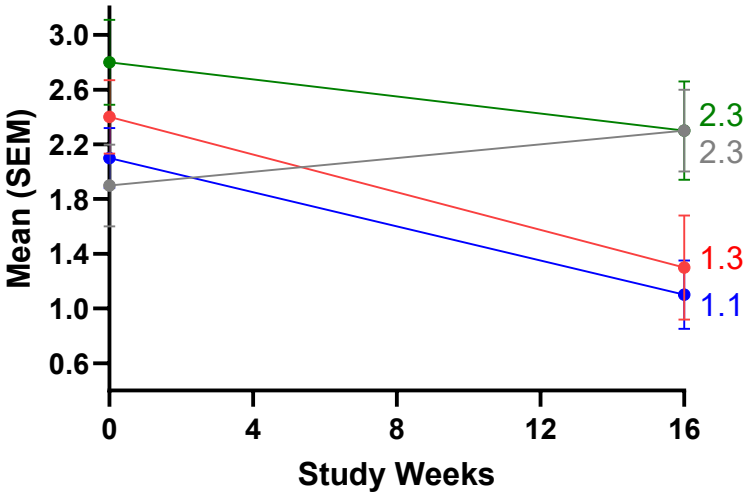
Only patients with both Baseline and Week 16 ACQ-5 data and baseline ACQ-5 ≥ 0.5 are included. The analysis for ACQ-5 data uses descriptive summary measures on observed data. P-value for change from baseline is from two-sample t-test and p-value for response is from Cochran-Mantel-Haenszel test.

ACQ-5 Response in Patients with Self-Reported *Uncontrolled* Asthma at Baseline

Improvement in ACQ-5 From Baseline to Week 16 in Rezpegaldesleukin Treated Patients with Baseline ACQ-5 Score ≥ 1.5

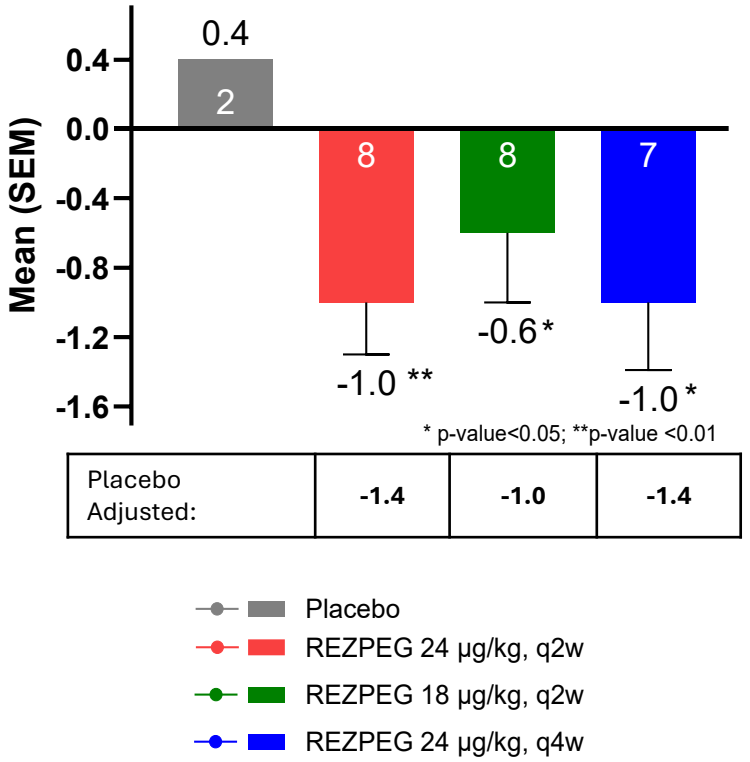
ACQ-5 at Baseline and Week 16

(As Observed)



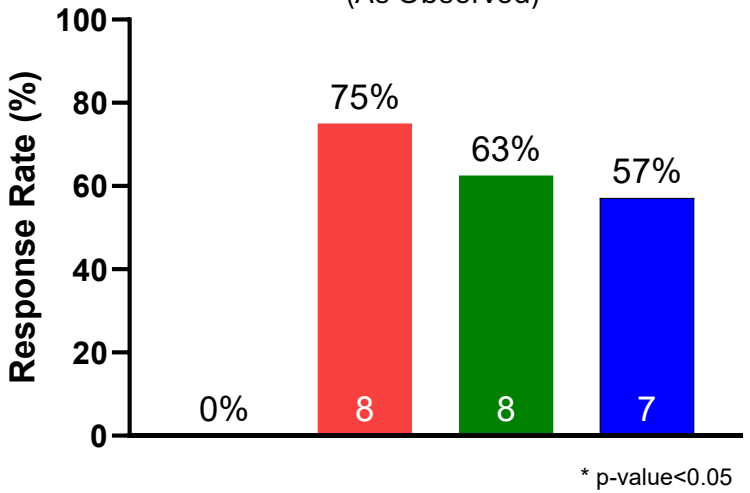
ACQ-5 Change From Baseline at Week 16

(As Observed)



Proportion of Patients with ACQ-5 Improvement of ≥ 0.5 at Week 16

(As Observed)

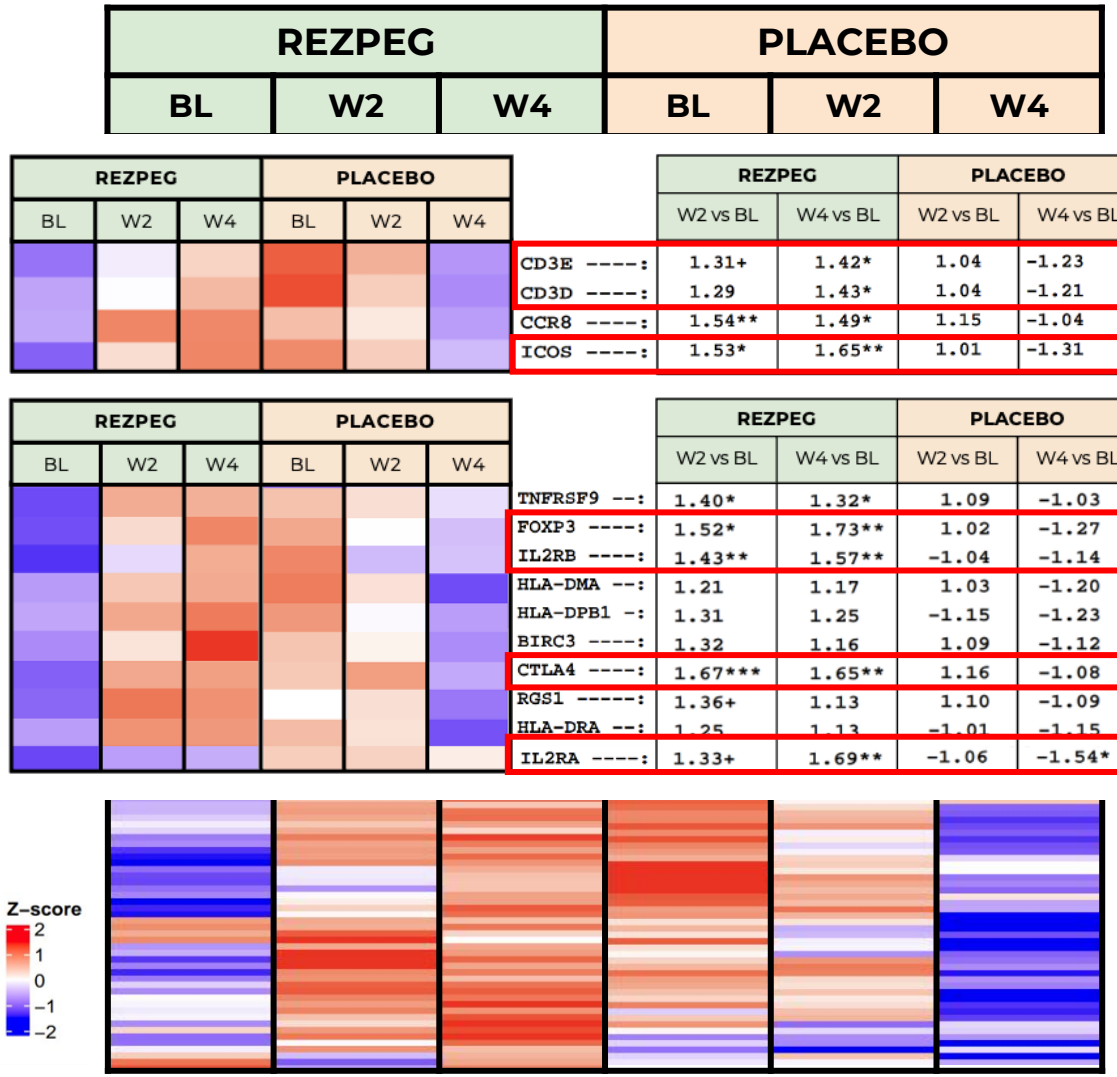


Only patients with both Baseline and Week 16 ACQ-5 data and baseline ACQ-5 ≥ 1.5 are included. The analysis for ACQ-5 data uses descriptive summary measures on observed data. P-value for change from baseline is from two-sample t-test and p-value for response is from Cochran-Mantel-Haenszel test.



Biomarker Analysis

REZPEG increased Treg-associated and regulatory gene expression as early as week 2



	REZPEG		PLACEBO		REZPEG v PBO	
	W2 vs BL	W4 vs BL	W2 vs BL	W4 vs BL	W2 vs BL	W4 vs BL
CD3E ----:	1.31+	1.42*	1.04	-1.23	1.26	1.75*
CD3D ----:	1.29	1.43*	1.04	-1.21	1.25	1.73*
CCR8 ----:	1.54**	1.49*	1.15	-1.04	1.34	1.56+
ICOS ----:	1.53*	1.65**	1.01	-1.31	1.49	2.16**

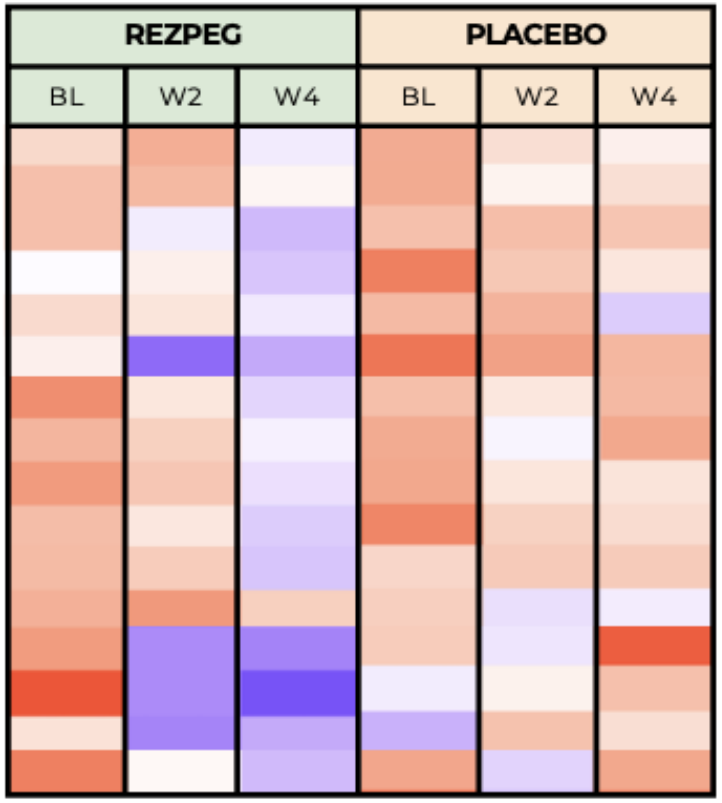
	REZPEG		PLACEBO		REZPEG v PBO	
	W2 vs BL	W4 vs BL	W2 vs BL	W4 vs BL	W2 vs BL	W4 vs BL
TNFRSF9 --:	1.40*	1.32*	1.09	-1.03	1.29	1.36
FOXP3 ----:	1.52*	1.73**	1.02	-1.27	1.48	2.19**
IL2RB ----:	1.43**	1.57**	-1.04	-1.14	1.49+	1.79**
HLA-DMA --:	1.21	1.17	1.03	-1.20	1.16	1.40
HLA-DPB1 -:	1.31	1.25	-1.15	-1.23	1.51	1.55
BIRC3 ----:	1.32	1.16	1.09	-1.12	1.21	1.28
CTLA4 ----:	1.67***	1.65**	1.16	-1.08	1.45	1.79*
RGS1 -----:	1.36+	1.13	1.10	-1.09	1.23	1.24
HLA-DRA --:	1.25	1.13	-1.01	-1.15	1.26	1.29
IL2RA ----:	1.33+	1.69**	-1.06	-1.54*	1.40	2.62***

- REZPEG induced early upregulation of T-cell biomarkers, including **CD3D**, **CD3E**, **ICOS**.
- **FOXP3** and **IL2RA**, hallmark genes identifying Tregs, increased with REZPEG treatment by week 2.
- These changes highlight early expansion and activation of regulatory T-cell programs.

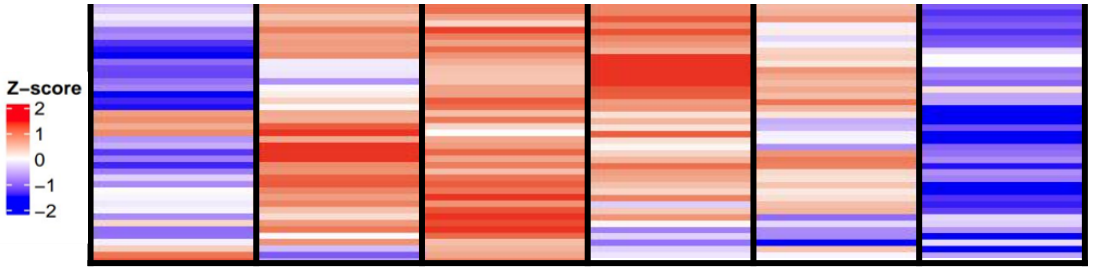
Abbreviations: BL, baseline; FCH, fold change; PBO, Placebo; REZPEG, Rezpegaldesleukin; W, week.

+p<0.1 *p<0.05 **p<0.01 ***p<0.001

REZPEG drives early changes in immune pathways implicated in AD



	REZPEG		PLACEBO		REZPEG v PBO	
	W2 vs BL	W4 vs BL	W2 vs BL	W4 vs BL	W2 vs BL	W4 vs BL
CXCL2 ---:	-1.19	-1.65**	-1.07	1.03	-1.11	-1.69+
CXCL1 ---:	-1.27	-1.61*	1.01	1.07	-1.28	-1.72
IL6 -----:	-1.26	-1.57*	-1.31	-1.25	1.04	-1.26
CXCL3 ---:	-1.16	-1.71**	-1.12	-1.12	-1.04	-1.54
CCL20 ---:	-1.21	-1.61*	1.04	-1.21	-1.27	-1.34
CCR2 ----:	-1.52*	-1.09	-1.12	-1.31	-1.36	1.20
CAMP ----:	-1.55*	-1.85**	-1.10	1.13	-1.40	-2.08*
CXCL10 --:	-1.20	-1.39	-1.47	-1.02	1.23	-1.37
S100A12 -:	-1.54*	-1.84**	-1.13	1.06	-1.37	-1.97*
IL36A ---:	-1.36	-1.79*	-1.10	1.01	-1.23	-1.80
S100P ---:	-1.30	-1.51*	-1.02	1.06	-1.27	-1.60+
IL36G ---:	-1.30	-1.68*	-1.39	1.06	1.06	-1.78
IL36RN --:	-1.88**	-1.88**	-1.23	1.60+	-1.53	-3.01***
CXCL17 --:	-2.14**	-2.19**	1.27	1.23	-2.71*	-2.69*
CCL7 ----:	-1.66*	-1.38	1.89*	1.38	-3.14**	-1.91
OASL ----:	-1.61*	-1.72**	-1.45	-1.13	-1.11	-1.53

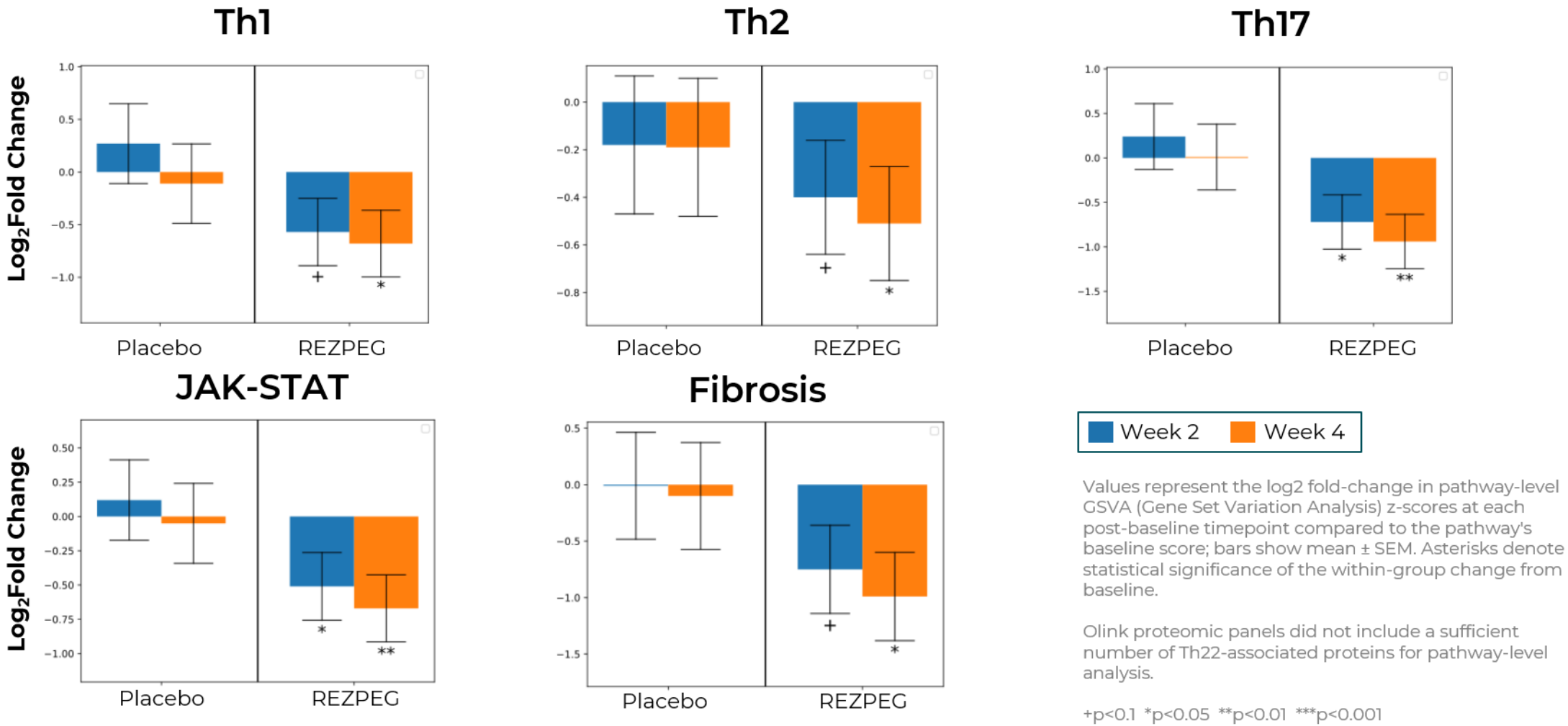


Th1 Th2 Th17 Th22

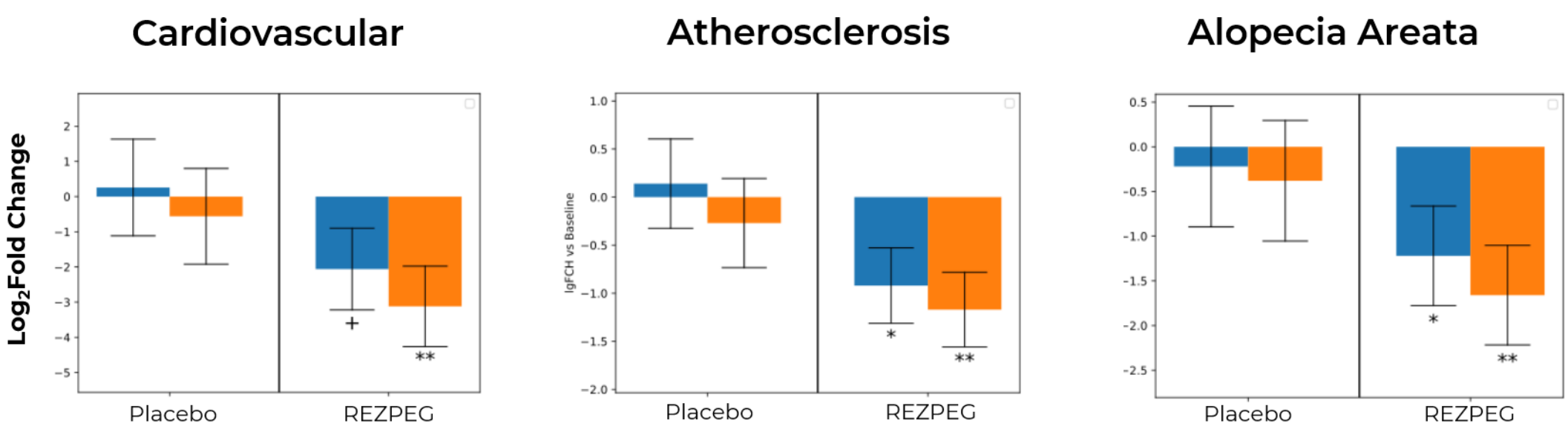
Abbreviations: BL, baseline; FCH, fold change; PBO, Placebo; REZPEG, Rezpegaldesleukin; W, week.

+p<0.1 *p<0.05 **p<0.01 ***p<0.001

Tape-strip proteomics reveal significant modulation of key immune pathways by week 4



Tape-strip proteomics demonstrate early improvement of validated systemic and cutaneous disease pathways



Atherosclerosis & cardiovascular: Pavel et al. J Am Acad Dermatol 2020. The proteomic skin profile of moderate-to-severe atopic dermatitis patients shows an inflammatory signature (https://pubmed.ncbi.nlm.nih.gov/31669080/); Th1, Th2, Th17, Th22, and AA pathways: Glickman et al. Allergy 2021. An integrated scalp and blood biomarker approach suggests the systemic nature of alopecia areata. (https://pubmed.ncbi.nlm.nih.gov/33721346/); JAK-STAT: Del Duca et al. J Am Acad Dermatol 2023. Proteomic characterization of atopic dermatitis blood from infancy to adulthood. (https://pubmed.ncbi.nlm.nih.gov/36773824/); Fibrosis: Obi et al. Review Expert Rev Proteomics 2024. Proteomic alterations in patients with atopic dermatitis. (https://pubmed.ncbi.nlm.nih.gov/38753434/)

Early serum biomarker changes associated with improvement in EASI at week 16

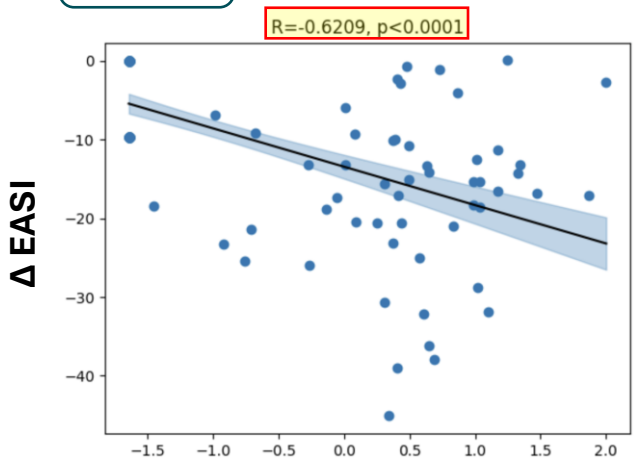
REZPEG

Placebo

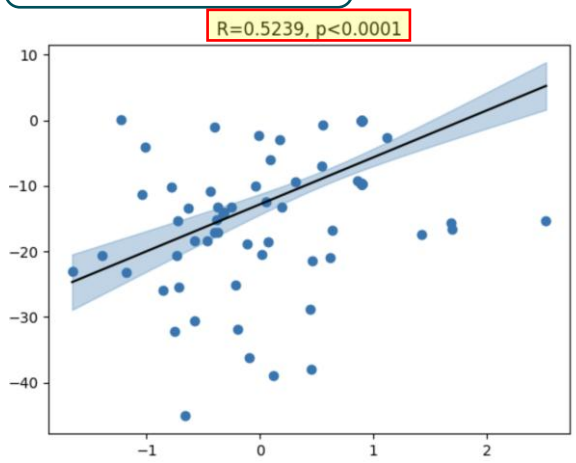
⇩ EASI

Th2

IL-10 ⇧

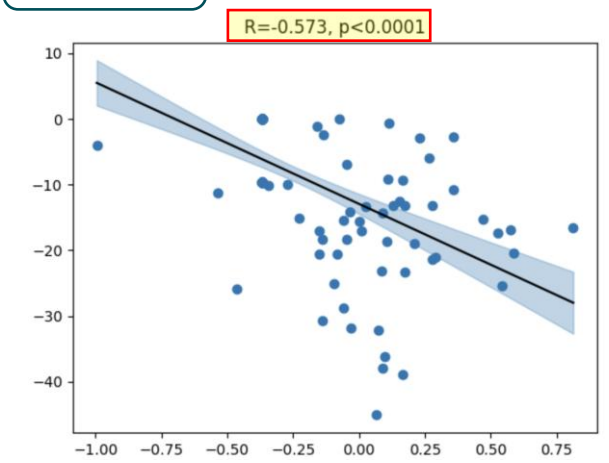


CCL17/TARC ⇩



Th17

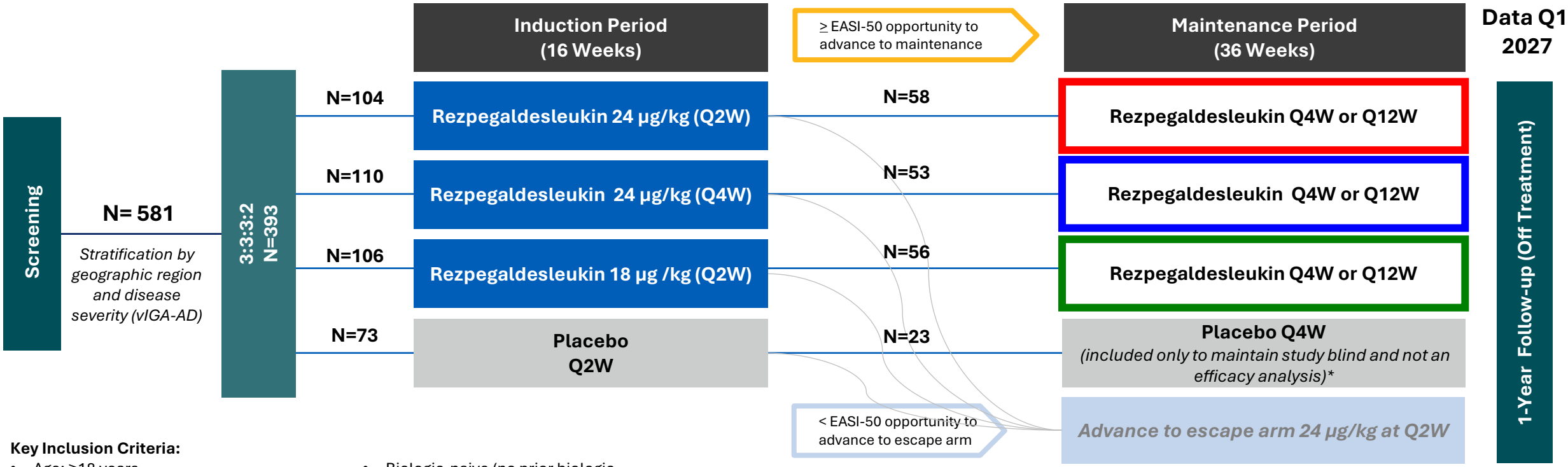
TGFβ1 ⇧



All correlations in REZPEG arm were significant with p-values <0.001

- Increases in IL-10 and TGFβ1 expression were associated with greater reductions in EASI at week 16.
- Reduction in CCL17/TARC expression was also associated with greater clinical improvement at week 16.

REZOLVE-AD: Phase 2b Maintenance Designed to Evaluate Monthly and Quarterly Dosing

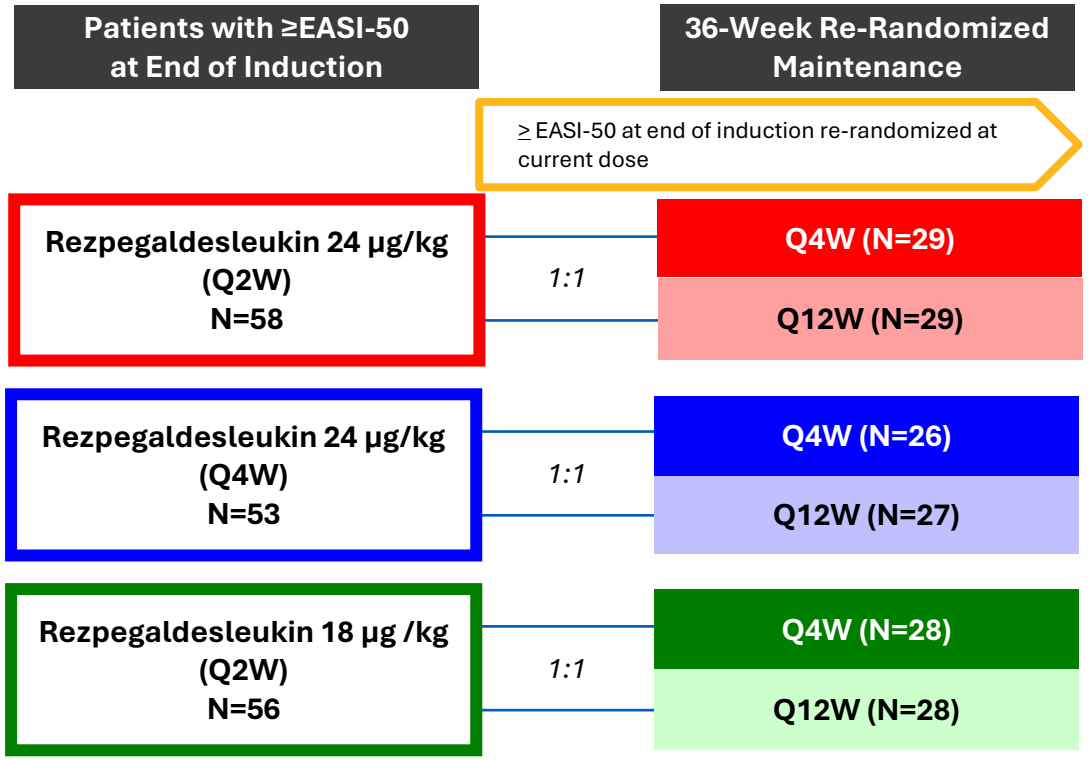


Key Inclusion Criteria:

- Age: ≥18 years
- Moderate/severe AD diagnosis for ≥ 12 months
  - EASI ≥ 16
  - vIGA-AD of 3 or 4
  - BSA ≥ 10%
- Biologic-naive (no prior biologic systemic therapy) and systemic JAKi-naïve
- Failure of prior therapy, including TCS of medium or higher potency, within last 6 months

*Placebo-treated clinical responders are not included in the efficacy analyses after week 16; however, they continued receiving placebo to maintain blinding (as was done in dupilimab Phase 3 SOLO-CONTINUE Study, amlitelimab Phase 2 STREAM-AD program, and tralokinimab Phase 3 ECZTRA Program)

Multiple Efficacy Endpoints Assessed in Maintenance Portion of Trial



Efficacy Endpoints at Week 52 Among Patients with Responses at Week 16

- Maintaining EASI-75
- Maintaining vIGA-AD 0/1 (Clear/Almost Clear)
- Maintaining EASI-90
- Maintaining Itch NRS (≥4-point reduction)

Assess New and Deepening Responses at Week 52 Among Patients Without Response at Week 16

- New EASI-75 responders
- New EASI-90 responders
- New vIGA-AD 0/1 responders

Conversions to EASI-100 from Week 16 to Week 52



Durability of Effect: Maintaining Responses

All Monthly and Quarterly Arms Demonstrated Durability of Responses Over 36 Weeks of Maintenance Dosing Following Induction

At Week 52

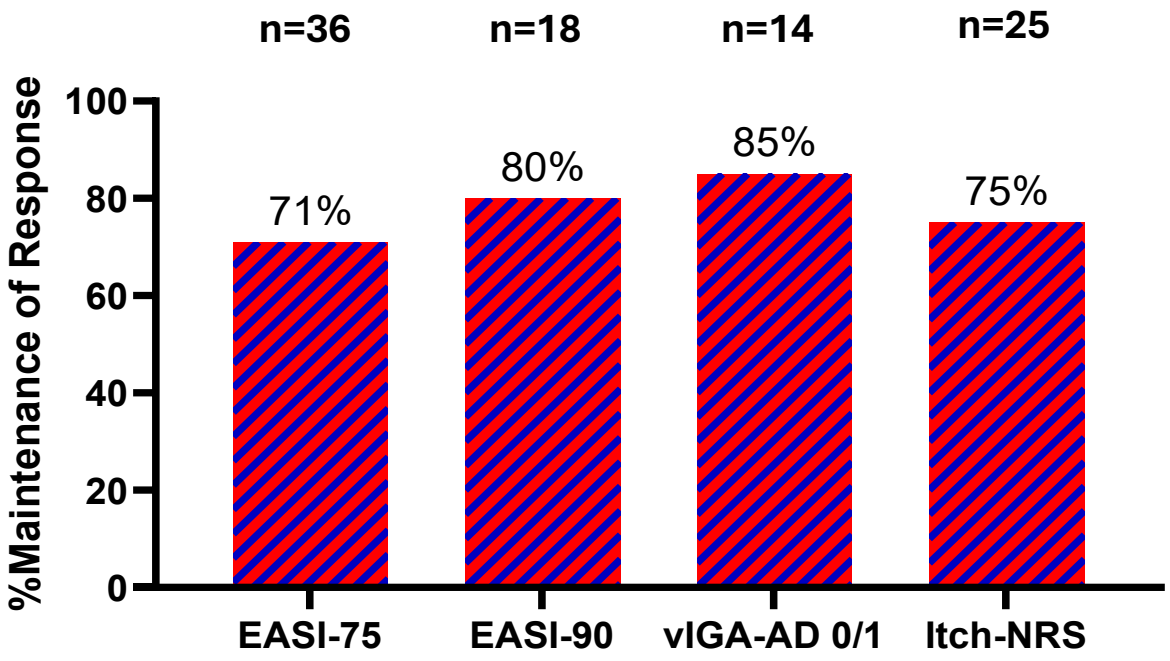
16-Week Induction Dose:	Rezpeg 24 µg/kg Q2W		Rezpeg 24 µg/kg Q4W		Rezpeg 18 µg/kg Q2W	
36 -Week Maintenance Dose:	**24 µg/kg Q4W N=29**	**24 µg/kg Q12W N=29**	**24 µg/kg Q4W N=26**	**24 µg/kg Q12W N=27**	**18 µg/kg Q4W N=28**	**18 µg/kg Q12W N=28**
Maintaining EASI-75	74% (n=19)	74% (n=18)	67% (n=17)	92% (n=17)	81% (n=20)	76% (n=19)
Maintaining EASI-90	80% (n=10)	77% (n=11)	81% (n=8)	78% (n=9)	57% (n=8)	57% (n=7)
Maintaining vIGA-AD 0/1	83% (n=8)	59% (n=8)	86% (n=6)	65% (n=13)	81% (n=12)	62% (n=9)
Maintaining Itch NRS (≥4-point reduction)	71% (n=18)	85% (n=9)	85% (n=7)	68% (n=8)	56% (n=14)	61% (n=6)

(N=xx) is the entire maintenance population
(n=xx) is the denominator which equals the number of responders at Week 16
% represents proportion of patients who maintained that response at Week 52
Missing data is imputed using multiple imputation

Maintenance of Responses in the Pooled Monthly and Quarterly High Dose Maintenance Arms

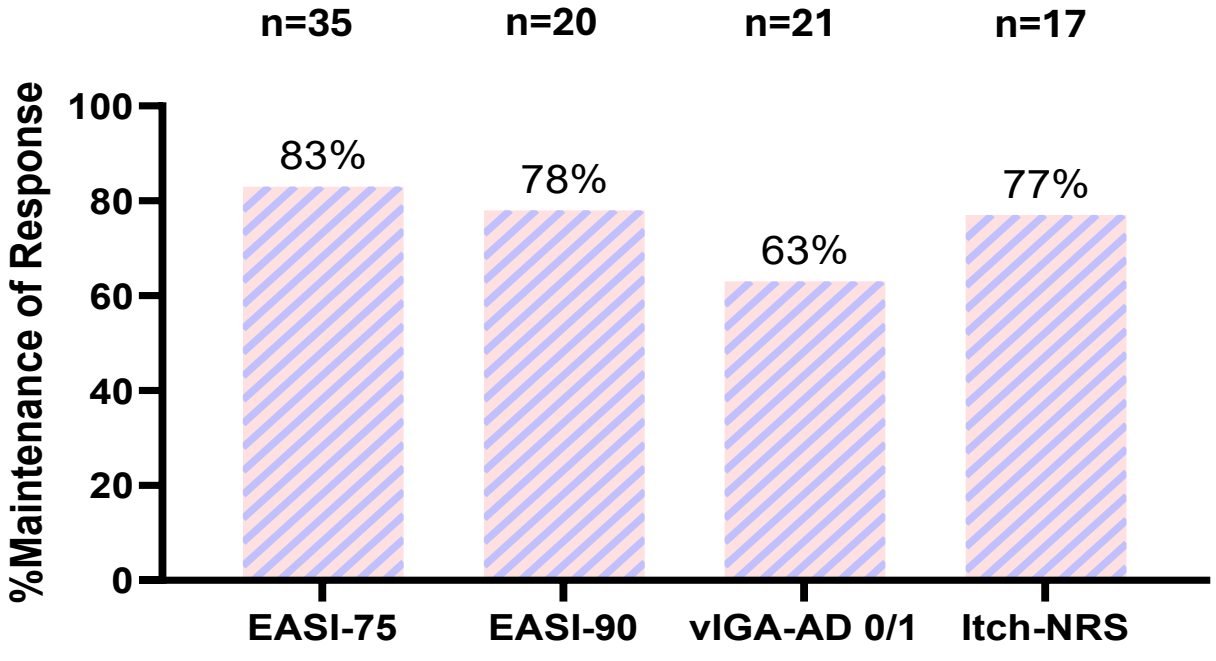
Maintenance at Week 52 in the Q4W Cohorts

24 µg/kg



Maintenance at Week 52 in the Q12W Cohorts

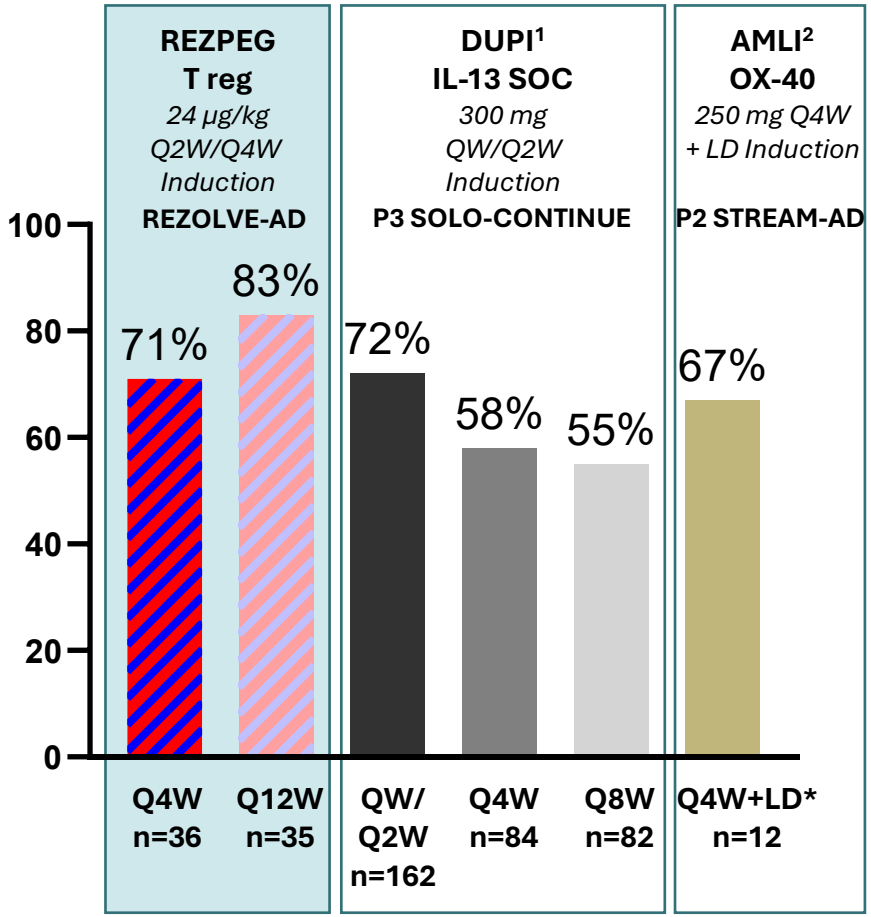
24 µg/kg



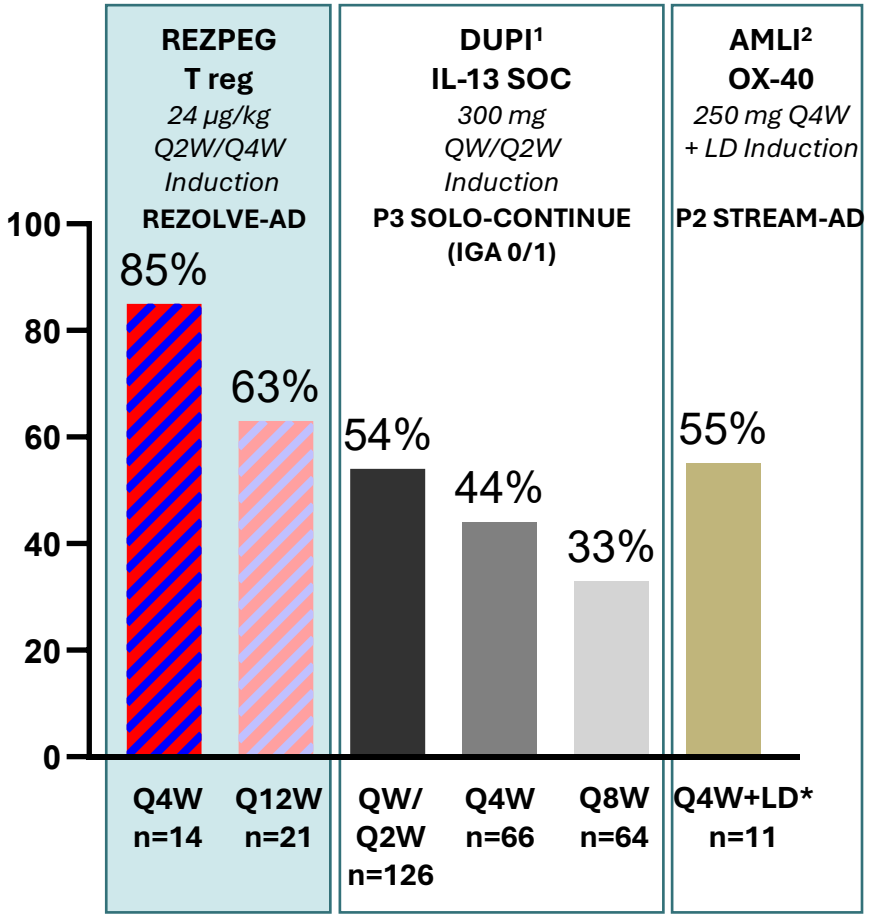
(n=xx) is the denominator which equals the number of responders at Week 16

Maintenance of EASI-75 and vIGA-AD 0/1

Percent Maintaining EASI-75 at Week 52



Percent Maintaining vIGA-AD 0/1 at Week 52

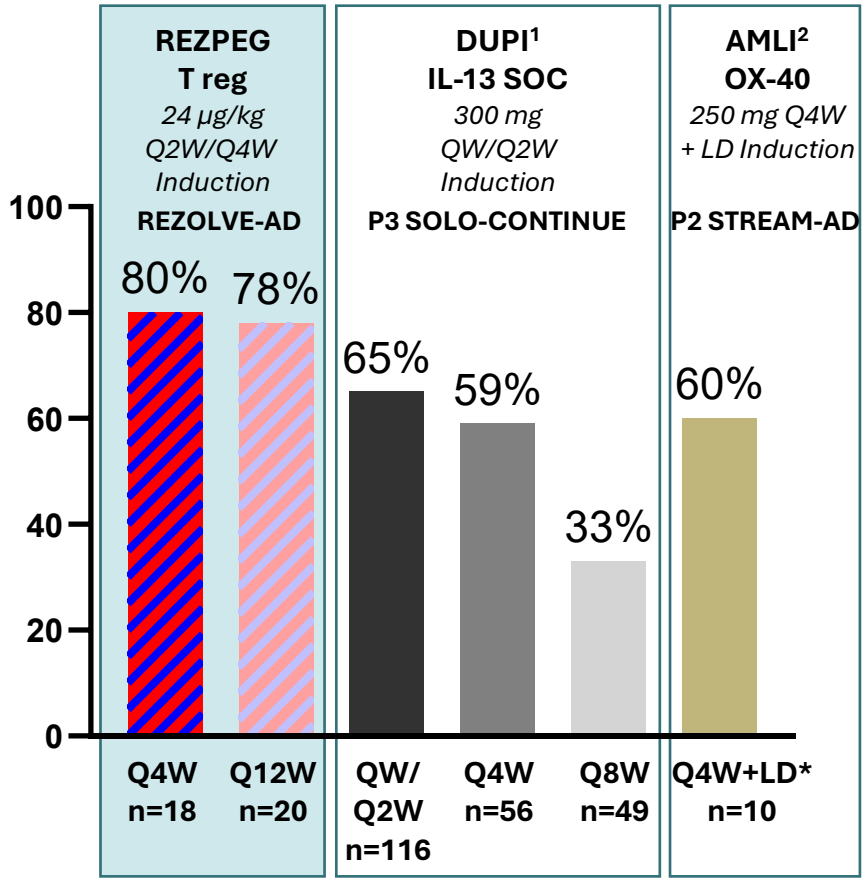


For REZOLVE-AD, data after escape are set to be missing. All other data regardless of rescue medication use and/or treatment discontinuation are used as is. Missing data is imputed using multiple imputation.
*Amlitelimab dose evaluated in Phase 3; Sources: 1. Phase 3 SOLO-CONTINUE Trial (Worm et al. 2019, JAMA Derm 156:131-143); 2. Phase 2 STREAM-AD (Weidinger et al. 2025, JACI 155:1264-75)

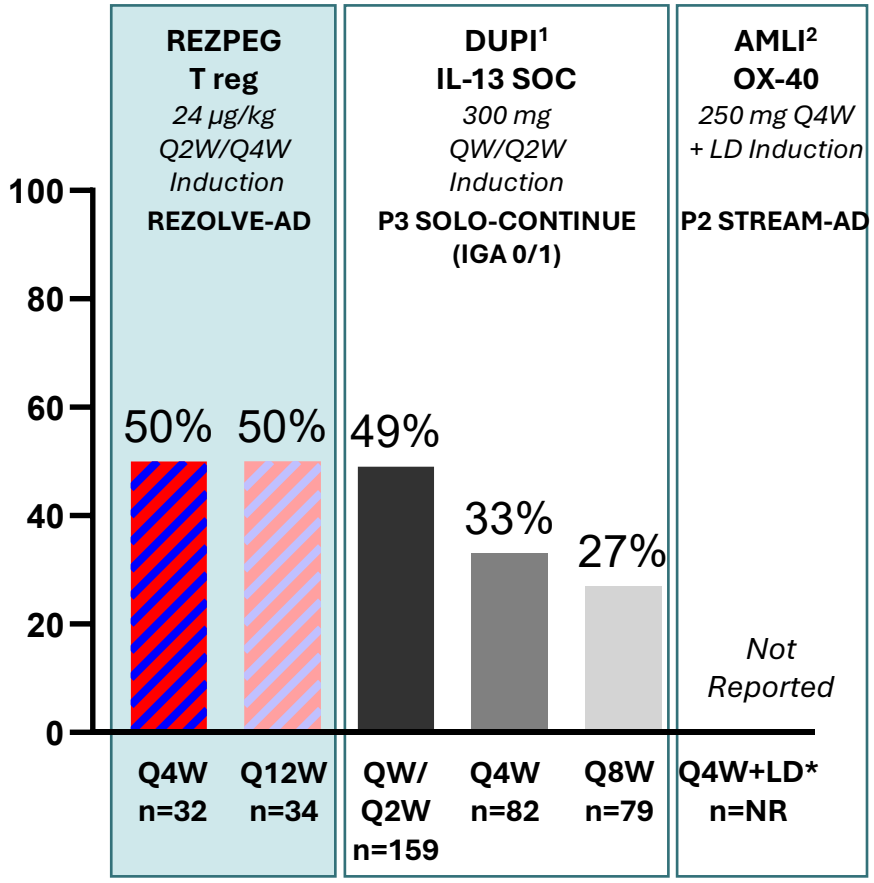
This is a cross-trial comparison and includes data from different clinical studies and is not intended to provide a head-to-head comparison.

Maintenance of EASI-90 and the Itch Response Rate at End of Maintenance

Percent Maintaining EASI-90 at Week 52



Percent Itch NRS (≥4-point reduction) Response Among EASI-75 or vIGA Responders at Re-Randomization



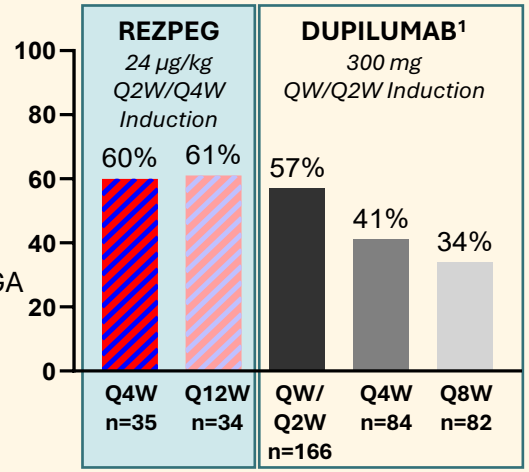
For REZOLVE-AD, data after escape are set to be missing. All other data regardless of rescue medication use and/or treatment discontinuation are used as is. Missing data is imputed using multiple imputation.
*Amlitelimab dose evaluated in Phase 3; Sources: 1. Phase 3 SOLO-CONTINUE Trial (Worm et al. 2019, JAMA Derm 156:131-143); 2. Phase 2 STREAM-AD (Weidinger et al. 2025, JACI 155:1264-75)
For percent itch NRS, SOLO-CONTINUE reported only 35 weeks of maintenance dosing

Measurements of Improvements and Worsening for Itch and vIGA/IGA

Improving

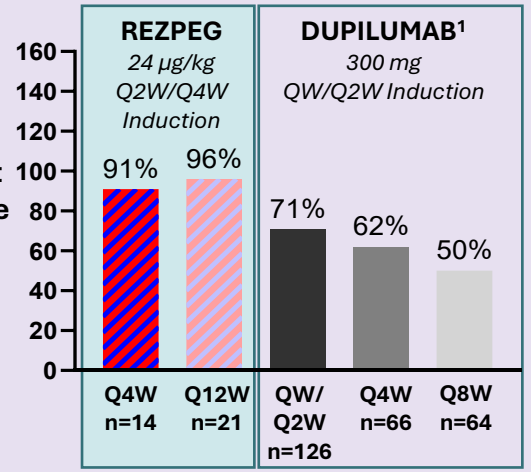
Itch NRS

≥3-pt reduction from induction baseline at end of maintenance among EASI-75 or vIGA/IGA Responders at Re-Randomization



vIGA/IGA

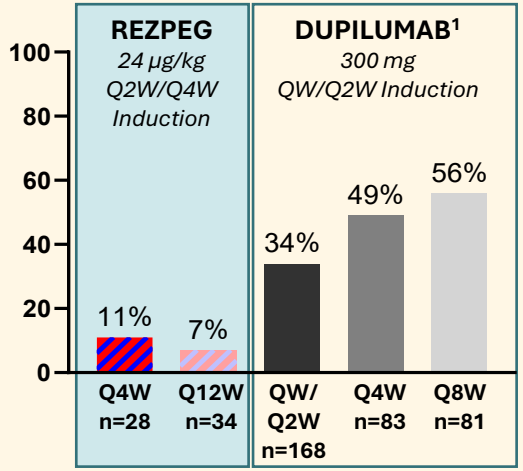
Maintained within 1 point from start of maintenance at end of maintenance among vIGA/IGA Responders at Re-Randomization



Worsening

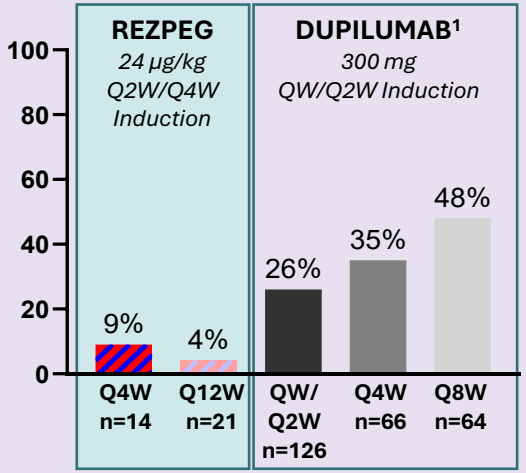
Itch NRS

≥3-pt increase from start of maintenance at end of maintenance among EASI-75 or vIGA/IGA Responders at Re-Randomization after Induction



vIGA/IGA

Worsening to 3/4 at end of maintenance among vIGA/IGA Responders at Re-Randomization



For REZOLVE-AD, data after escape are set to be missing. All other data regardless of rescue medication use and/or treatment discontinuation are used as is. Missing data is imputed using multiple imputation.

Sources: 1. Phase 3 SOLO-CONTINUE Trial (Worm et al. 2019, JAMA Derm 156:131-143)

For percent itch NRS, SOLO-CONTINUE reported only 35 weeks of maintenance dosing

This is a cross-trial comparison and includes data from different clinical studies and is not intended to provide a head-to-head comparison.



New and *Deepening* Responses in Maintenance Among Re-Randomized Patients with ≥ EASI-50

Rezpegaldesleukin Monthly and Quarterly Induced *New* and *Deepening* Responses

At Week 52

Induction Dose:	Rezpeg 24 µg/kg Q2W		Rezpeg 24 µg/kg Q4W		Rezpeg 18 µg/kg Q2W	
Maintenance Dose:	**24 µg/kg Q4W N=29**	**24 µg/kg Q12W N=29**	**24 µg/kg Q4W N=26**	**24 µg/kg Q12W N=27**	**18 µg/kg Q4W N=28**	**18 µg/kg Q12W N=28**
New EASI-75 Responders	43% (n=10)	35% (n=11)	59% (n=9)	44% (n=10)	17% (n=8)	62% (n=9)
New EASI-90 Responders	33% (n=19)	12% (n=18)	33% (n=18)	40% (n=18)	37% (n=20)	33% (n=21)
New vIGA-AD 0/1 Responders	38% (n=21)	35% (n=21)	44% (n=20)	46% (n=14)	23% (n=16)	36% (n=19)
New Itch Responder (≥4-point improvement)	13% (n=9)	9% (n=17)	44% (n=17)	29% (n=15)	31% (n=13)	18% (n=17)

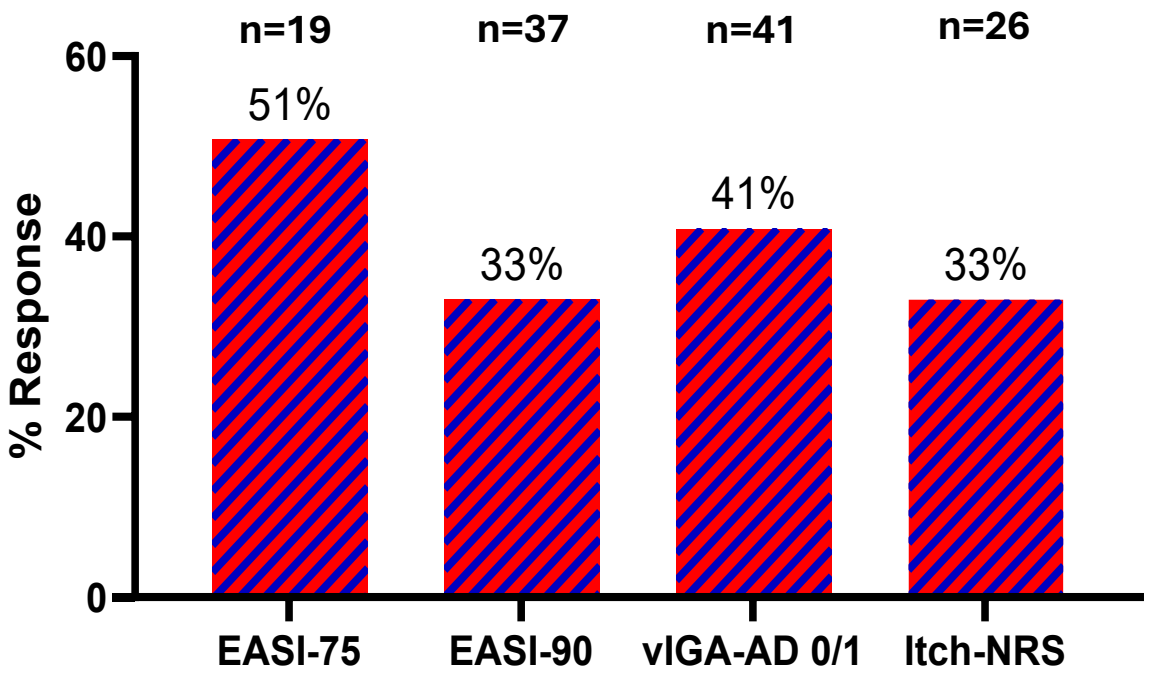
New and deepening responses among re-randomized patients achieving EASI-50 in 16-week induction

(N=xx) is the entire maintenance population; (n=xx) is the denominator which equals the number of non-responders for each endpoint at re-randomization; % represents proportion of patients who achieved that response at Week 52; missing data is imputed using multiple imputation

New and *Deepening* Responses at Week 52 in Pooled Monthly and Quarterly Rezpegaldesleukin (High Dose) Maintenance Arms

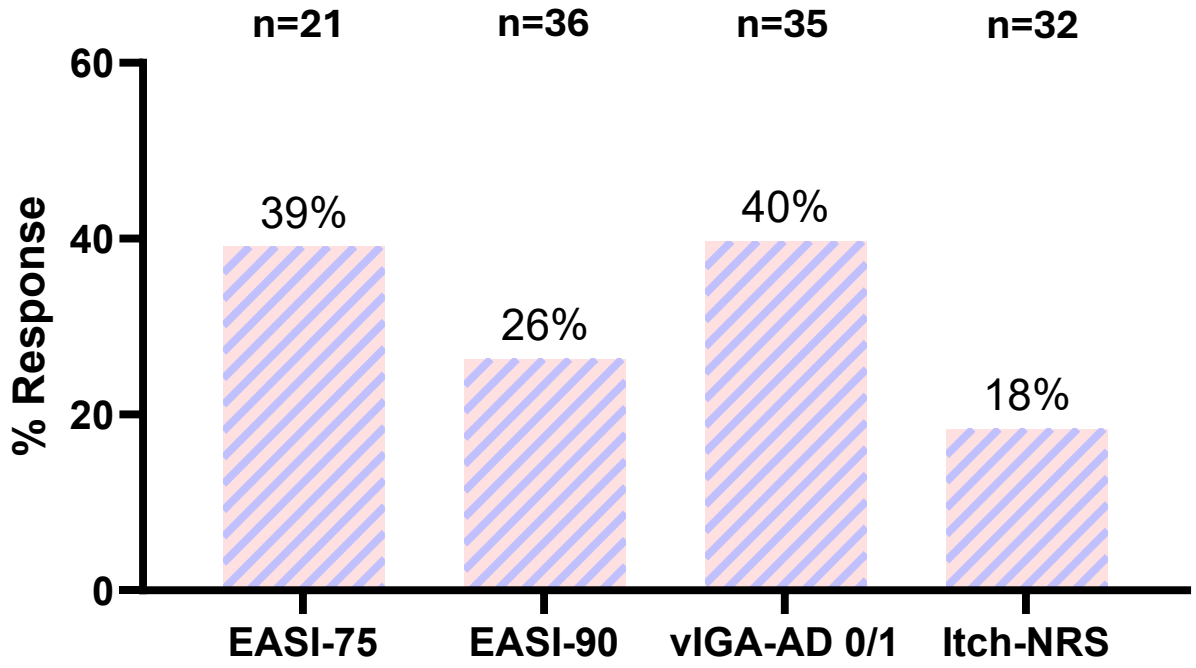
New Responses at Week 52 in Q4W Cohorts

24 µg/kg



New Responses at Week 52 in Q12W Cohorts

24 µg/kg



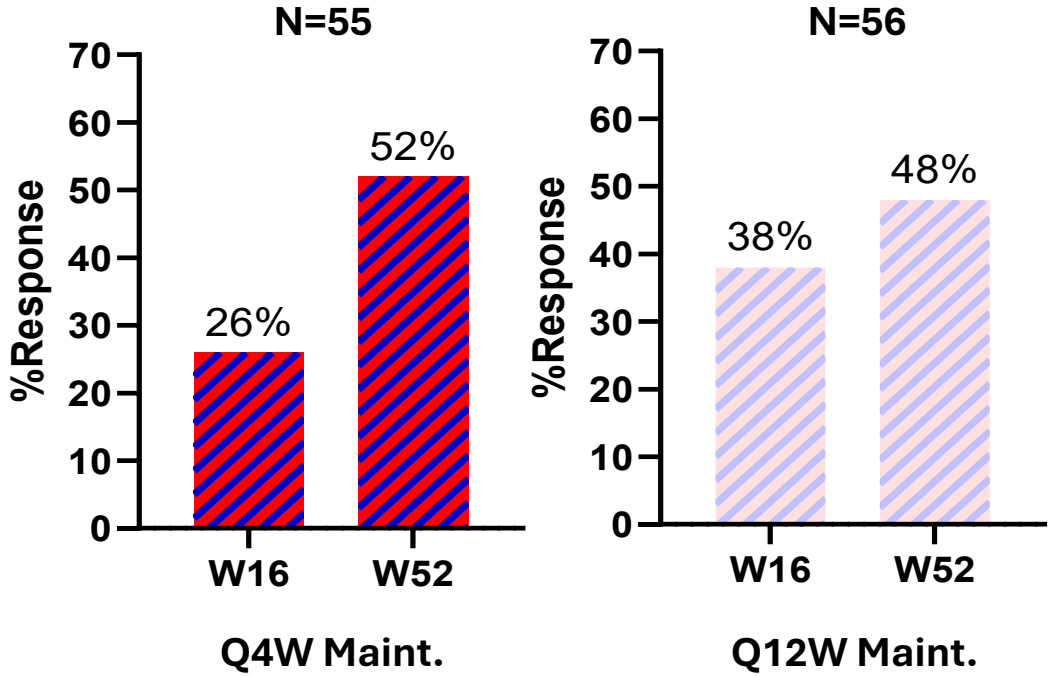
New and deepening responses among re-randomized patients achieving EASI-50 in 16-week induction

(n=xx) is the denominator which equals the number of non-responders for each endpoint at re-randomization

vIGA-AD 0/1 Response Rates Increased at Week 52 in Pooled Monthly and Quarterly Rezpegaldesleukin (High Dose) Maintenance Arms

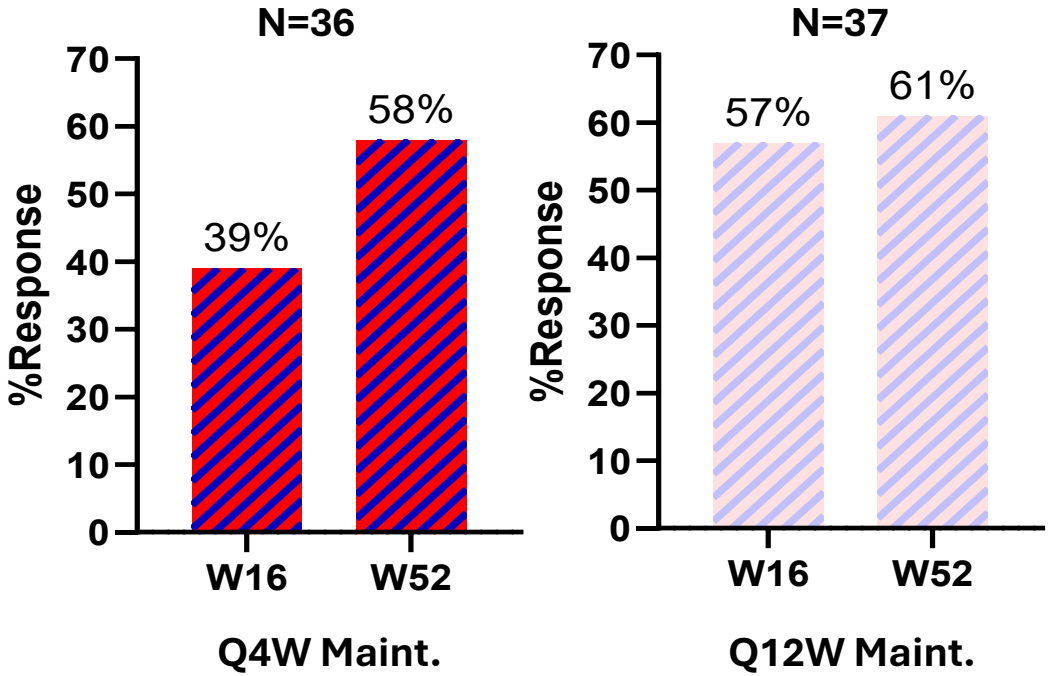
vIGA-AD 0/1 Response Rate at Week 52 Among ≥ EASI-50 Responders at Re-Randomization

24 µg/kg



vIGA-AD 0/1 Response Rate at Week 52 Among ≥ EASI-75 or vIGA-AD 0/1 Responders at Re-Randomization

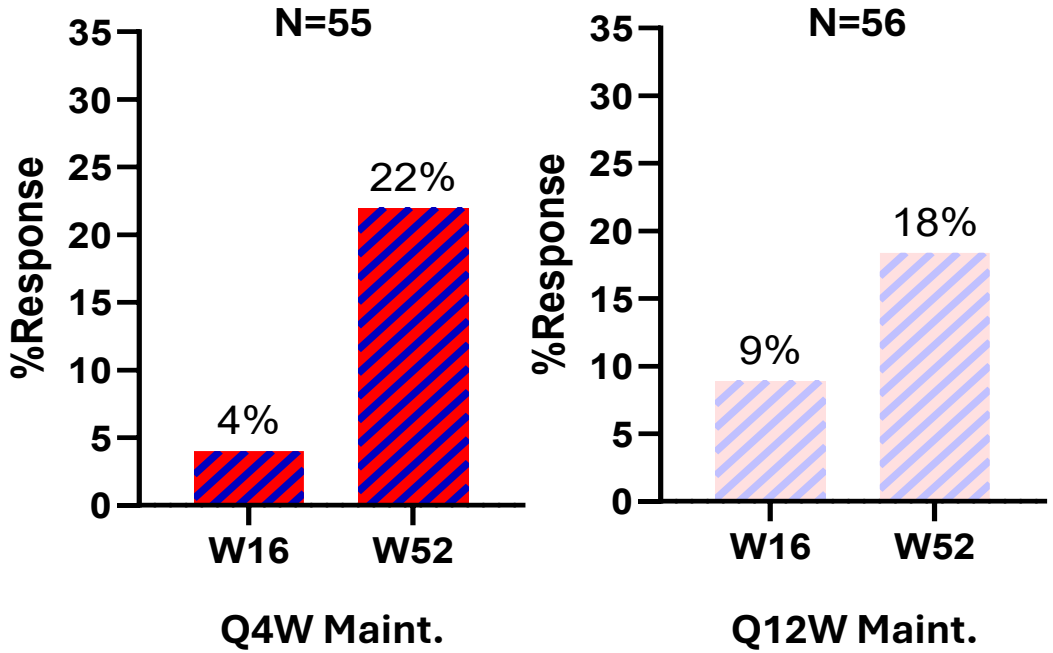
24 µg/kg



EASI-100 Response Rates Increased at Week 52 in Pooled Monthly and Quarterly Rezpegaldesleukin (High Dose) Maintenance Arms

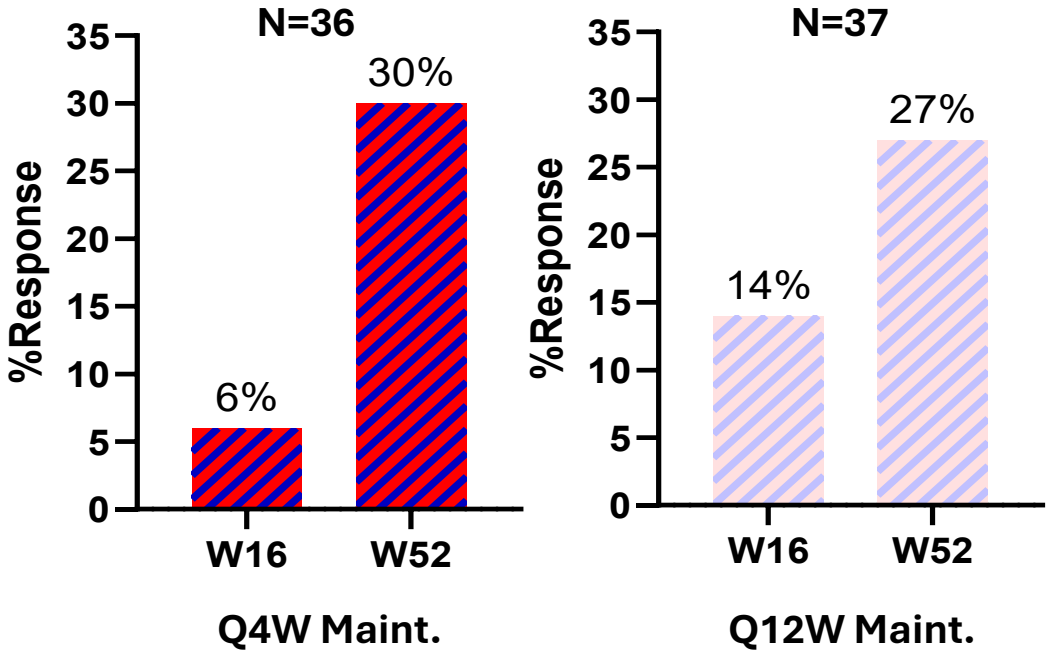
EASI-100 Rate at Week 52 Among ≥ EASI-50 Responders at Re-Randomization

24 µg/kg



EASI-100 Rate at Week 52 Among ≥ EASI-75 or vIGA-AD 0/1 Responders at Re-Randomization

24 µg/kg



Safety Profile at 52-Weeks Consistent with Previously Reported Results

52-week safety of Rezpegaldesleukin across maintenance and escape patient populations is consistent with previously observed and reported safety profile

- Discontinuation rate due to AEs was low (3.5%) for Rezpeg-exposed patients and was within the range of rates seen in contemporary Phase 2b studies
- No imbalance to suggest an increased risk of infection over placebo

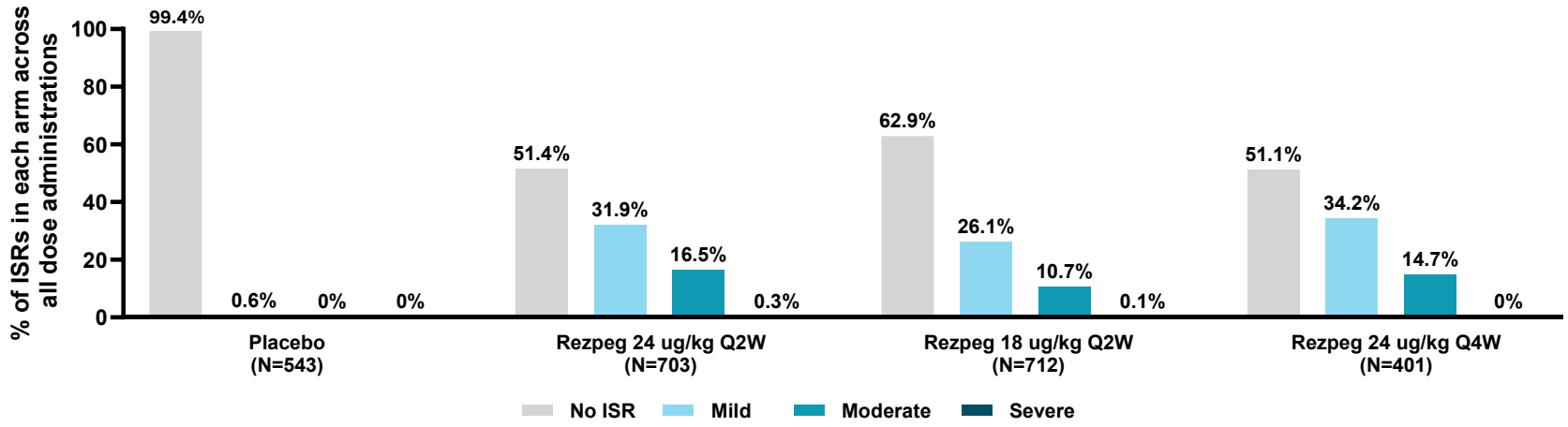
No observed increased risk or safety signal for: conjunctivitis, facial swelling or erythema, oral (aphthous) ulcers, myocardial infarction, pulmonary embolus, deep venous thrombosis and malignancy

Most frequently observed adverse event was injection site reactions (ISRs)

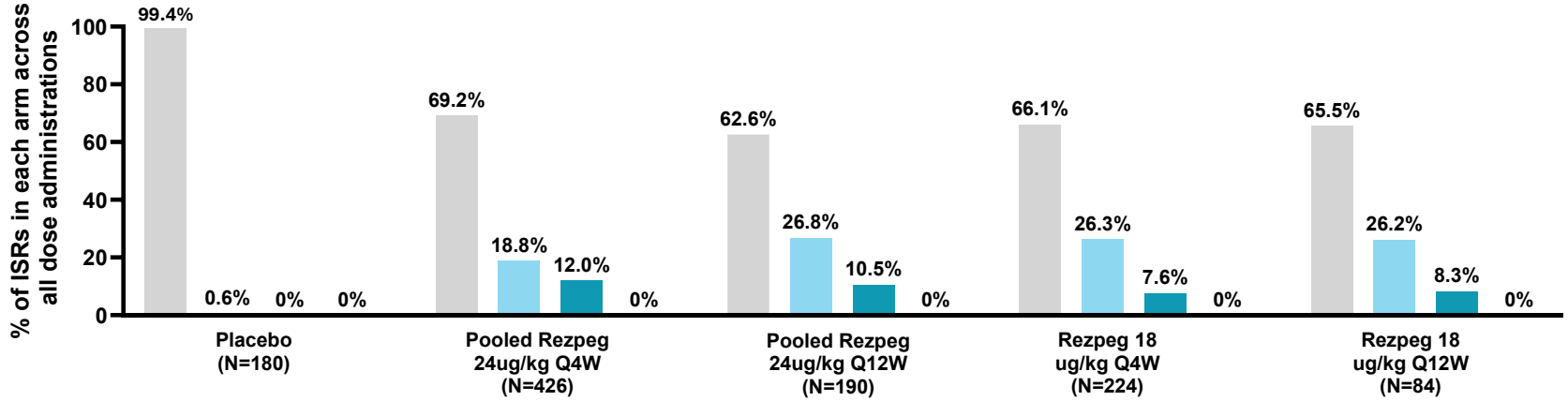
- Nearly all were mild-moderate in severity and self-resolving
- The treatment discontinuation rate due to ISRs overall was very low (0.7%) for Rezpegaldesleukin exposed patients
- Lower frequency of ISRs observed over longer dosing duration in maintenance

Lower Frequency of ISRs Observed Over Longer Dosing Duration in Maintenance

Induction Period



Maintenance Period



N= number of rezpegaldesleukin administrations in rezpegaldesleukin arms and number of placebo administrations in placebo arms
Mild: *Faint erythema, asymptomatic, no or mild itch, no or mild tenderness*
Moderate: *Notable/great erythema, widespread itch, readily apparent induration, moderate pain*
Severe: *Widespread and constant itch limiting daily life, gross deviation of normal anatomic contour for induration, severe pain*

REZOLVE-AD Phase 2 Validates Rezpegaldesleukin as First-in-Class Novel Treg Mechanism in Atopic Dermatitis

Novel Treg MoA differentiates from existing and in-development biologics

- **Up to 6-fold increase in Tregs**
- **Clear dose-dependent reduction in multiple AD biomarkers: IL-19, TARC/CCL17, Periostin, MDC/CCL22**
- **Mechanistic validation translating into sustained clinical efficacy**

All 3 dose arms met primary endpoint

- **% improvement in EASI at 16 weeks** ($p<0.001$)
- **Clear dose-dependent response**
- **Rapid onset of action** (early separation from placebo)
- **Similar efficacy data observed in severe patients as in moderate**

Highest dose achieved all 6 key secondaries and durable maintenance

- **Met all six key secondary endpoints EASI-75, vIGA-AD 0/1, Itch-NRS, EASI-90, BSA**
- **Q4W and Q12W maintenance regimens durable through Week 52**
- **Continued deepening of responses from Week 16 to Week 52**

Long-term safety consistent with previously-reported safety profile with no new safety concerns

- No increased risk of conjunctivitis, oral ulcers, or infections, including oral herpes, in study treatment arms
- Most frequent AEs were mild injection site reactions (ISRs) that were self-resolving (<1% discontinuations due to ISRs)
- Over 1,000 patients treated to date (~381 patient-years of exposure)

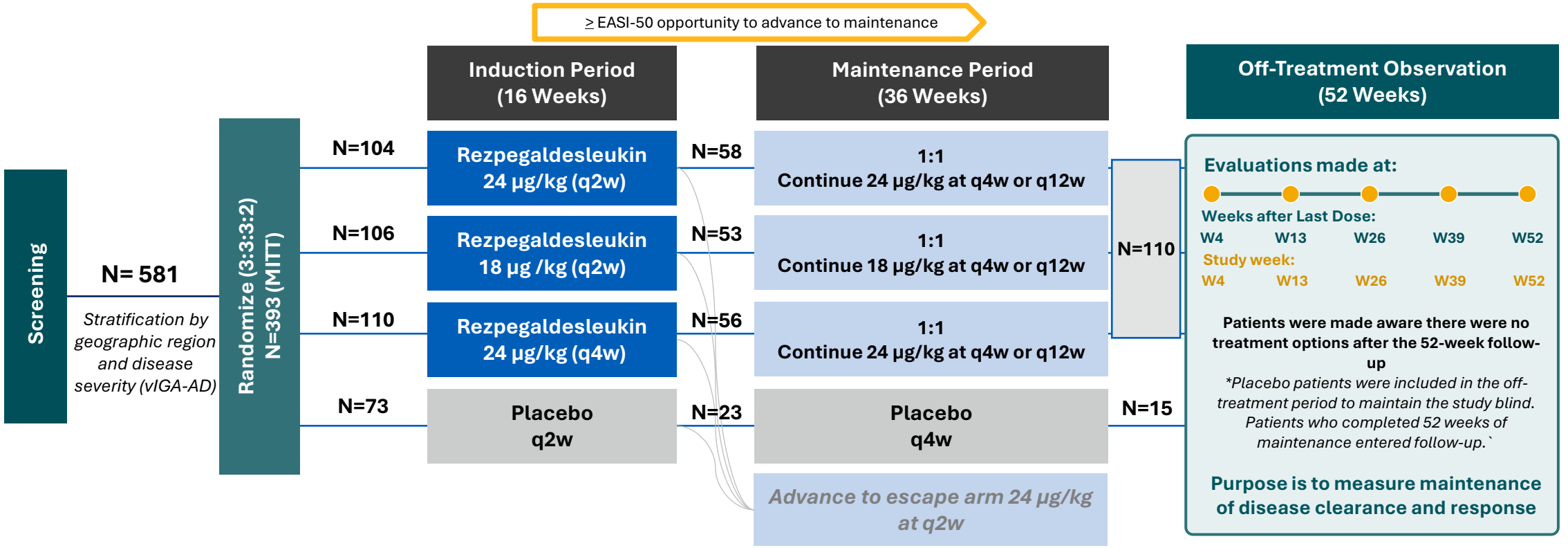
Source: Nektar Investor and Analyst Event (June 2025); EASI-75: Eczema Area and Severity Index ≥ 75; vIGA-AD: validated Investigator Global Assessment of Atopic Dermatitis; Itch-NRS: Itch Numerical Rating Scale; EASI-90: Eczema Area and Severity Index ≥ 90; BSA: Body Surface Area

Differentiating Features of Rezpegaldesleukin for Atopic Dermatitis

- **Treg MoA validated** for deep and durable efficacy in patients with moderate-to-severe atopic dermatitis with extended dosing out to 52 weeks
- **Rapid onset of action** for both EASI-75 and itch relief with rezpegaldesleukin arm separating from placebo early in treatment
- Demonstrated **control of asthma (ACQ-5 endpoint)** in patients with moderate-to-severe atopic dermatitis and co-morbid asthma (25% of population)
- **Maintenance regimens achieved durability and demonstrated a deepening of responses**
- **Extended dosing regimens with rezpegaldesleukin compare favorably** to historically reported longer term maintenance data across Phase 2/Phase 3 trials
- **Extended dosing regimens with rezpegaldesleukin resulted in new and deepening of responses** achieved from Week 16 to Week 52
- **Long-term Safety Profile Established** for 52 weeks of dosing
  - Consistent with previously-reported safety profile with no new safety concerns identified in study treatment arms

REZOLVE-AD: Phase 2b trial design

Patients with Moderate-to-Severe Atopic Dermatitis



Stratification

- ✓ Geographic region
- ✓ Disease severity by vIGA-AD

Key Inclusion Criteria:

- ✓ Age: ≥18 years
- ✓ Moderate/severe AD diagnosis for ≥ 12 months
  - EASI ≥ 16
  - vIGA-AD of 3 or 4
  - BSA ≥ 10%
- ✓ Biologic-naive (no prior biologic systemic therapy) and systemic JAKi-naïve
- ✓ Failure of prior therapy, including TCS of medium or higher potency, within last 6 months

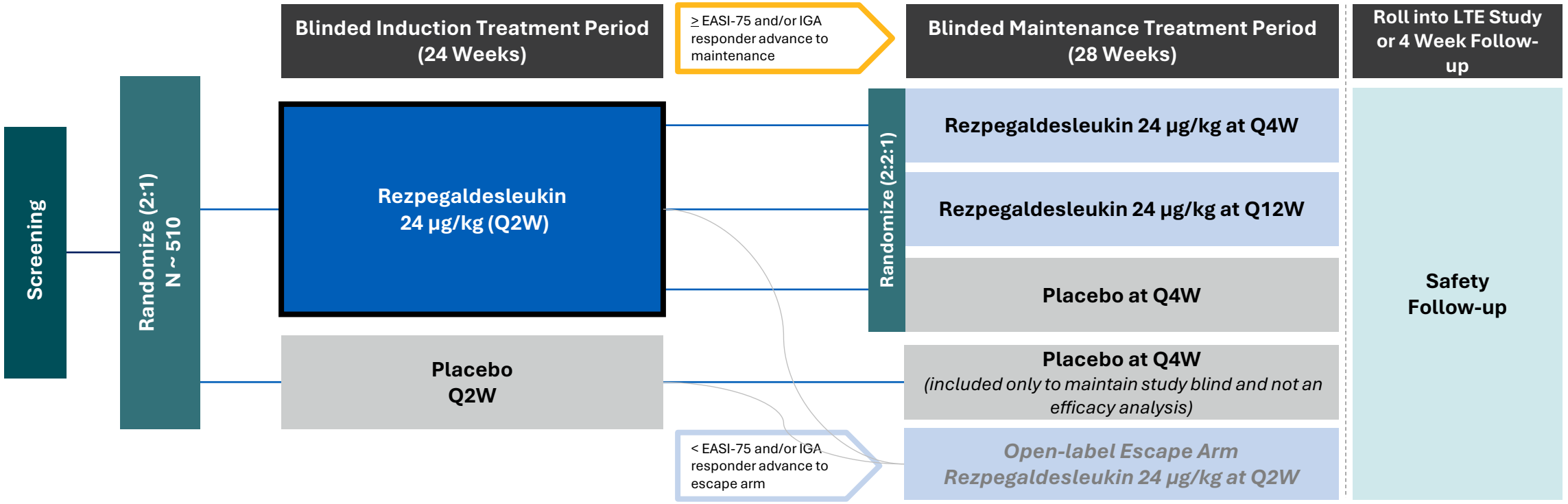
Key Pharmacodynamic Biomarkers:

- T regulatory cell
- TARC/CC17
- Periostin
- MDC/CCL22
- IL-19

MITT is defined as patients who were randomized and received at least one dose of study treatment or placebo.

Trial Design for ZENITH-AD Ph3 Program: 3 Trials in Atopic Dermatitis

ZENITH AD-1 (biologic and systemic JAK inhibitor naïve) , ZENITH AD-2 (TCS/TCI combination study) and ZENITH AD-3 (experienced patients)



Key Eligibility Criteria

- Age: ≥12 years
- Moderate/severe AD diagnosis for ≥ 12 months
  - EASI ≥ 16.0
  - IGA of 3 or 4
  - BSA ≥ 10.0%
- ***[ZENITH AD-1]*** No prior treatment with biologic or JAK inhibitors
- ***[ZENITH AD-3]*** Must have prior systemic biologic and/or JAK inhibitors experience

Stratification

Induction:

- Age
- Geographic region
- Disease severity by IGA
- Prior biologic/oral JAKi

Stratification

Maintenance:

- Age
- Disease severity by IGA

Endpoints

Co-Primary

- IGA-related endpoint
- EASI-75

Key Secondary

- EASI-90
- Itch NRS, ≥ 4-point reduction
- ACQ-5



Rezpegaldesleukin in Alopecia Areata

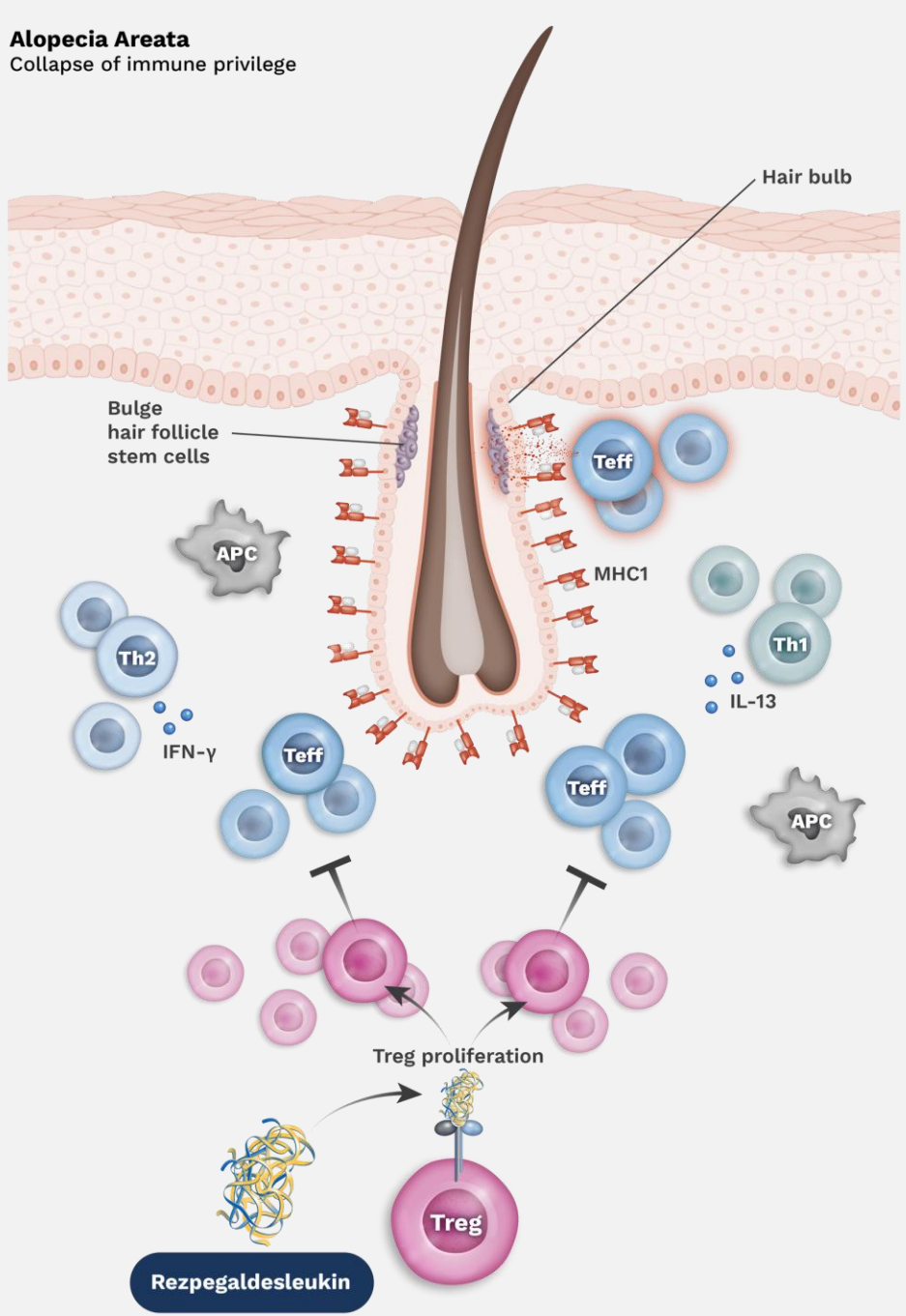
Rezpegaldesleukin
Alopecia Areata MOA

Scientific rationale

- By targeting receptors on regulatory T cells, rezpegaldesleukin stimulates the proliferation of regulatory T cells (Tregs), including FOX-P3+ Tregs

- In alopecia, a pro-inflammatory environment causes the collapse of immune privilege around the anagen hair bulb leading to hair follicle focal inflammation driven by NKG2D + T cells, NK cells, as well as auto-reactive CD8+ T cells

- Regulatory T cells act upstream of these inflammatory cytokines to reduce their activity; by increasing the number and functionality of regulatory T cells, rezpegaldesleukin aims to reduce the hair follicle local inflammation and restore immune privilege.



Rezpegaldesleukin in Alopecia Areata Overview

Topline data from Phase 2b study in severe-to-very severe alopecia areata in December 2025

Alopecia areata (AA) is a disease that happens when the immune system attacks hair follicles and causes hair loss[1]

- Nearly 6.7 million people in the US have had it or will have it in their lifetime. ~700,000 people currently have alopecia areata in US. [2]
- ~160 million people worldwide have alopecia areata or have had, or will have it[2]
- 80% of patients show signs of alopecia before 40[2]
- Many patients are refractory to available therapies, and long-term use is associated with troublesome side effects and safety risks[3]
- Only systemic treatments approved for alopecia are JAK inhibitors with multiple Blackbox warnings. High relapse rates upon discontinuation of these therapies[3]

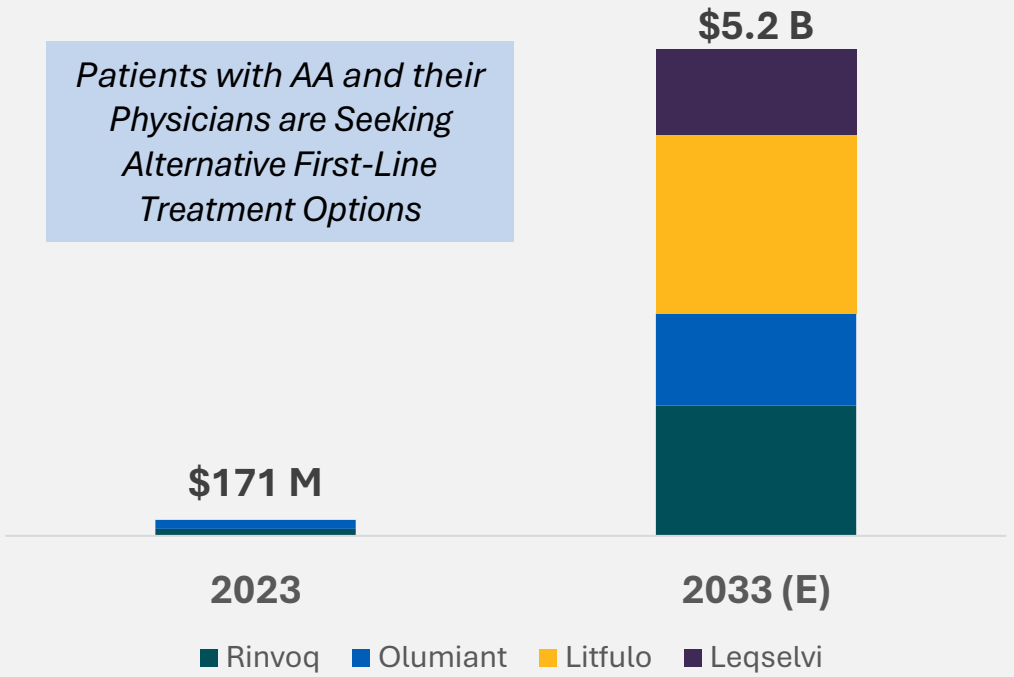
Represents additional opportunity to expand Rezpeg

Sources: 1. NIH; 2. National Alopecia Areata Foundation; 3. DRG – Unmet Needs of Alopecia Areata

Opportunity for Rezpegaldesleukin in Alopecia Areata (AA)

- **~160 million people worldwide are affected by alopecia areata** (AA), including those who currently have it, have had it, or are expected to develop it[1]
- In the US, **~6.7 million people will have AA** at some point in their lifetime, with **~700,000 individuals currently living with the condition**[1]
- Notably, **80% of patients show signs of AA before 40**[1]
- **Many patients are refractory to available therapies**, and long-term use is associated with troublesome side effects and safety risks[2]
- Currently, the only approved systemic treatments for AA are JAK inhibitors, which **carry multiple boxed warnings** and are also associated with high relapse rates upon discontinuation

Actual and Projected Sales of JAK inhibitors in AA[2] (WW Sales in USD, 2023 – 2033)



Sources: 1. National Alopecia Areata Foundation; 2. DRG – Unmet Needs of Alopecia Areata (accessed: 4.9.2026)
WW: worldwide; (E): Estimate; RINVOQ® (upadacitinib) is a registered trademark of AbbVie Biotechnology Ltd; Olumiant® (baricitinib) is a registered trademark (Registration #5745831) owned by Eli Lilly and Company; LITFULO® (ritlecitinib) is a registered trademark owned by Pfizer Inc.; Leqselvi™ (deuruxolitinib) is a registered trademark of Pharmaceutical Industries, Inc.

Phase 2b REZOLVE-AA Study Evaluating Rezpegaldesleukin for Alopecia Areata

Severe-to-Very-Severe Alopecia Areata (NCT06340360) - Granted Fast Track Designation in July 2025

Key Eligibility Criteria

- Adult patients (18+)
- Severe-to-very-severe AA
- SALT ≥50
- >6 months since diagnosis to exclude unstable AA
- No spontaneous improvement over the past 6 months
- 8-week washout of prior medication for AA

Stratification by baseline SALT Score ≥50 to <95 vs ≥95 to 100

Induction Q2W (Weeks 0-36)

3:3:2 N=92

- **Rezpegaldesleukin 24 µg/kg n=35**
- **Rezpegaldesleukin 18 µg/kg n=37**
- **Placebo n=20**

Week 36 Analyses

Primary:

- Mean % SALT reduction at Week 36

Key Secondaries:

- SALT ≥ 30% reduction from baseline ($SALT_{30}$)
- Absolute SALT Score ≤30
- Absolute SALT Score ≤20
- Absolute SALT Score ≤10
- Clinician-Reported Outcome (ClinRO) Eyebrow and Eyelash (exploratory)
- Safety

Exploratory Treatment Extension and Follow-up

Blinded 16-week treatment extension: **Patients with a SALT Score greater than 20 at Week 36 who also demonstrated hair growth**

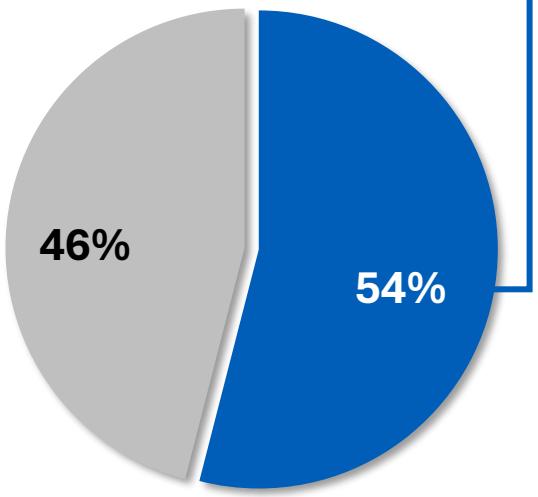
24-week follow-up period after 36 or 52 weeks of treatment

Rezolve AA

Severity of Alopecia Tool (SALT) is a validated endpoint to assess the extent of scalp-hair loss in patients with alopecia areata

Majority of Physicians Report They Would Try Patients on Alternate Therapies for AA Before Prescribing JAK inhibitors

54% of physicians report they would try patients on alternate therapies for AA before prescribing JAKi[1]



Challenges with JAKi Class

- **Boxed warnings** for serious infections, mortality, malignancy, major adverse cardiovascular events (MACE), and thrombosis
- Class-related risks such as cytopenias, hepatic enzyme elevations, and lipid changes require **routine safety monitoring**
- **Extensive testing** required prior to initiating therapy and while on therapy to monitor TB, CBC, LFTs, and lipids
- 80% of patients who go off low-dose Olumiant eventually rebound (90% SALT Score ≤20 responders rebound)[2]

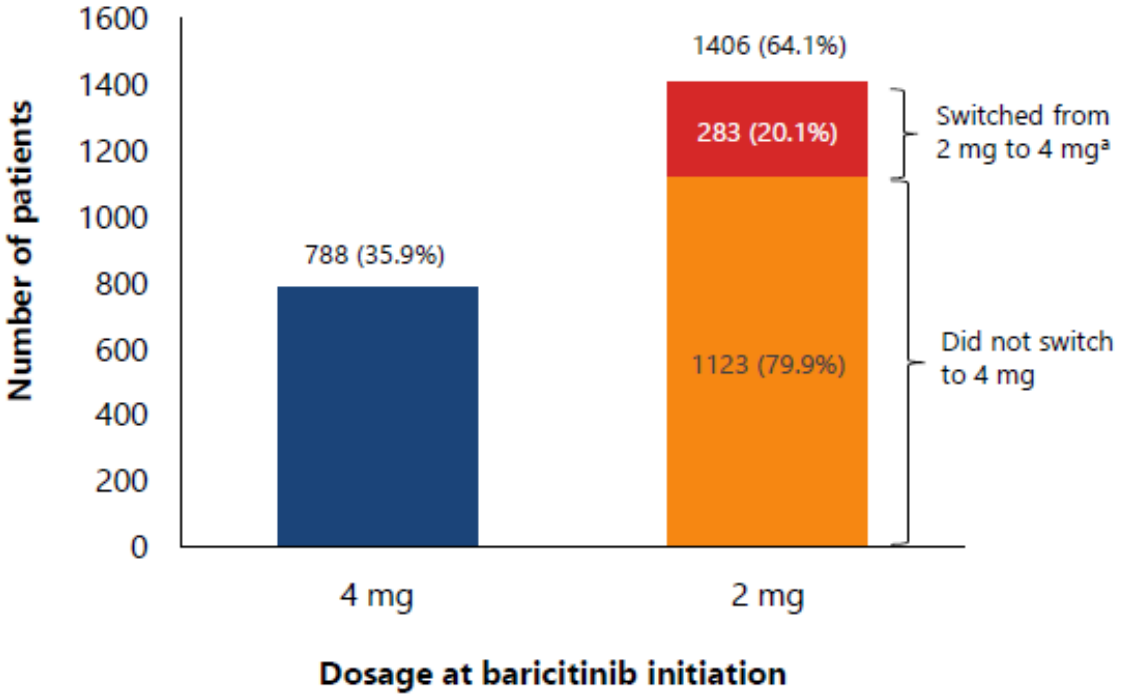
Source: 1. Adapted from Nohria et al., Journal of the American Academy of Dermatology 2024; 2. King et al., JAMA Dermatol. 2024

Unmet Need for Patients with Alopecia Areata

AAD 2025: Baricitinib Real World Claims Data

"Poor persistence observed among patients treated with baricitinib suggest there is an unmet need for effective treatment for patients with AA"[1]

Dose Patterns Among Patients With AA Treated With Baricitinib



[a]Only switches from 2 to 4 mg are shown. A total of 775 (98.4%) of the 788 patients who initiated on baricitinib 4 mg remained on 4 mg during treatment; 13 (1.6%) patients who initiated on baricitinib 4 mg had a claim during the follow-up period for baricitinib 2 mg.

	Initiated on baricitinib 4 mg[a] n = 788	Initiated on baricitinib 2 mg n = 1406	Initiated on baricitinib 2 mg, did not switch to 4 mg n = 1123
TTD using Kaplan-Meier analysis[b,c] (months), median (IQR)	5.3 (2.1, 10.9)	5.0 (2.0, 11.8)	3.7 (1.2, 8.7)

[a]A total of 775 (98.4%) of the 788 patients who initiated on baricitinib 4 mg remained on 4 mg during treatment; 13 (1.6%) of the patients who initiated on baricitinib 4 mg had a claim during the follow-up period for baricitinib 2 mg.
[b]The discontinuation date was defined as the date of the last claim (or last claim before a large gap) + days supply + 1. Patients who did not discontinue treatment were censored at the end of clinical activity.
[c]Discontinuation was defined as twice the amount of typical days of supply following each claim date, determined by the most frequent days supply. Specifically, 97.0% of baricitinib claims had a supply of 30 days.

Source: 1. Mostaghimi et al., AAD 2025

An Efficacious and Safe Biologic with Novel MoA Could Redefine First-line Systemic Therapy in Alopecia Areata

We believe there is a strong need for a non-JAKi based Sub-Q biologic to treat patients with AA, which could provide:

- **Better suitability for chronic use:** Circumvents JAKi class safety issues, including boxed warnings, that limit JAKi use in AA
- **Easier adherence:** Infrequent twice-monthly dosing of a biologic may be advantageous over oral daily dosing for long-term treatment
- **Extended biologic pharmacodynamic effect:** Opportunity for more durable and stable efficacy even in the setting of non-compliance
- **No need for lab monitoring:** Simplifies prescribing in dermatology clinics, which are not optimized for chronic lab management
- **Payer-friendly profile:** Fewer restrictions and risk-based exclusions; more straightforward access and broader eligibility

Blinded 16-Week Exploratory Treatment Extension for REZOLVE-AA

A Total of 31 Patients Entered into Treatment Extension

Blinded 16-week treatment extension:
Patients with a SALT Score greater than 20 at Week 36 who also demonstrated hair growth
n=31

Extension Q2W (Weeks 36-52)

Patient with a SALT Score greater than 20 at Week 36 who also demonstrated hair growth
Patients continued at same dose from induction

- **Rezpegaldesleukin 24 µg/kg n=13**
- **Rezpegaldesleukin 18 µg/kg n=14**
- **Placebo n=4**

52-Week Exploratory Endpoints

- New SALT Score ≤20 Responders Weeks 36-52 (80% or more hair coverage on scalp)
- Overall SALT Score ≤20 at Week 52*
- Overall SALT Score ≤30 at Week 52* (70% or more hair coverage on scalp)
- SALT Score $SALT_{30}$ at Week 52* (30% improvement from baseline SALT)
- Overall $SALT_{50}$ at Week 52* (50% improvement from baseline SALT)

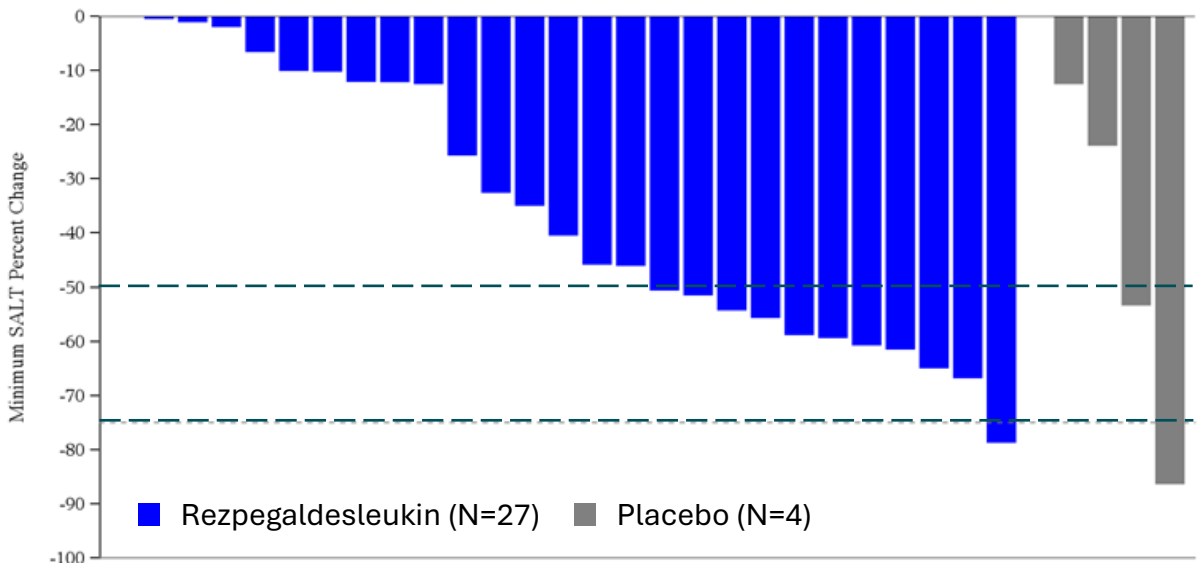
**Modified intent-to-treat adapted (mITT^{A}): excludes 4 patients with major study eligibility violations (post-hoc); No patient with study eligibility violations entered into the 16-week treatment extension*

REZPEG-Treated Patients in Extension Achieved Deepening of Response

Best Percent Improvement in SALT Score from Baseline While on Study Treatment

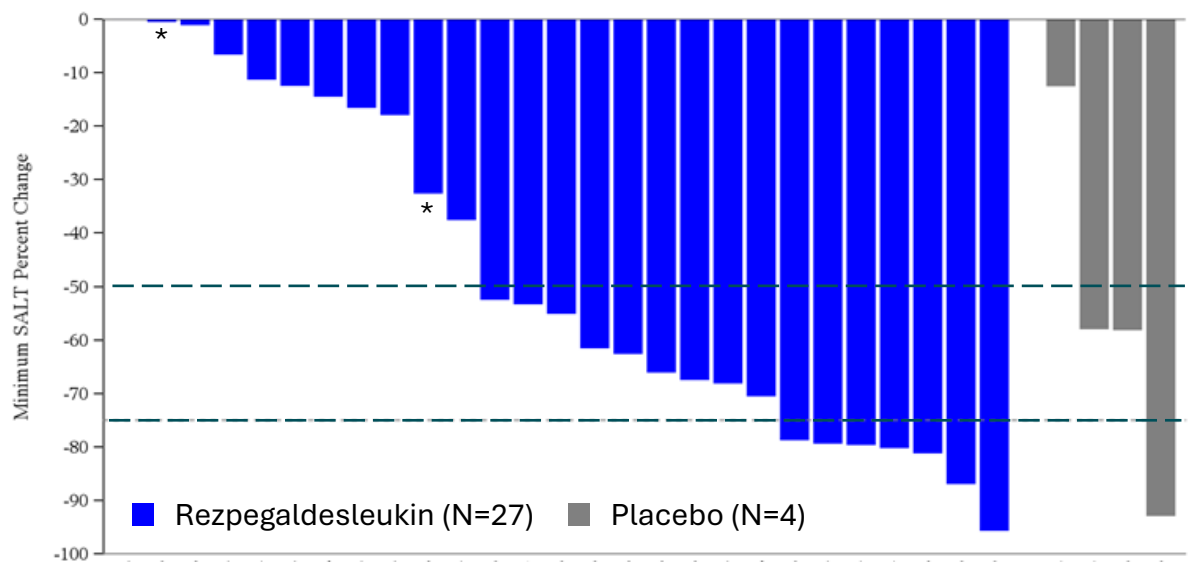
94% of patients in extension completed treatment to week 52

Extension Patients 36-week Induction (N=31)



4% (1/27) achieved ≥75% reduction from baseline SALT

Extension Patients 52-week Treatment (N=31)

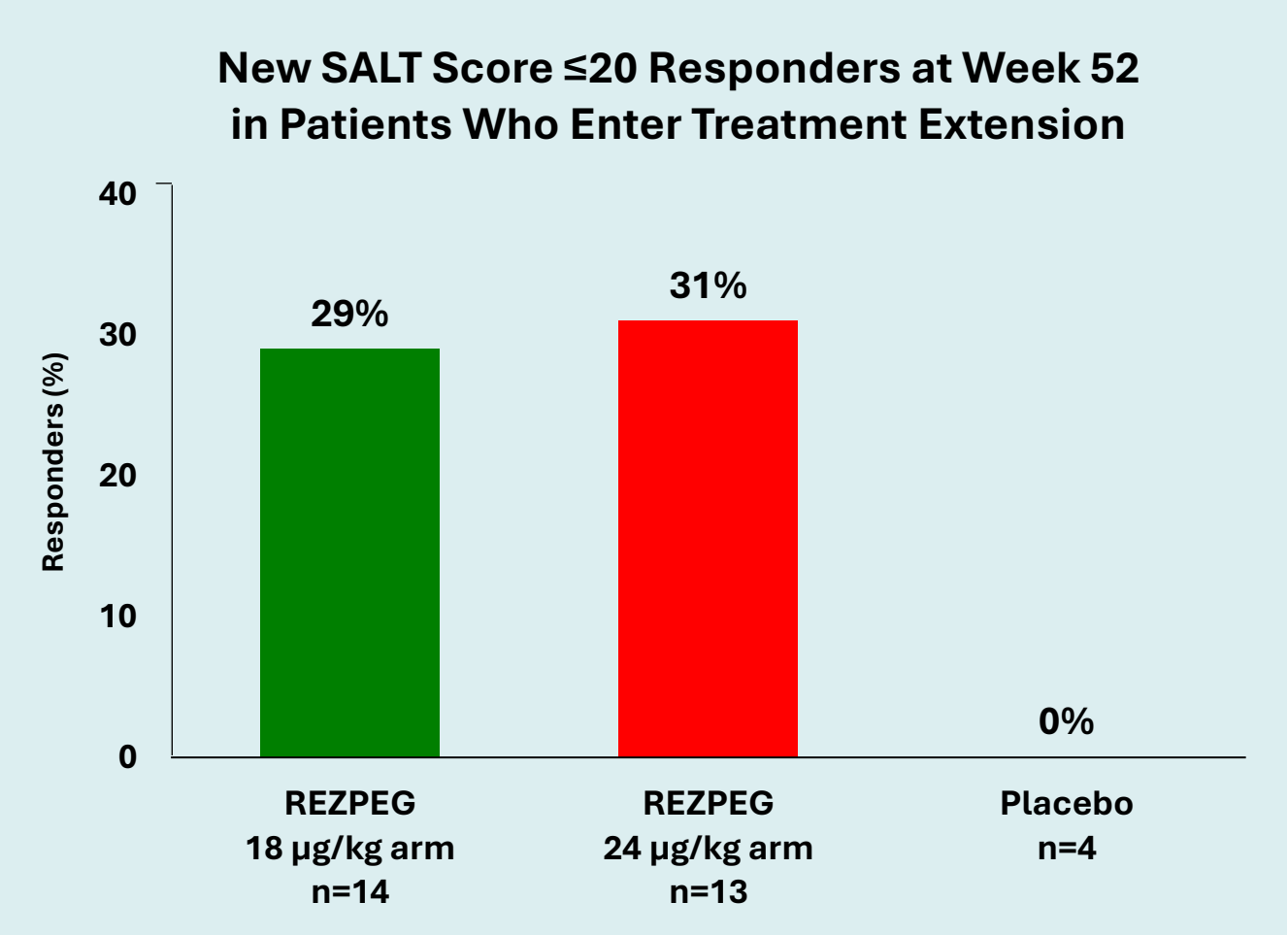


26% (7/27) achieved ≥75% reduction from baseline SALT

**Discontinued prior to week 52 due to patient decision; one placebo patient with a SALT Score ≤20 at week 36 entered into extension based on investigator's request, which was granted as an exception*

Conversions to SALT Score ≤20 with Additional 16 Weeks of Treatment

A Total of 31 Patients Entered into Treatment Extension



- There were 8 new SALT Score ≤20 responses in 27 patients treated with REZPEG
- There were no new SALT Score ≤20 responses in placebo
- Data strongly support a 52-week dosing induction in Phase 3

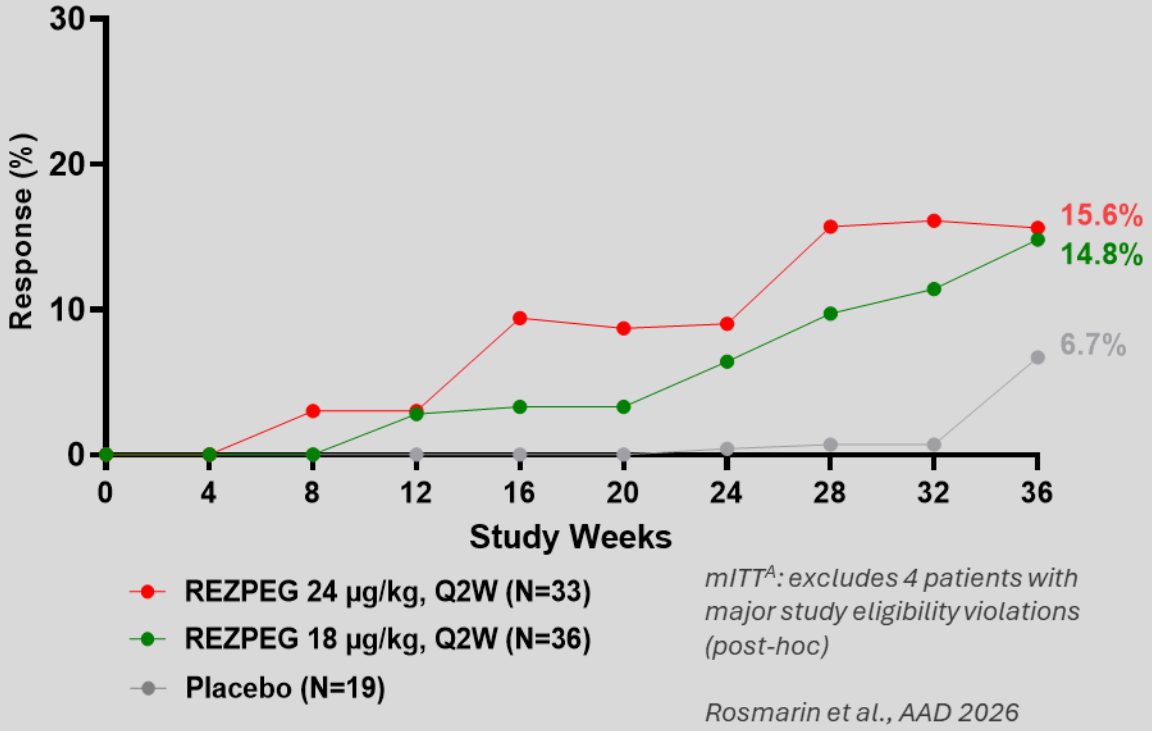
Analysis by multiple imputation (slide 31); two patients discontinued prior to week 52 due to patient decision

More Patients Treated with Rezpegaldesleukin Achieved SALT Score ≤20 at Week 52

Overall SALT Score ≤20 (80% or more hair coverage on scalp)

36-week Treatment Data

SALT Score ≤20 at Week 36 (mITT[A])

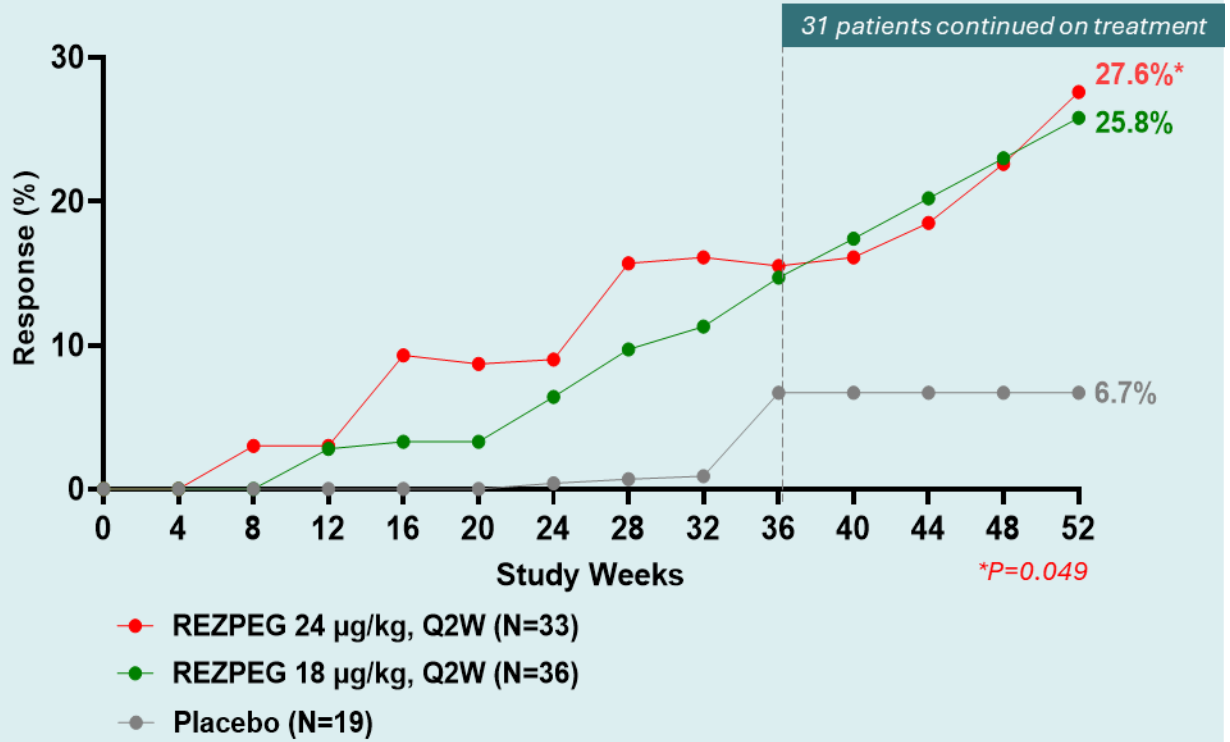


mITT[A]: excludes 4 patients with major study eligibility violations (post-hoc)

Rosmarin et al., AAD 2026

52-week Treatment Data

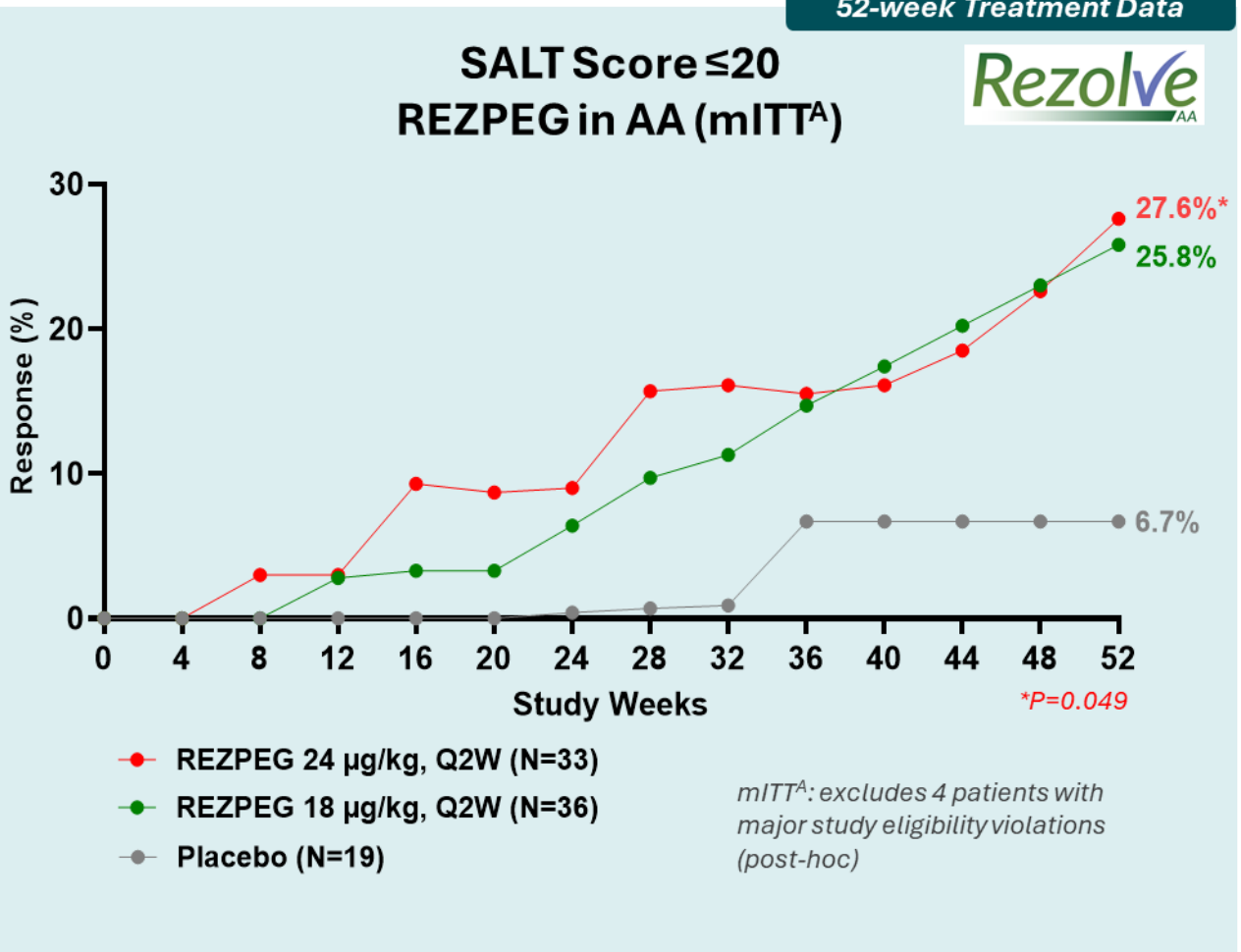
SALT Score ≤20 at Week 52 (mITT[A])



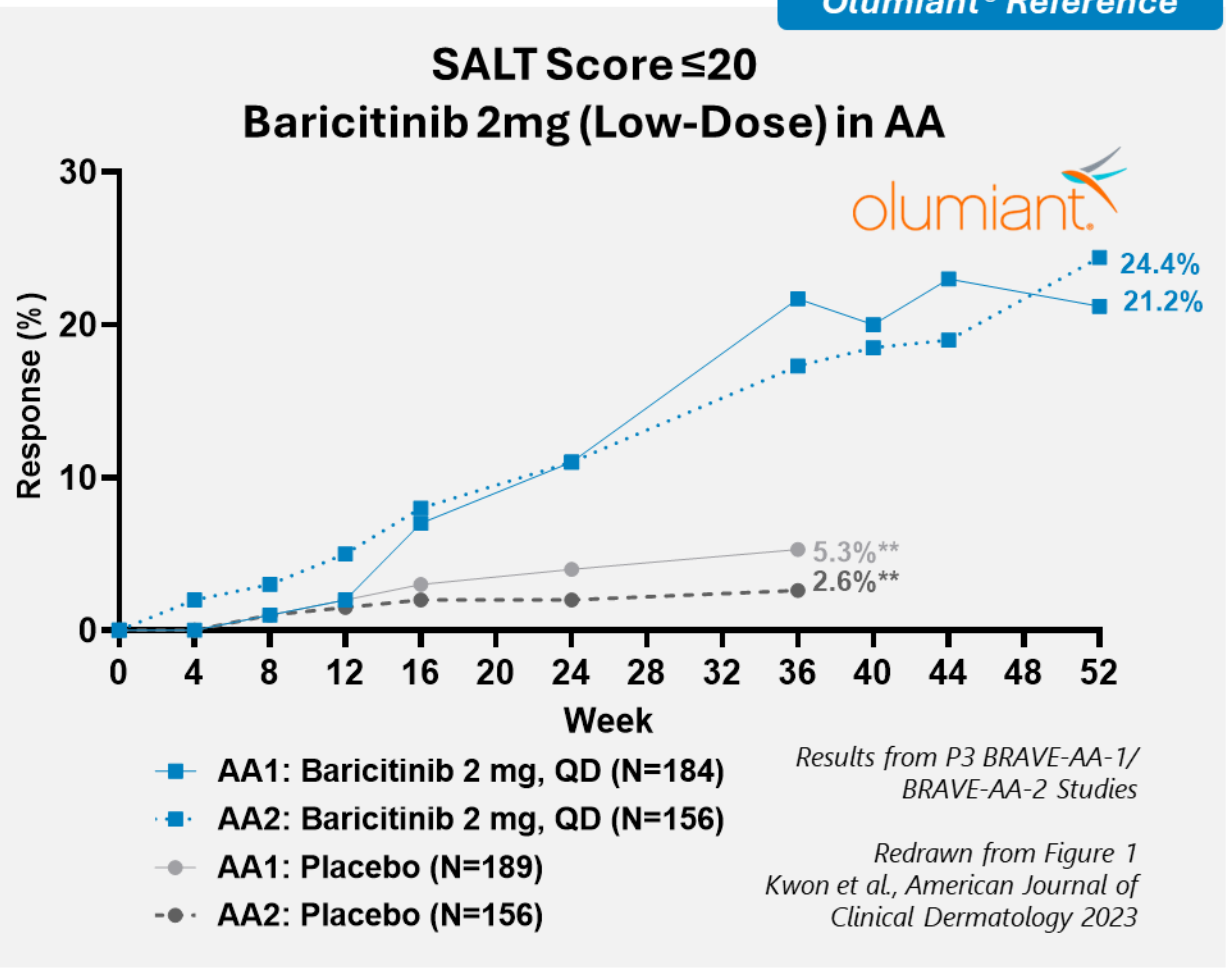
Data for mITT[A] analysis set are imputed from week 0 to week 36 following primary estimand. Data for patients in non-treatment extension set in week 40, 44, 48 and 52 are carried forward from week 36 data. Missing data for patients in treatment extension set for week 40, 44, 48 and 52 are imputed using the multiple imputation method.

Rezpegaldesleukin Met Our Target Product Profile

52-week Treatment Data



Olumiant® Reference



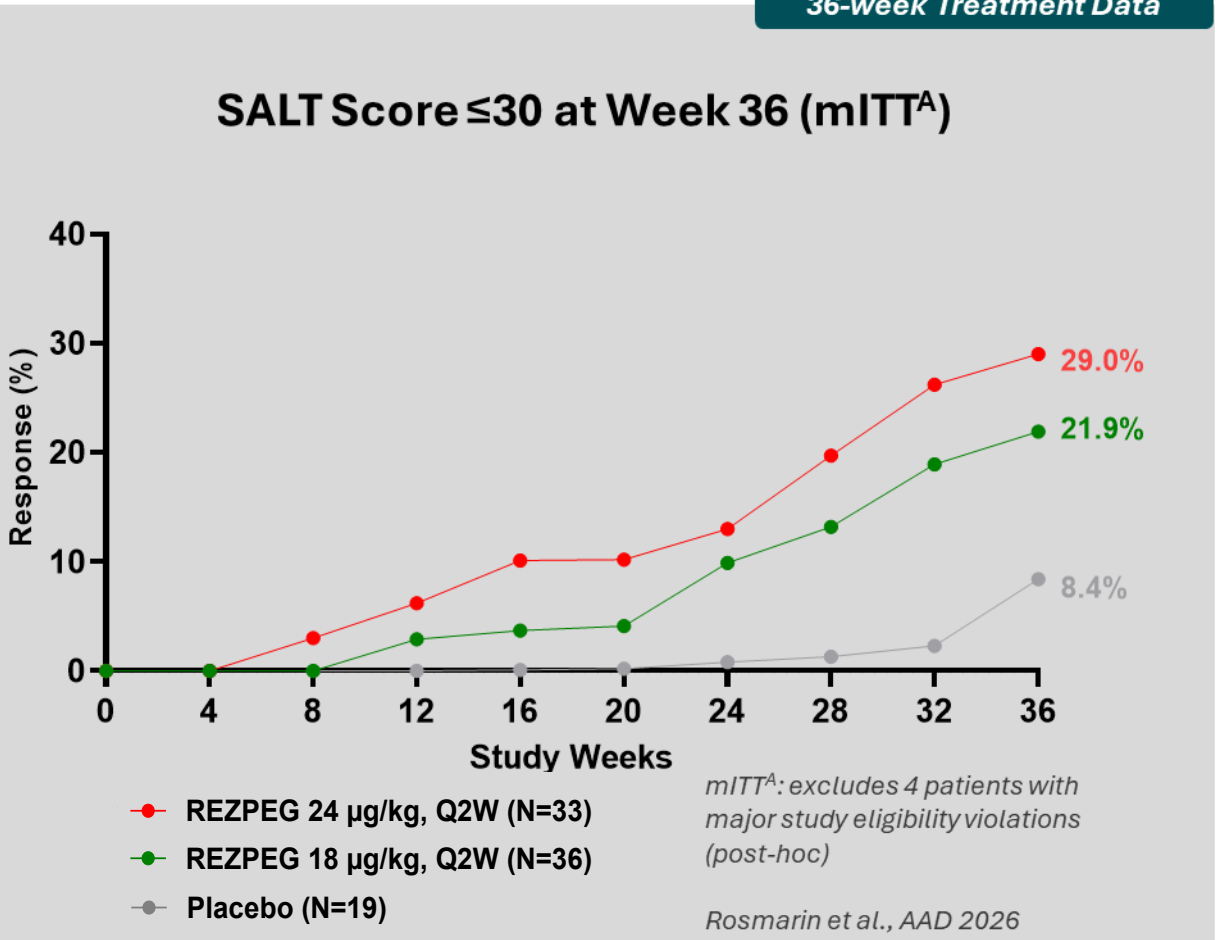
*Olumiant® is a registered trademark owned or licensed by Eli Lilly and Company, its subsidiaries, or affiliates.**Placebo data based on Figure S9 from King et al., NEJM 2022*

This is a cross-trial comparison and includes data from different clinical studies and is not a head-to-head comparison.

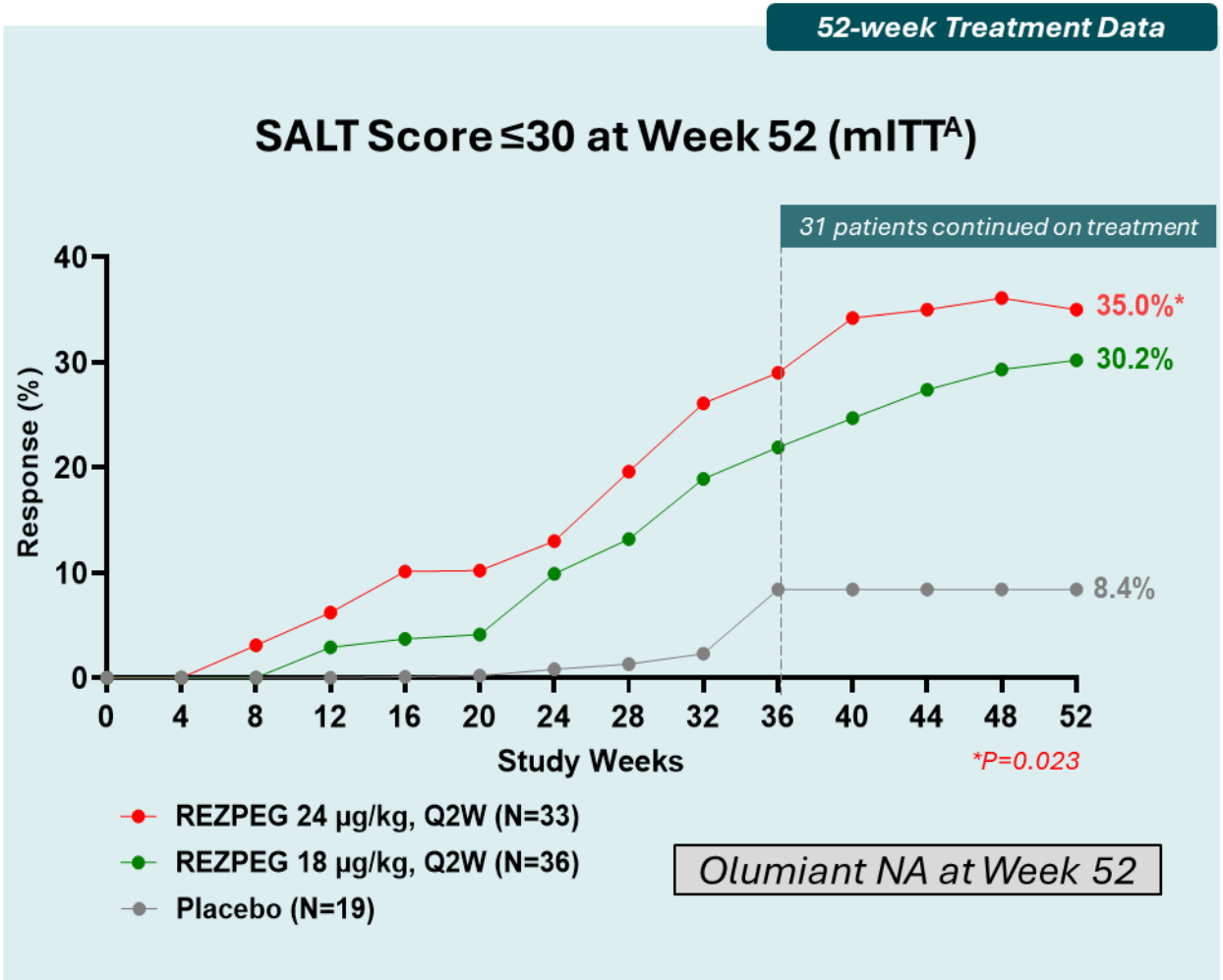
More Patients Treated with Rezpegaldesleukin Achieved SALT Score ≤30 at Week 52

SALT Score ≤30 (70% or more hair coverage on scalp)

36-week Treatment Data



52-week Treatment Data



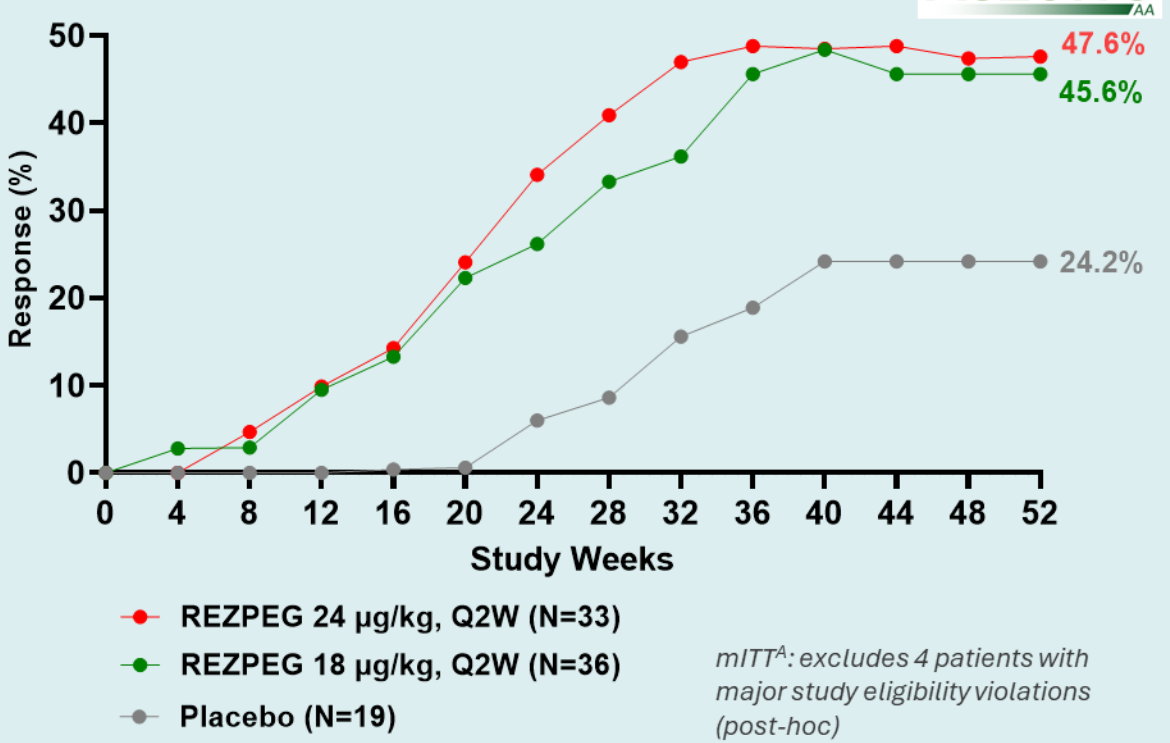
Data for mITT^A analysis set are imputed from week 0 to week 36 following primary estimand. Data for patients in non-treatment extension set in week 40, 44, 48 and 52 are carried forward from week 36 data. Missing data for patients in treatment extension set for week 40, 44, 48 and 52 are imputed using the multiple imputation method.

Promising Data for a Biologic in AA

$SALT_{30}$ (At Least 30 Percent Improvement from Baseline in SALT)

52-week Treatment Data

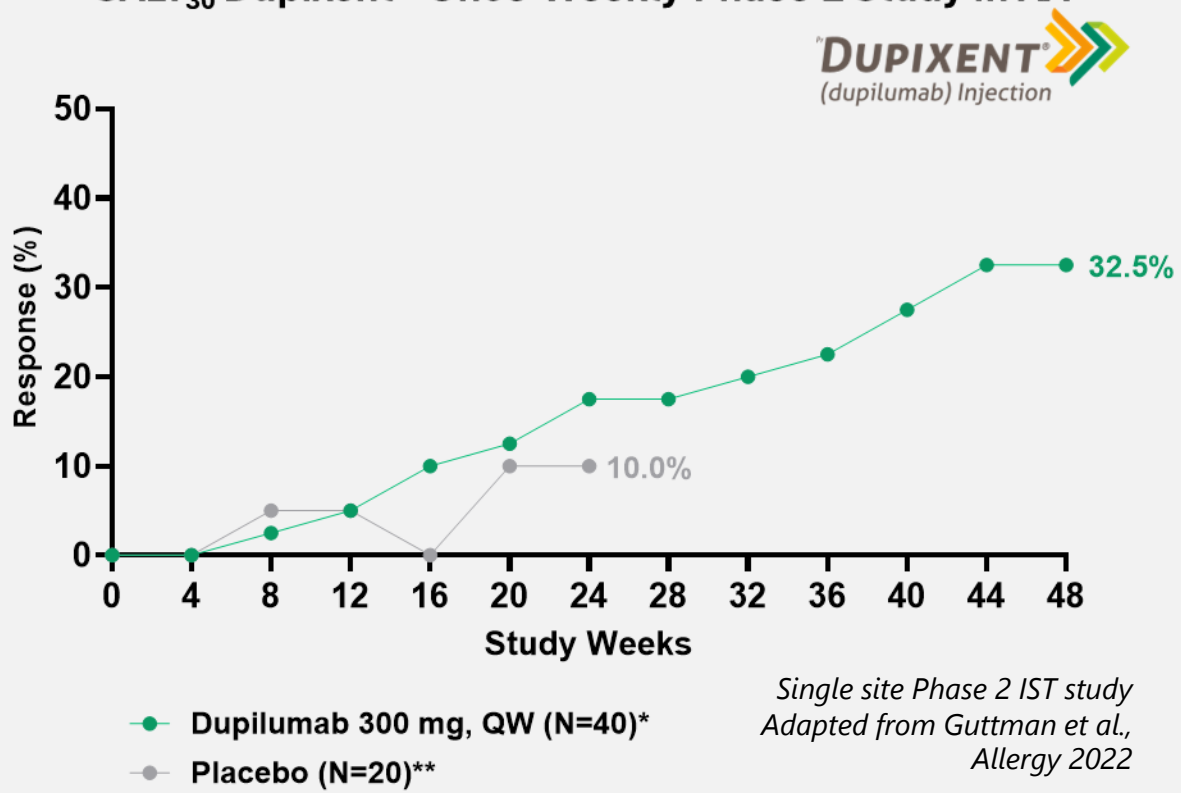
$SALT_{30}$ REZPEG Twice-Monthly Phase 2 Study in AA (mITT[A])



mITT[A]: excludes 4 patients with major study eligibility violations (post-hoc)

Dupixent® Reference

$SALT_{30}$ Dupixent® Once-Weekly Phase 2 Study in AA



Single site Phase 2 IST study Adapted from Guttman et al., Allergy 2022

*DUPIXENT is a registered trademarks of Sanofi or an affiliate. Study went to 48 weeks of treatment with $SALT_{50}$ at 22.5%; *Two 300 mg doses administered on cycle one as a loading dose; **Placebo patients not available past week 24*

US DELPHI Consensus Guidelines "In patients with active atopy or history of atopic dermatitis, dupilumab may be considered as a long-term AA treatment" (Dec'25)

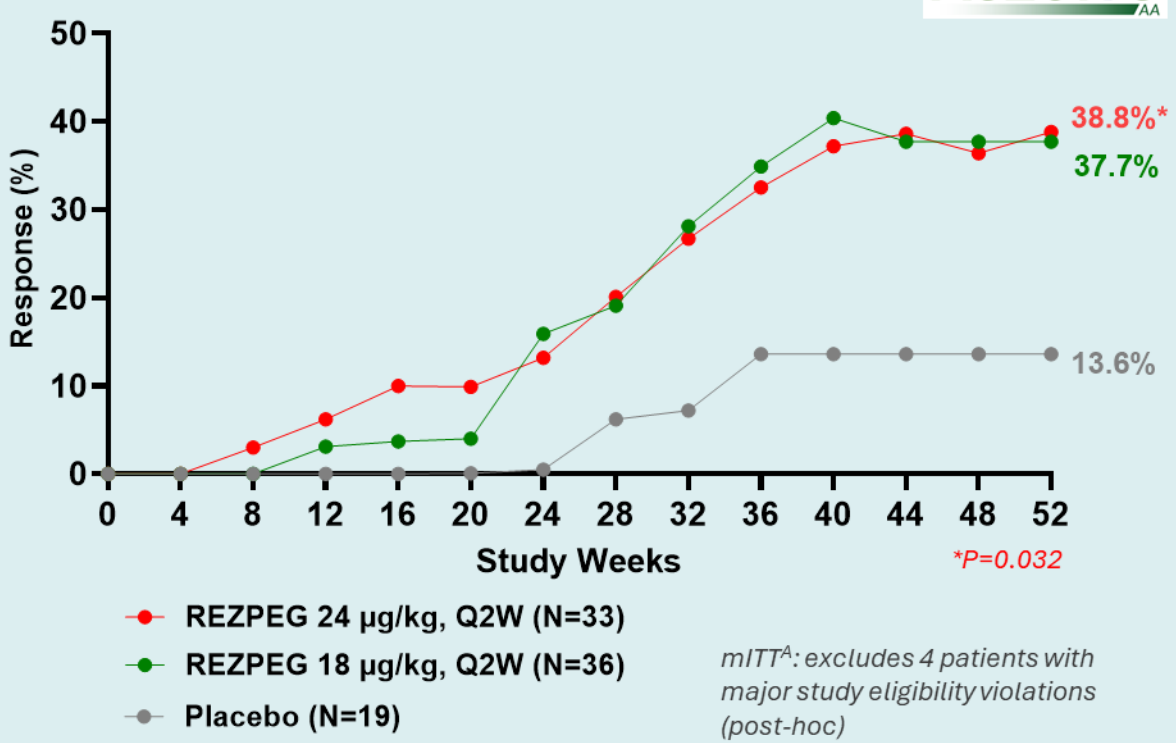
This is a cross-trial comparison and includes data from different clinical studies and is not a head-to-head comparison.

Promising Data for a Biologic in AA

$SALT_{50}$ (At Least 50 Percent Improvement from Baseline in SALT)

52-week Treatment Data

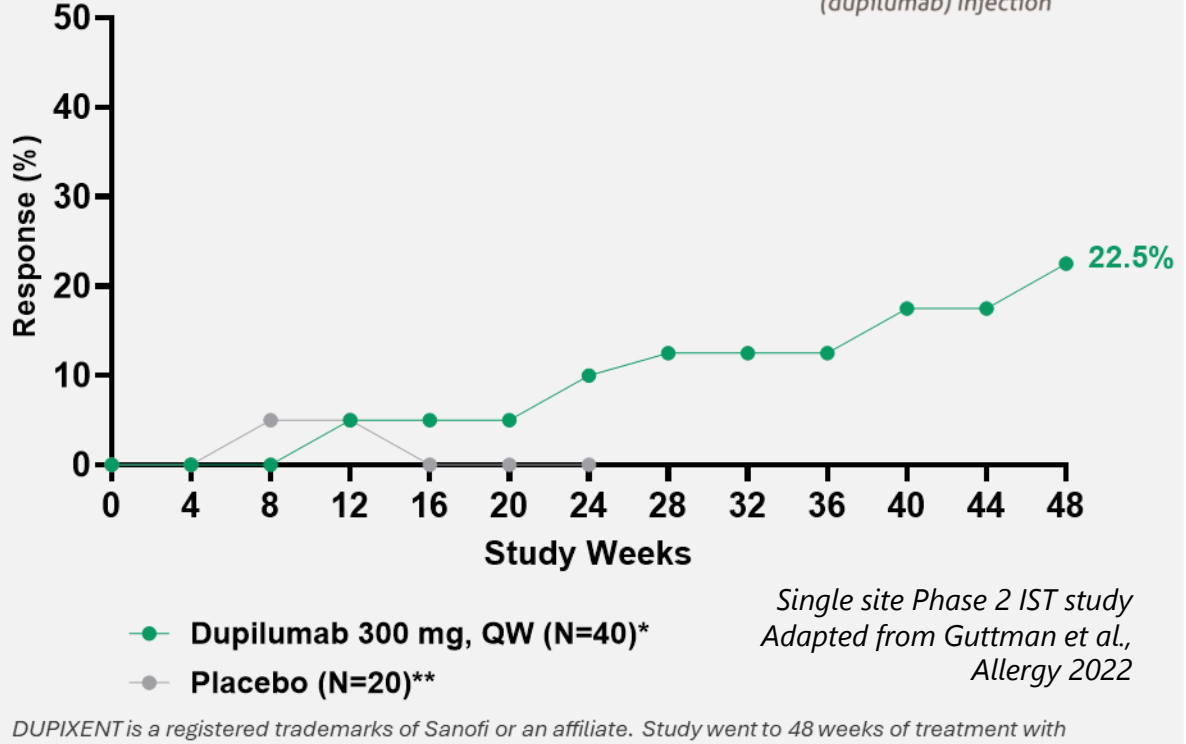
$SALT_{50}$ REZPEG Twice-Monthly Phase 2 Study in AA (mITT[A])



mITT[A]: excludes 4 patients with major study eligibility violations (post-hoc)

Dupixent® Reference

$SALT_{50}$ Dupixent® Once-Weekly Phase 2 Study in AA



Single site Phase 2 IST study Adapted from Guttman et al., Allergy 2022

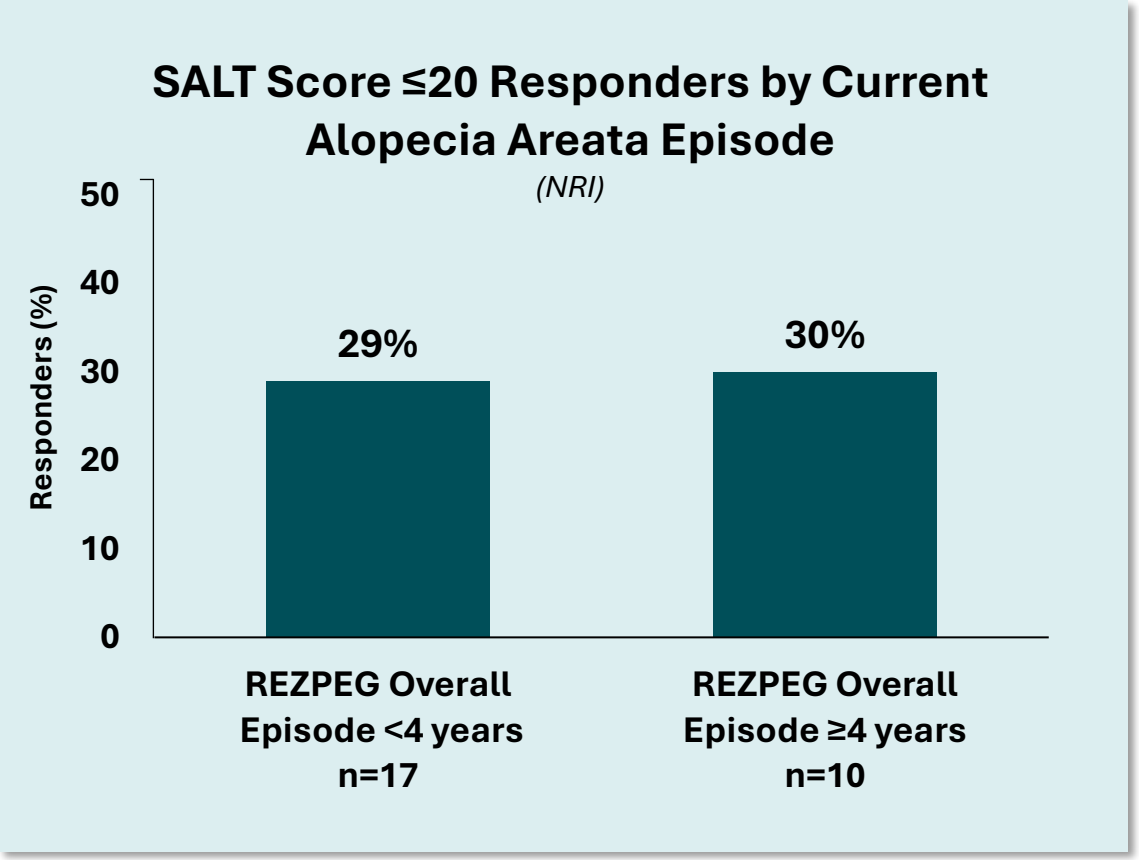
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This is a cross-trial comparison and includes data from different clinical studies and is not a head-to-head comparison.

New Data: Comparable SALT Score ≤20 Response Rates Seen at Week 52 in Patients with Current Alopecia Areata Episode < 4 years vs ≥ 4 years at Baseline

SALT Score ≤20 Response Rates by Duration of Current Alopecia Areata Episode



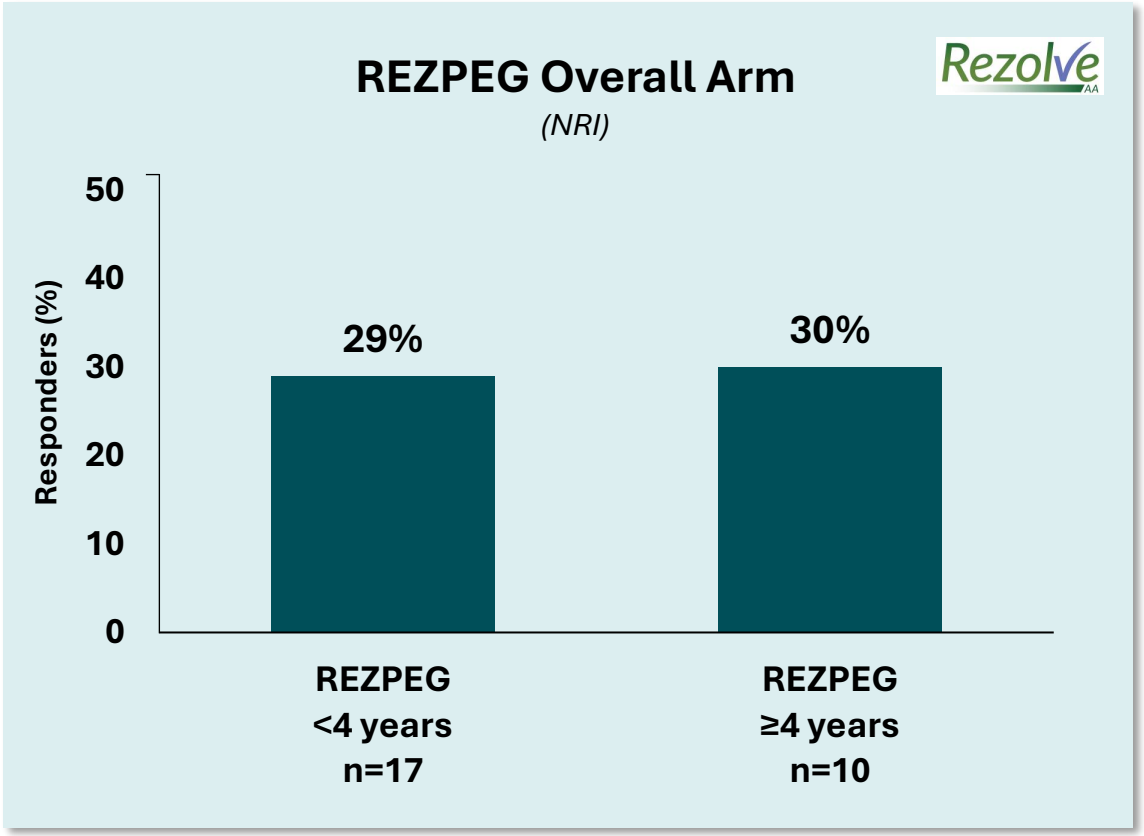
- Clinically meaningful hair growth with REZPEG was observed irrespective of duration of episode
- Current episode duration is an important prognostic factor in alopecia areata
- Patients with 4 years or greater current episode represent approximately one third of population and are more difficult to treat
- 37% of REZPEG-treated patients in REZOLVE-AA had a current continuous episode of 4 years or greater

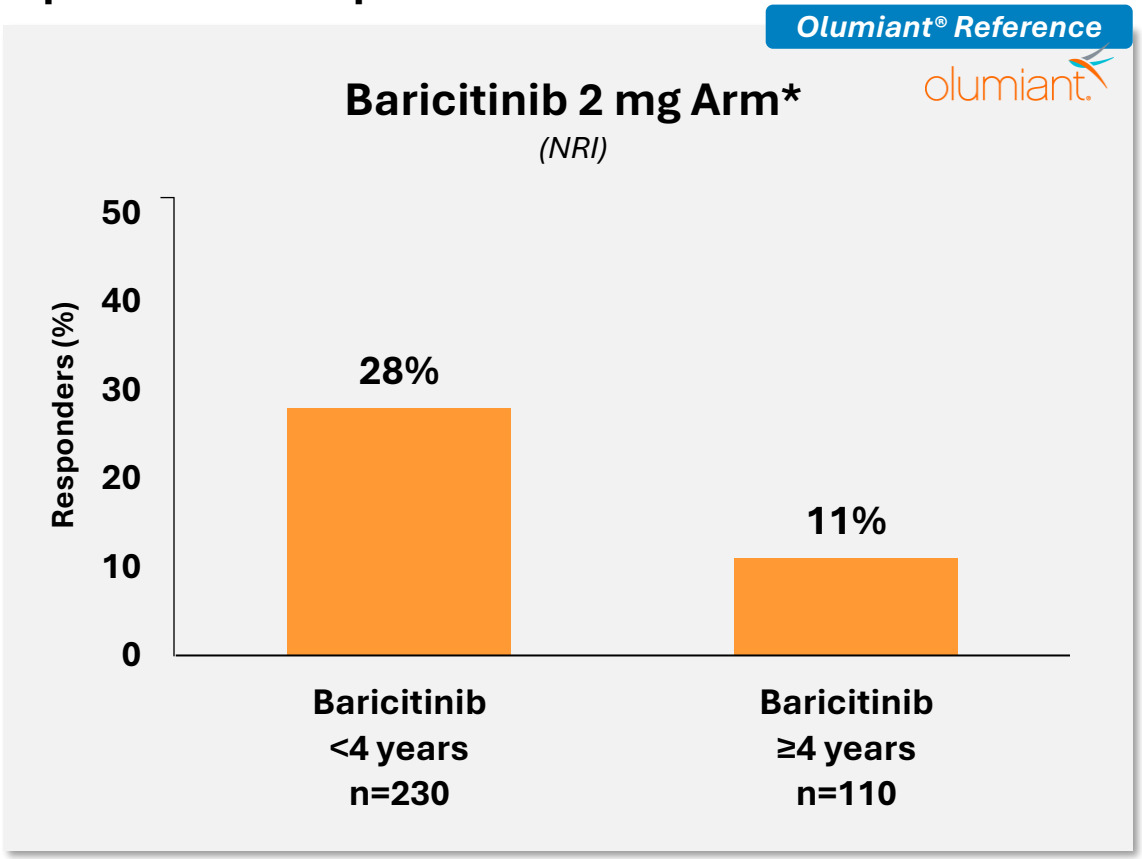
(n=xx) is the denominator which equals the number of patients who entered extension

Non-responder imputation (NRI): missing data are treated as non-responders

SALT Score ≤20 Response Rates in Patients with Current Alopecia Areata Episode < 4 years vs ≥ 4 years

SALT Score ≤20 Response Rates at Week 52 by Duration of Current Alopecia Areata Episode





(n=xx) is the denominator which equals the number of patients who entered extension

Olumiant® is a registered trademark owned or licensed by Eli Lilly and Company, its subsidiaries, or affiliates. *Baricitinib SALT≤20 response rates for baricitinib are estimated from Table 1 in Senna et al. (2023)
Non-responder imputation (NRI): missing data are treated as non-responders

Phase 2b REZOLVE-AA Study Evaluating REZPEG for Alopecia Areata

Severe-to-Very-Severe Alopecia Areata (NCT06340360) - Granted Fast Track Designation in July 2025

Key Eligibility Criteria

- Adult patients (18+)
- Severe-to-very-severe AA
- SALT ≥50
- >6 months since diagnosis to exclude unstable AA
- No spontaneous improvement over the past 6 months
- Maximum episode duration of 8 years
- 8-week washout of prior medication for AA

Stratification by baseline SALT Score ≥50 to <95 vs ≥95 to 100

Induction Q2W (Weeks 0-36)

3:3:2 N=92

- **REZPEG 24 µg/kg n=35**
- **REZPEG 18 µg/kg n=37**
- **Placebo n=20**

Extension (Weeks 36-52) /Off treatment Follow-up (24 Weeks After Last Dose)

Blinded treatment extension out to 52 weeks total treatment for patients with a SALT score greater than 20 at Week 36 who also demonstrated hair growth n=31

24-week off-treatment follow-up period after 36 or 52 weeks of treatment

Inclusion of placebo group ensures blinding is maintained

Primary:
- Mean % SALT reduction at Week 36

Key Secondaries:
- Absolute SALT Score ≤20
- Safety

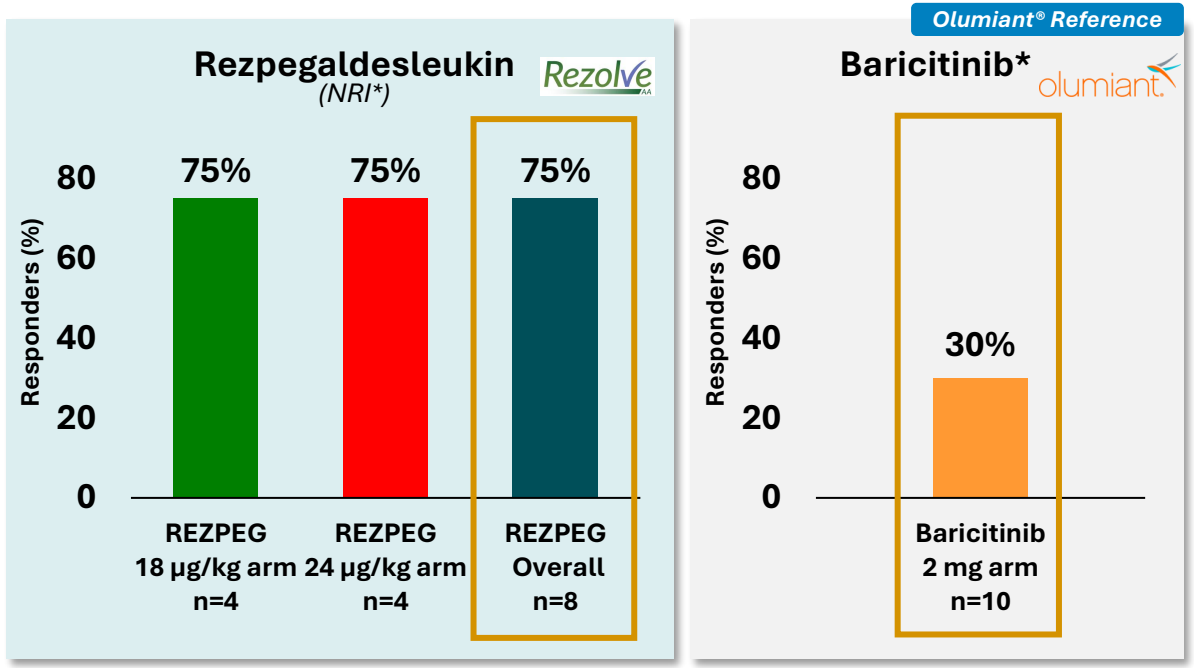
Severity of Alopecia Tool (SALT) is a validated endpoint to assess the extent of scalp-hair loss in patients with alopecia areata

Rezolve AA

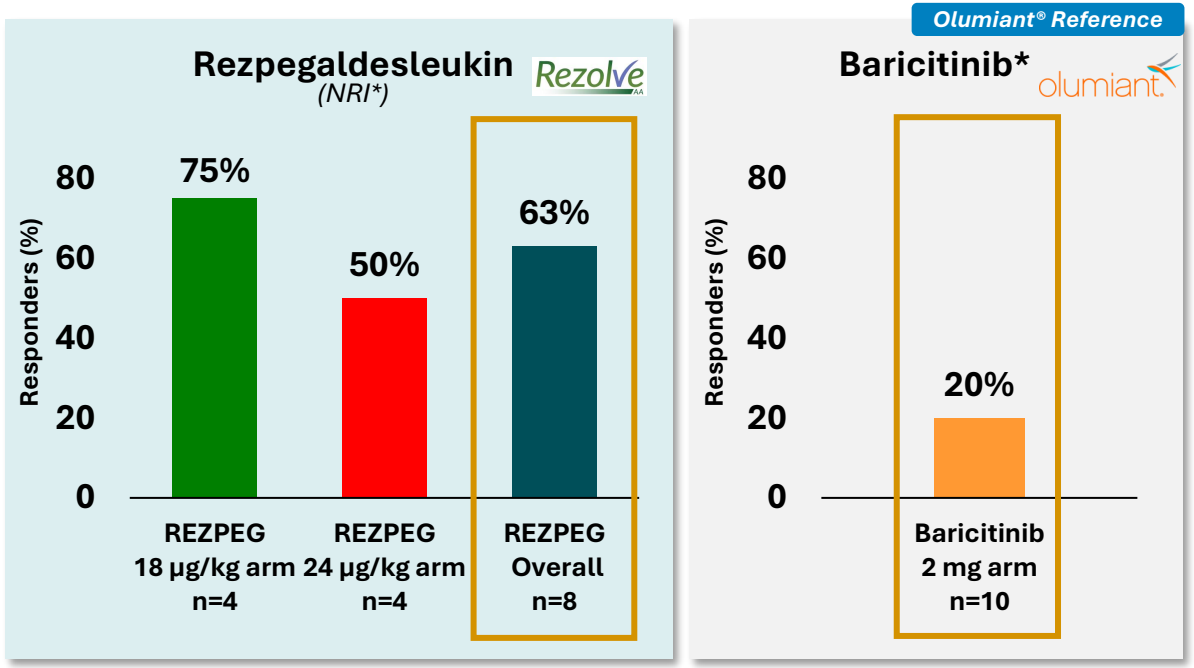
Majority of Patients Treated with REZPEG for 52 Weeks Maintained SALT Score ≤20 at 4 Months and 6 Months Off Treatment

Maintenance of SALT Score ≤20 Among Patients Who Received 52 Weeks of Treatment Prior to Off-Treatment Period

4 Month (16 Weeks) Off Treatment



6 Month (24 Weeks) Off Treatment



(n=x) is the denominator which equals the number of SALT Score ≤20 responders at Week 52 among patients who entered extension

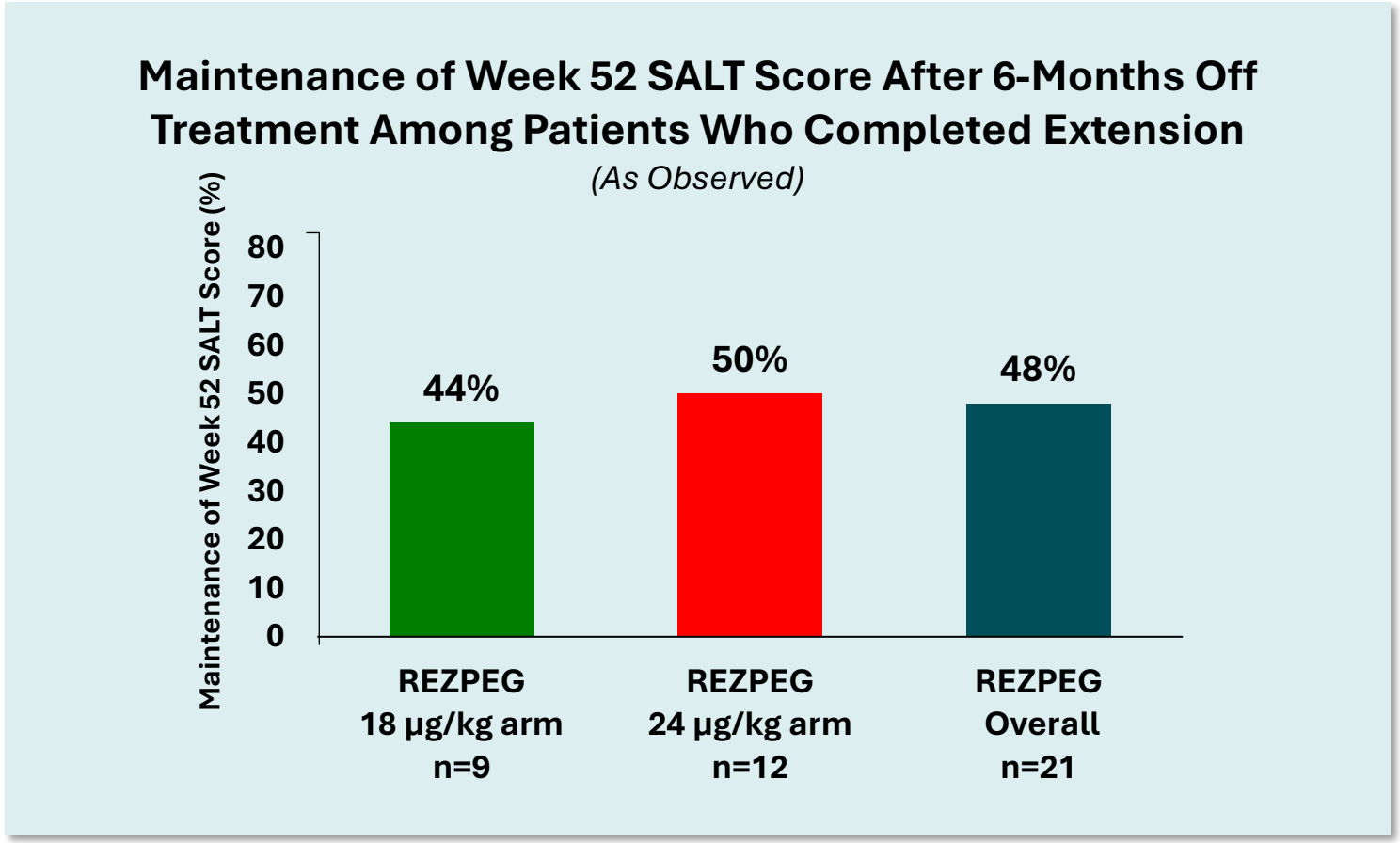
*Analysis based upon non-responder imputation (NRI): all patients were available for off-treatment assessments; as a result, NRI analysis is identical to an as observed analysis for this patient cohort.

- For patients who received 36 weeks of treatment with REZPEG, 67% (4/6) or 40% (4/10) maintained SALT Score ≤20 at 4 months off treatment and 17% (1/6) or 10% (1/10) maintained SALT Score ≤20 at 6 months off treatment (as observed and NRI, respectively)

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Data for rezpegaldesleukin are Non-responder imputation (NRI) analyses: missing data are treated as non-responders; Data for baricitinib are last observation carried forward (LOCF) analysis

For Patients Who Completed 6 Months Off Treatment, Nearly Half of Patients Maintained Hair Regrowth at 6 Months

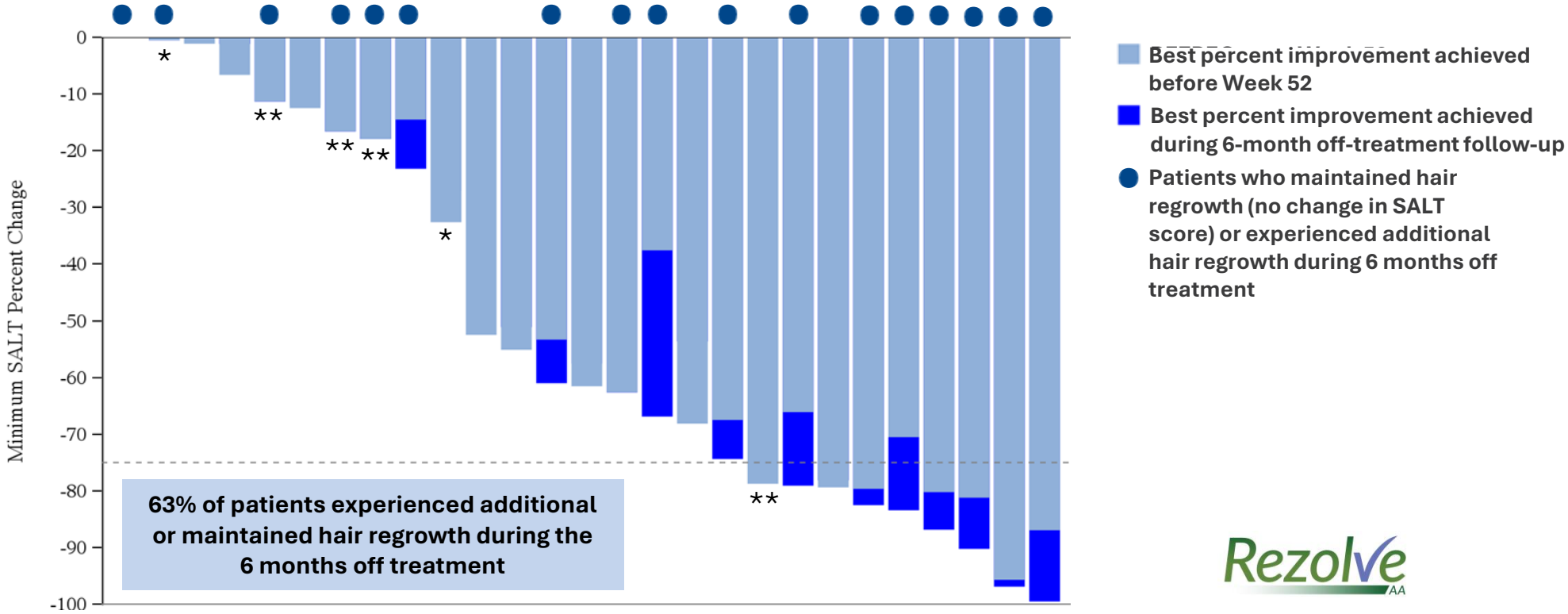


- Consistent durability observed across both REZPEG dose groups
- Maintenance of response defined as having no worsening of SALT score from the end of treatment through 6 months off treatment
- Results suggest REZPEG may alter the underlying disease process over time

n=xx is the denominator which equals number of patients with observed data at 6 month follow-up among patients who completed 52 weeks of treatment

During the 6 Month Off-Treatment Period, 41% of Patients Achieved Deeper Responses and an Additional 22% Maintained Hair Regrowth

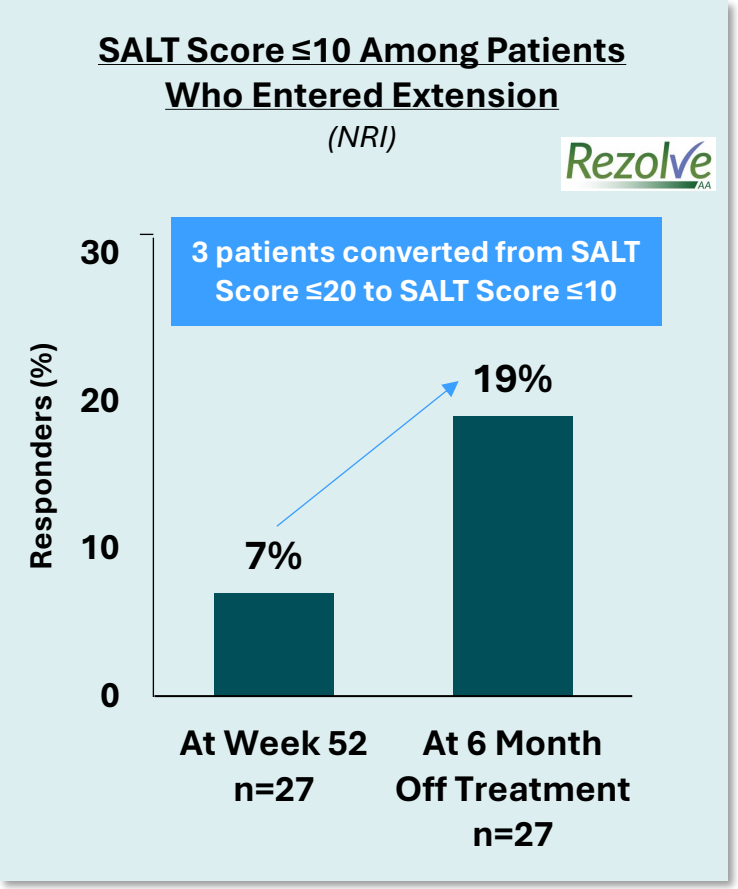
Best Percent Improvement in SALT Score from Baseline in the 52-Week Treatment Cohort (N=27)



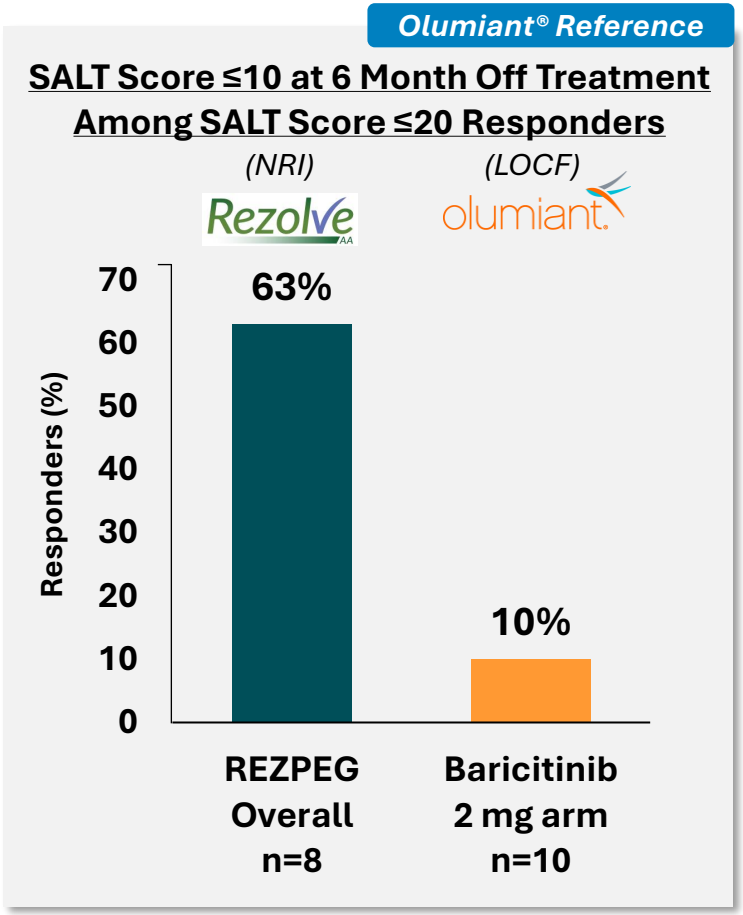
Over the On and Off Treatment Periods, 33% (9/27) Achieved ≥75% Reduction from Baseline SALT

**discontinued treatment before week 52 and were followed up to 6 months post treatment; **discontinued in the 6-month off-treatment follow-up; best response during follow-up shown*

Proportion of Patients Who Achieved SALT Score ≤10 Doubled in the 6 Months Off Treatment



(n=xx) is the denominator which equals the number of patients who entered extension



(n=xx) is the denominator which equals the number of SALT Score ≤20 responders at Week 52 among patients who entered extension

- The proportion of patients achieving near-complete scalp hair regrowth (SALT ≤10) doubled during the 6-month off-treatment period.
- Clinical responses continued to deepen after treatment discontinuation, demonstrating durable biological activity.
- One patient reached SALT Score 0 during 6 month off treatment
- Findings suggest continued hair regrowth beyond the active treatment period, supporting a Treg-mediated mechanism that could address the underlying immune dysregulation driving disease.

Olumiant® is a registered trademark owned or licensed by Eli Lilly and Company, its subsidiaries, or affiliates. 6-month off-treatment data is estimated based on Figure S1 in King et al. JAMA Dermatology (2024)

Data for rezpegaldesleukin are Non-responder imputation (NRI) analyses: missing data are treated as non-responders; Data for baricitinib are last observation carried forward (LOCF) analysis

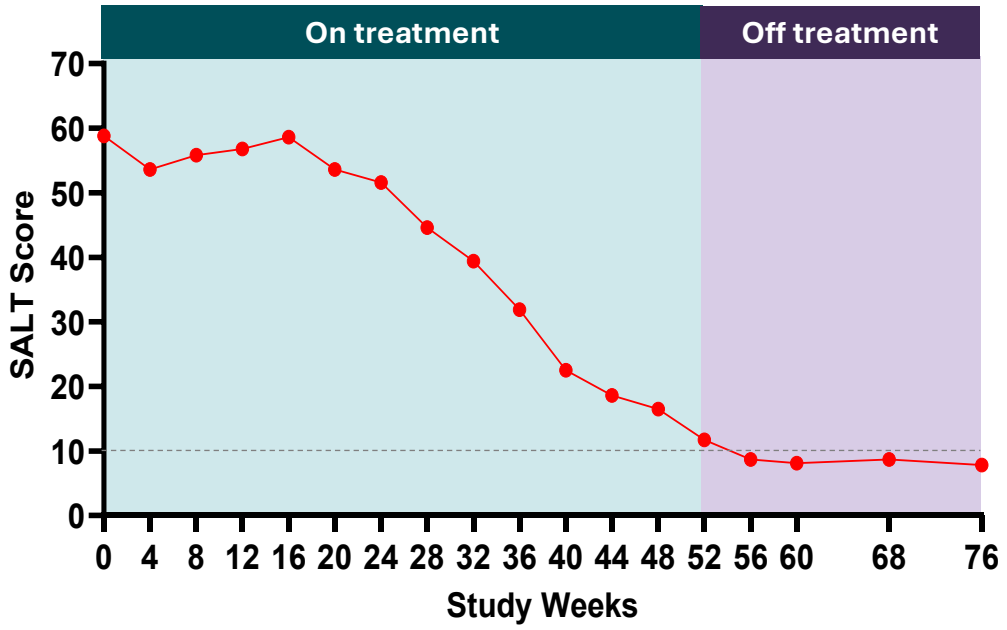
This is a cross-trial comparison and includes data from different clinical studies and is not a head-to-head comparison.

REZOLVE-AA: Safety Profile in Alopecia Areata at 52 Weeks Consistent With Previously Reported Studies

- No new safety findings observed with longer Q2W dosing out to 52 weeks
- Nearly all AEs were mild to moderate in severity and self-resolved
- No patients discontinued during 16-week extension due to an adverse event
  - Discontinuation rate due to AEs over 52 weeks of treatment was low (1.4%) for all REZPEG-exposed patients
- No patients discontinued treatment due to an ISR over 52 weeks of treatment
  - Lower frequency of ISRs observed over longer dosing duration in extension
  - Majority of ISRs were mild to moderate (erythema) and self-resolved within 5 days
- No observed increased risk or safety signal for: oral herpes, conjunctivitis, facial swelling or erythema, oral (aphthous) ulcers, myocardial infarction, pulmonary embolus, deep venous thrombosis and malignancy
- No AEs observed that could require JAKi-like laboratory testing and monitoring

Deepening of Response from SALT Score ≤20 after One Year of Treatment to a SALT Score ≤10 Off Treatment

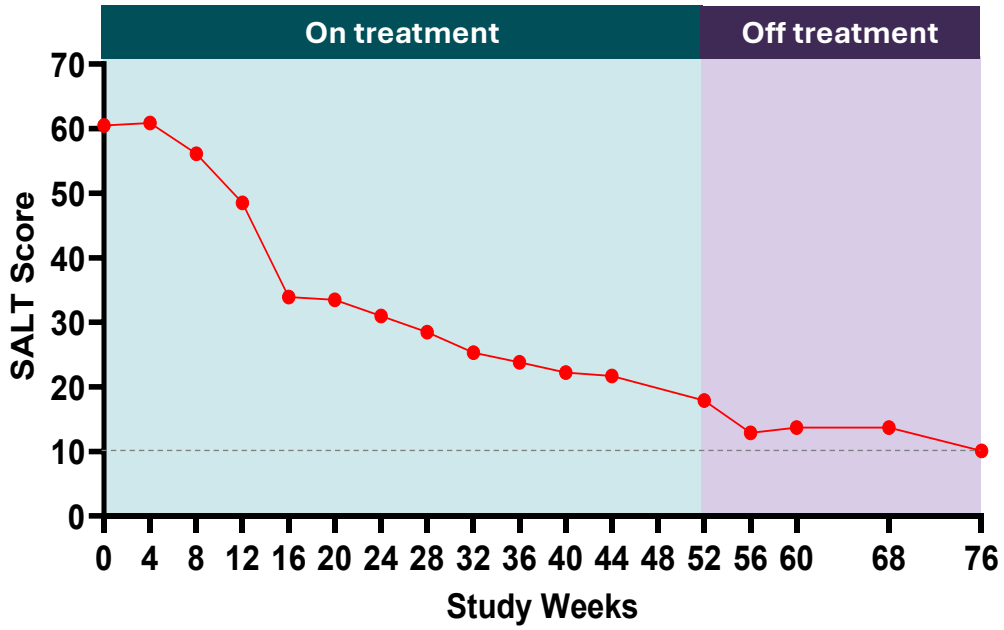
- 40-year-old white male
- Diagnosis 8 months prior to treatment
- 52 weeks of 24 µg/kg REZPEG treatment





Deepening of Response from SALT Score ≤20 after One Year of Treatment to a SALT Score ≤10 Off Treatment

- 64-year-old white female
- Diagnosed 13 years prior to treatment
- 52 weeks of 24 µg/kg REZPEG treatment





Rezpegaldesleukin in Severe-to-Very-Severe Alopecia Areata Patients

Key Takeaways from the Phase 2b REZOLVE-AA Study

52-Week Treatment Data:

- Q2W dosing of REZPEG demonstrates clear and consistent separation from placebo on all measures of efficacy
- Similar SALT Score ≤20 in the subgroup of patients with current AA episode < vs ≥4 years after 52 weeks of treatment
  - Patients with current AA episode <4 years: 29% and patients with current AA episode ≥4 years: 30%
- Safety profile consistent with prior studies and highly differentiated from previously reported data on JAKi

Six Months Off-Treatment Data:

- Six months off-treatment data demonstrate durability of hair regrowth after REZPEG twice monthly dosing for one year
- Robust off drug durability of SALT Score ≤20 after 52 weeks of treatment
  - SALT Score ≤20 response is maintained at 6 months off treatment in 63%
- SALT Score ≤10 deepened from 7% at Week 52 to 19% at six month off-treatment follow-up
- Based on maintenance of SALT Score ≤20 response, REZPEG demonstrates superior off-treatment durability versus historical low-dose JAK inhibitor data following 52 weeks of treatment
- Data support evaluation of Q4W or Q12W dosing after 52 weeks of Q2W dosing in patients who achieved SALT Score ≤20

Phase 3 ZENITH AA trial in 850 patients to initiate in December

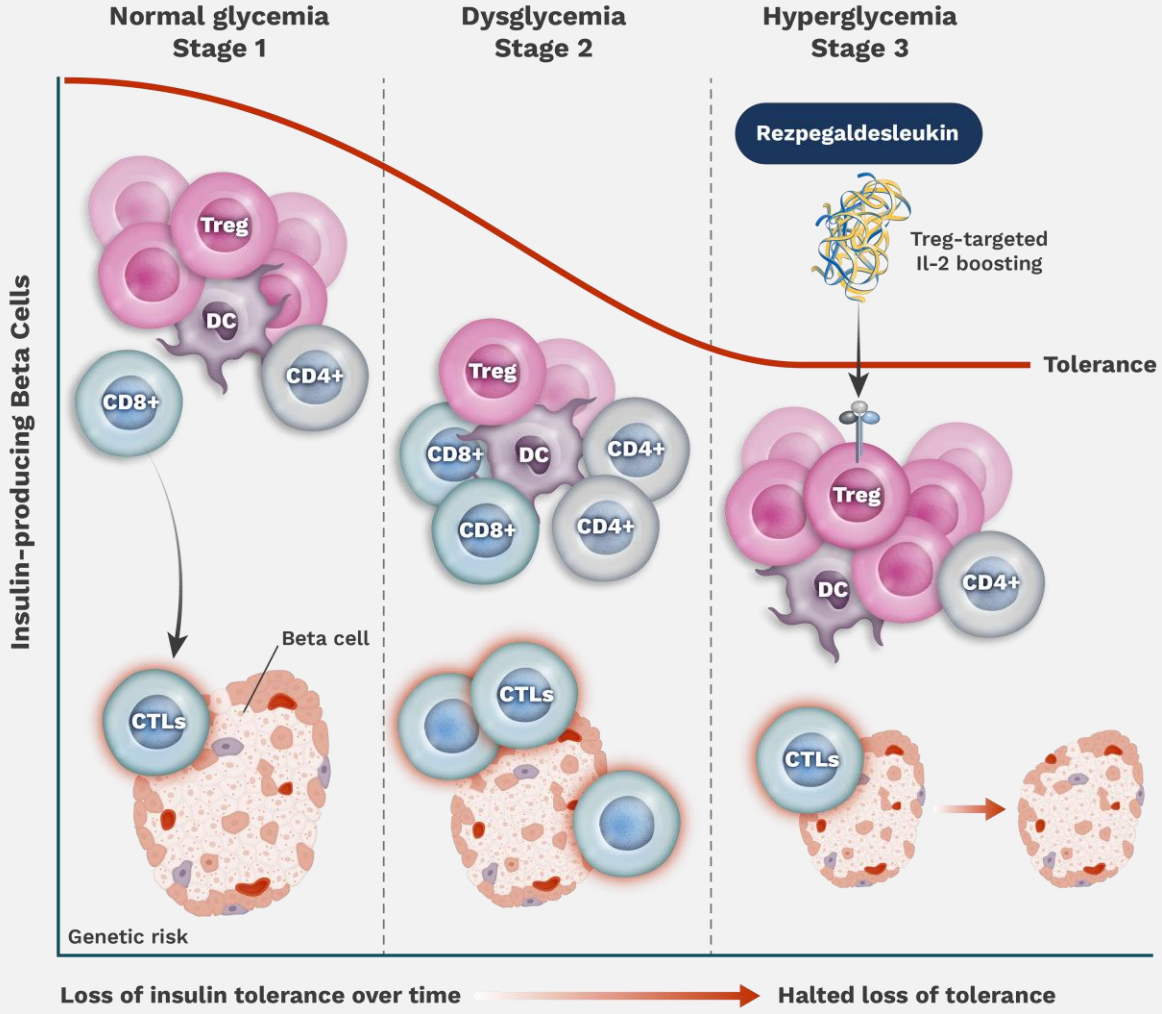


Rezpegaldesleukin in Type 1 Diabetes

Rezpegaldesleukin
Type 1 Diabetes MOA

Scientific rationale

- By targeting receptors on regulatory T cells, rezpegaldesleukin stimulates the proliferation of regulatory T cells (Tregs), including FOX-P3+ Tregs
- In Type 1 diabetes, the destruction of insulin-producing pancreatic beta cells is caused by T cells of the immune system
- Regulatory T cells act upstream of these T cell and pro-inflammatory cytokines to reduce their activity; by increasing the number and functionality of regulatory T cells, this investigational therapy aims to slow the progression of new onset Type 1 diabetes.



Proposed study design

Type 1 Diabetes (Stage 3)

Type 1 Diabetes TrialNet

Eligibility

Key Inclusion:

- ✓ Ages starting at minimum of 18 and then decreasing to 12 and then 8 pending data review
- ✓ New onset T1D within 100 days
- ✓ Positive for ≥1 autoantibody (+AAB)
- ✓ Peak C-peptide >0.2pmol/mL

Treatment

Randomize (2:1) N=~66

- Rezpegaldesleukin Q2W regimen for 6 months
- Placebo

Patient Enrollment

Part 1 Cohort: 18 Adult Subjects (18-45 yrs.)

Complete remaining 48 subjects in adults if data not supportive of 12 yrs. and up

Safety Review at 6 months (DSMB/FDA)

Part 2 Cohort: 17 Pediatric & Adult Subjects (12-45 yrs.)

Complete remaining 31 subjects in pediatric and adults if data not supportive of 8 yrs. of and up

Safety Review at 6 months (DSMB/FDA)

Part 3 Cohort: 31 Pediatric & Adult Subjects (8-45 yrs.)

Outcome Measures

ENDPOINTS:

Primary:
C-peptide response to Mixed Meal Tolerance Test (MMTT) compared to placebo at 12 months

Secondary/Exploratory:

- Comparisons of MMTT-stimulated C-peptide and glucose AUCs at 3 and 6 months to placebo
- Comparisons of MMTT-stimulated C-peptide at 3, 6, and 12 months to historical model-adjusted placebo controls
- Glucose monitoring data and hypoglycemia events
- Adverse Events

Additional Assessments:

- Metabolic Assessments (HbA1c, insulin usage, etc.)
- Immunologic Assessments

Ongoing Phase 2 Study Sponsored and Funded by TrialNet (NIH/NIDDK) Type 1 Diabetes Consortium

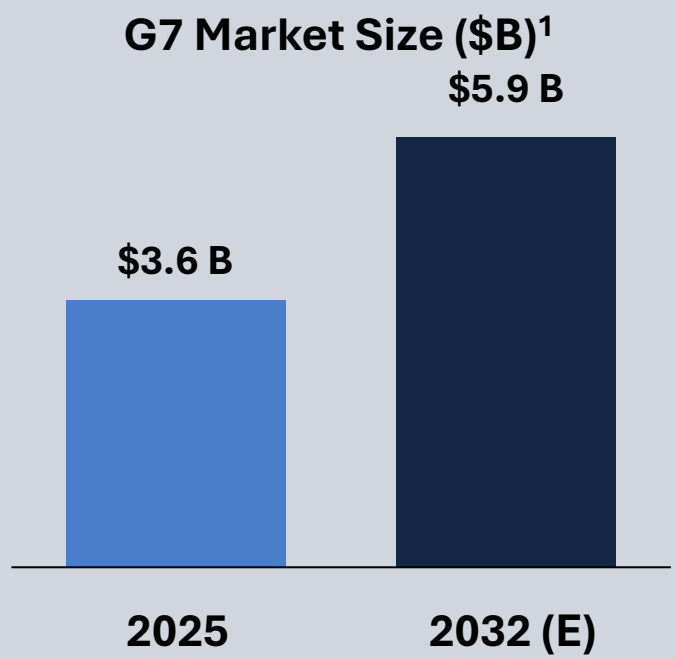
About the Study:

- Ongoing phase 2 placebo-controlled clinical trial in approximately 66 adults and children with new onset stage 3 T1D
- Evaluating REZPEG's Treg MoA for preservation of beta cell function in Stage 3 New Onset T1D
- Data from first cohort expected in 2027

Scientific Rationale

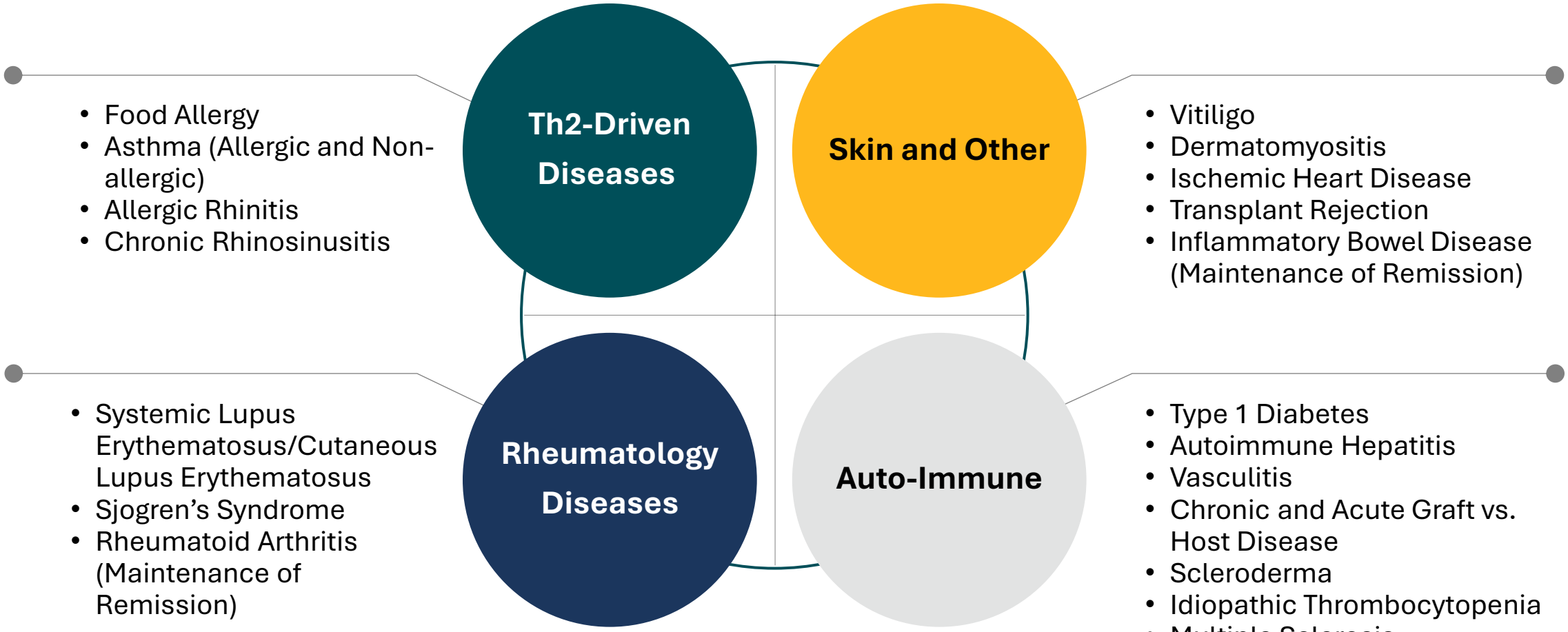
- ✔ In T1D, the destruction of insulin-producing pancreatic beta cells is caused by T cells of the immune system
- ✔ Regulatory T cells (Tregs) act upstream of these T cell and pro-inflammatory cytokines to reduce their activity; by increasing the number and functionality of regulatory T cells, this investigational therapy aims to slow the progression of new onset T1D.

Commercial Opportunity for Type 1 Diabetes



Sources: 1. Evaluate Pharma WW Market Size Estimates
(E): Estimate

Expanding Potential Opportunities for Rezpegaldesleukin (Treg MOA Activity)



- Food Allergy
- Asthma (Allergic and Non-allergic)
- Allergic Rhinitis
- Chronic Rhinosinusitis

- Vitiligo
- Dermatomyositis
- Ischemic Heart Disease
- Transplant Rejection
- Inflammatory Bowel Disease (Maintenance of Remission)

- Systemic Lupus Erythematosus/Cutaneous Lupus Erythematosus
- Sjogren's Syndrome
- Rheumatoid Arthritis (Maintenance of Remission)

- Type 1 Diabetes
- Autoimmune Hepatitis
- Vasculitis
- Chronic and Acute Graft vs. Host Disease
- Scleroderma
- Idiopathic Thrombocytopenia
- Multiple Sclerosis
- Amyotrophic Lateral Sclerosis

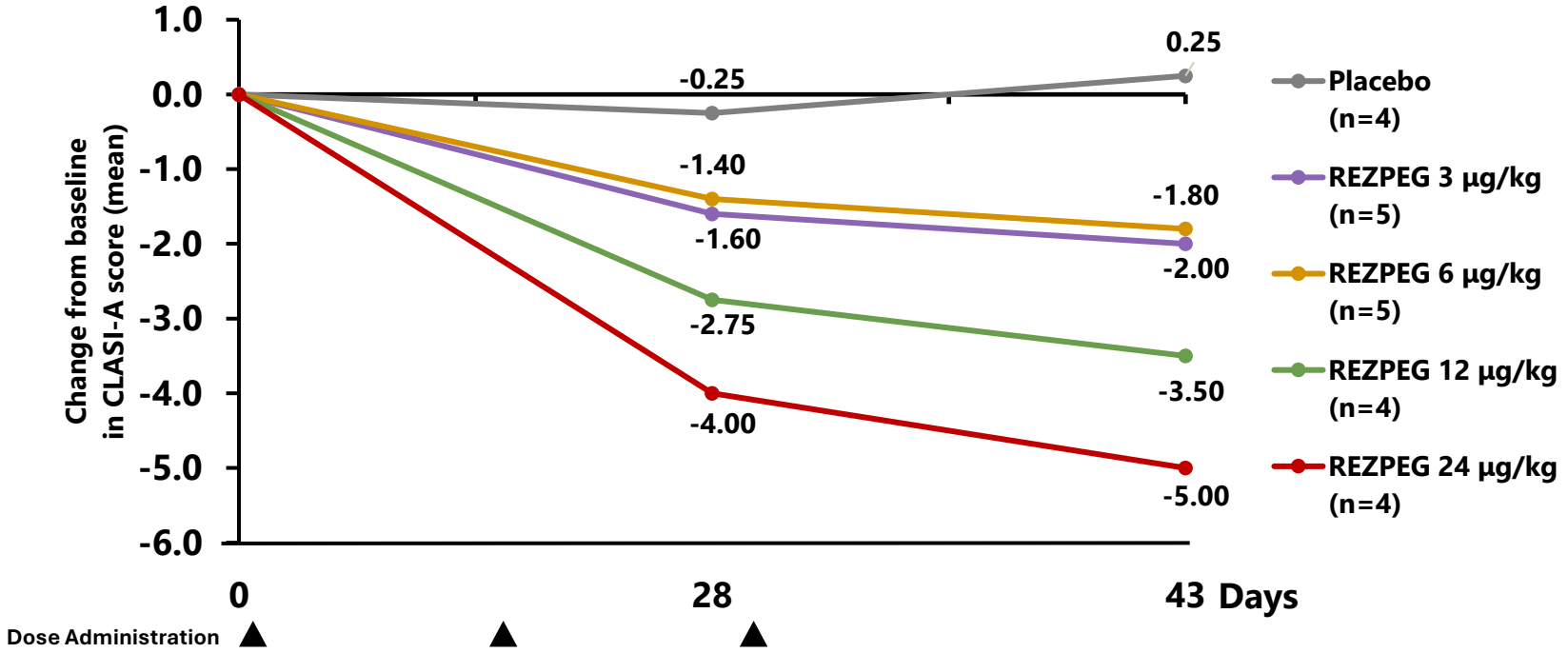
Anticipated Next Steps in Alopecia Areata and for Rezpegaldesleukin

Atopic Dermatitis	• Additional data readout from REZOLVE-AD Study: 52-week off treatment data in Q1 2027 • Topline data from ZENITH AD Phase 3 program in 2028
Alopecia Areata	• Initiation of a single trial Phase 3 ZENITH AA program in patients with severe-to-very-severe alopecia areata in December • Initiation of investigator-sponsored study at Mount Sinai which will include moderate alopecia areata patients
Type 1 Diabetes	• Data from the first cohort of patients in Phase 2 Type 1 diabetes trial in 2027
Other Indications	• Initiation of proof-of-concept study in vitiligo for rezpegaldesleukin with initial data coming in late 2027 or early 2028

Opportunity in Cutaneous Lupus Erythematosus

Rezpegaldesleukin Demonstrated a Dose-Dependent Reduction in CLASI-A Score in Patients with Lupus

Patients with Systemic Lupus Erythematosus and Cutaneous Involvement
Mean Change in CLASI-A Score from Phase 1 Study
Patients with a CLASI-A score of ≥4 at baseline (N=22)



Source: 1. Fanton et al., Journal of Translational Autoimmunity 2022
CLASI-A, cutaneous lupus erythematosus disease area and severity index–activity; SLE: systemic lupus erythematosus



NKTR-0165

TNFR2 Agonist Antibody

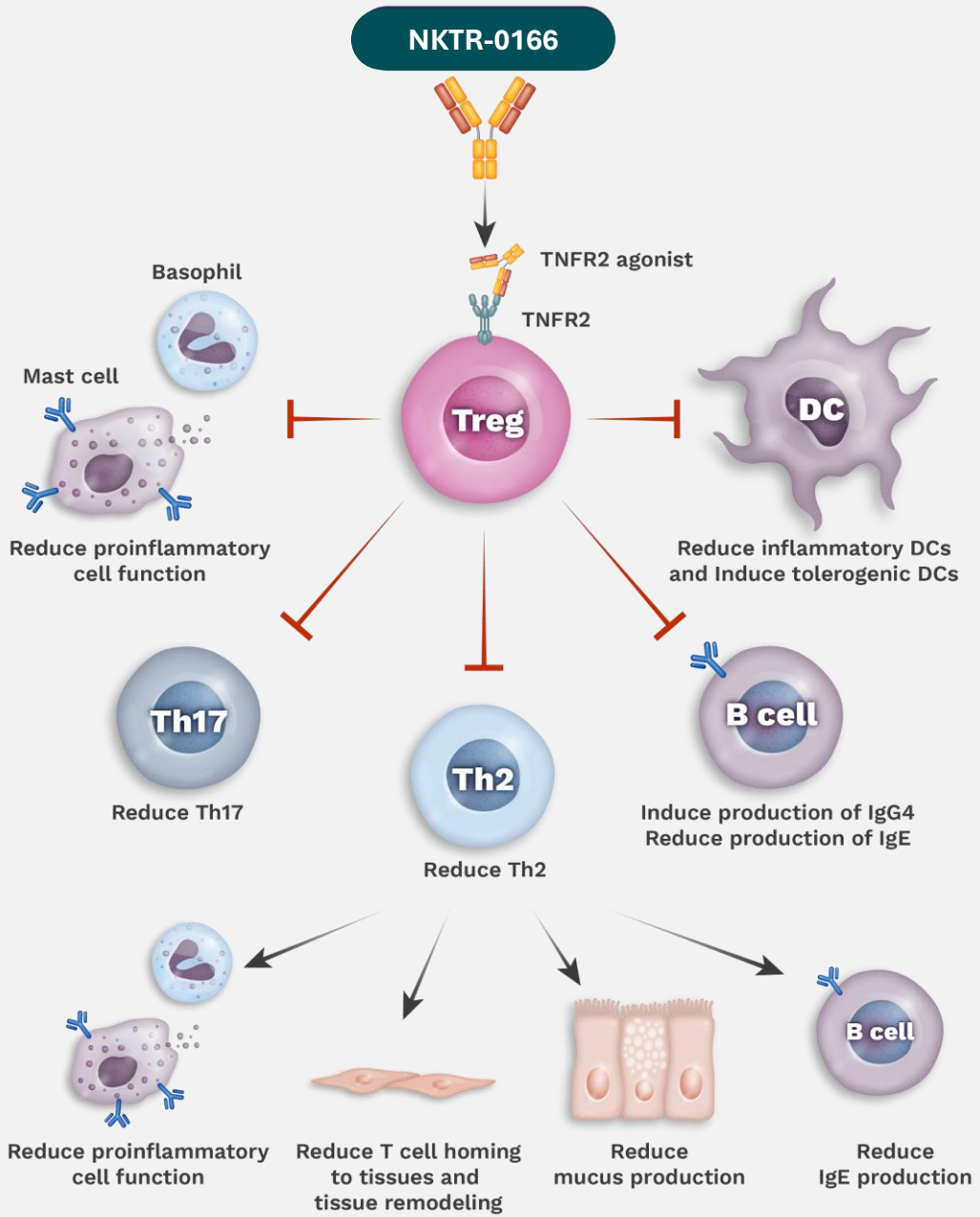
TNFR2 Agonist Bivalent Antibody

Scientific rationale

- By targeting TNFR2, a co-stimulatory receptor preferentially expressed on the surface of highly suppressive tissue-specific regulatory T cells, B-regulatory cells, neuronal cells and endothelial cells, NKTR-0165 has been shown to promote the activation, function, proliferation, and phenotypic stability of these cells

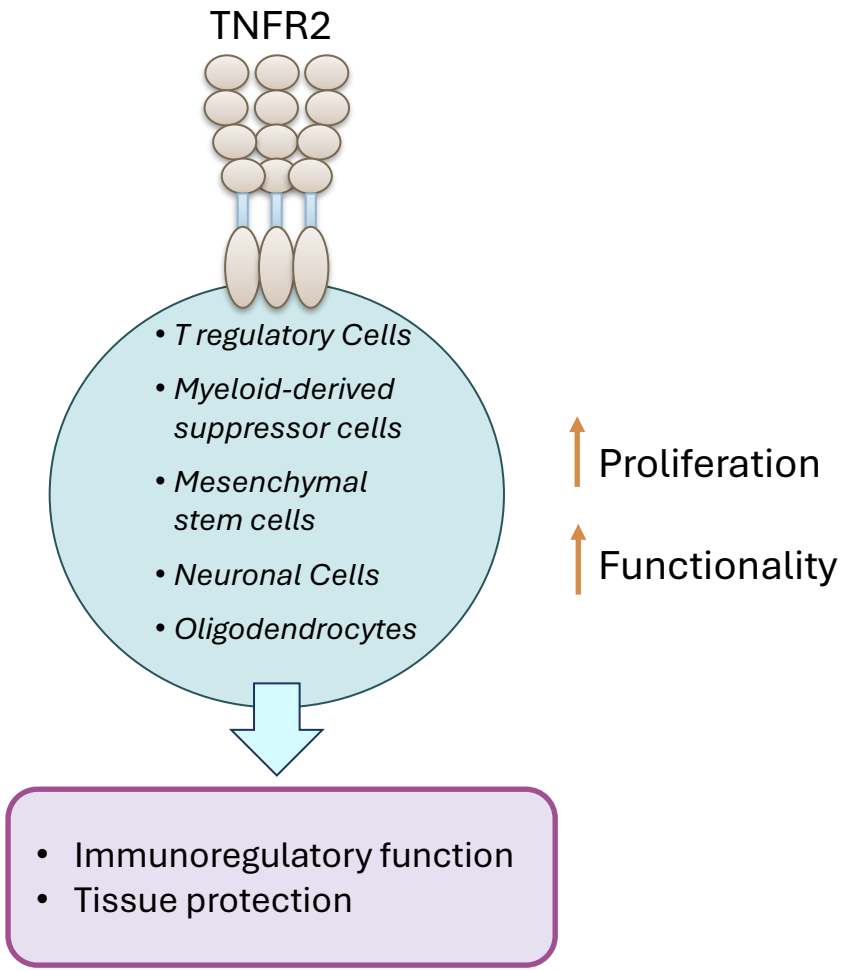
- TNFR2 signaling is an important gatekeeper of inflammation and its absence or deficit is associated with a broad range of autoimmune diseases

- As a monomeric bivalent antibody with a unique epitope, NKTR-0165 selectively stimulates TNFR2 receptor activity, without modulation of TNFR1 signaling; this novel first-in-class compound has the potential to modulate acute exacerbations and chronic trajectory of a number of autoimmune diseases



NKTR-0166: TNFR2 agonist antibody program

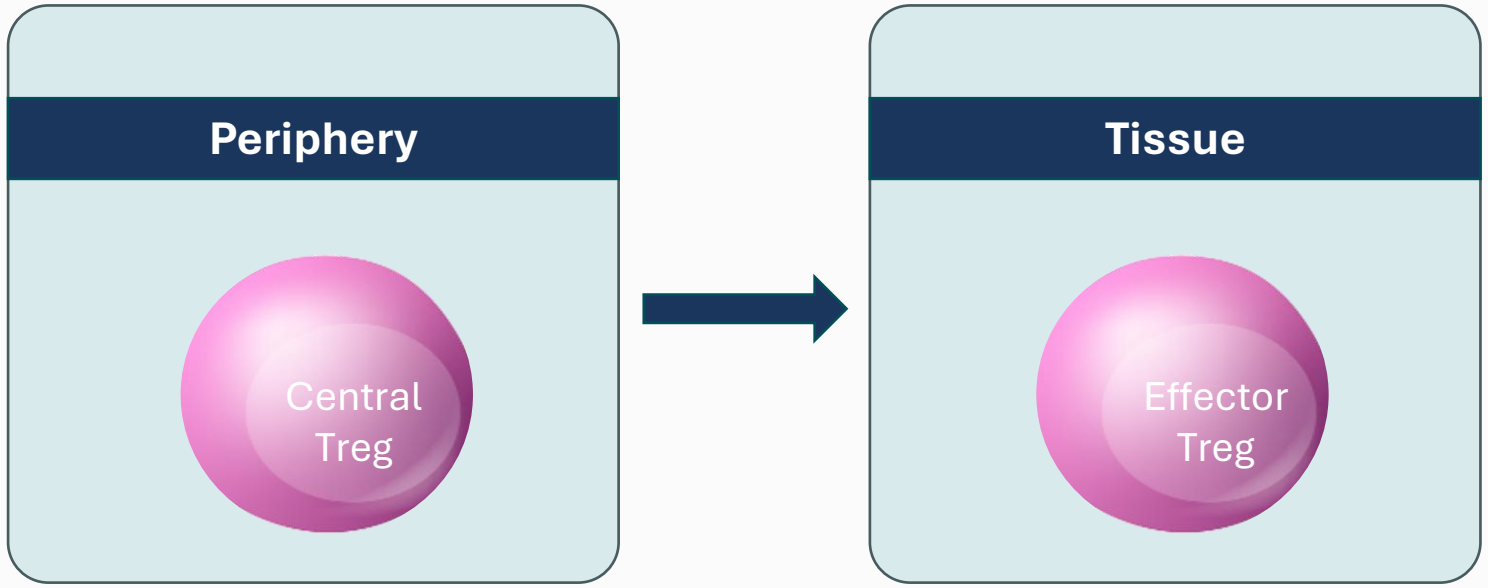
Targeting TNF Receptor 2 (TNFR2) for the treatment of autoimmune conditions



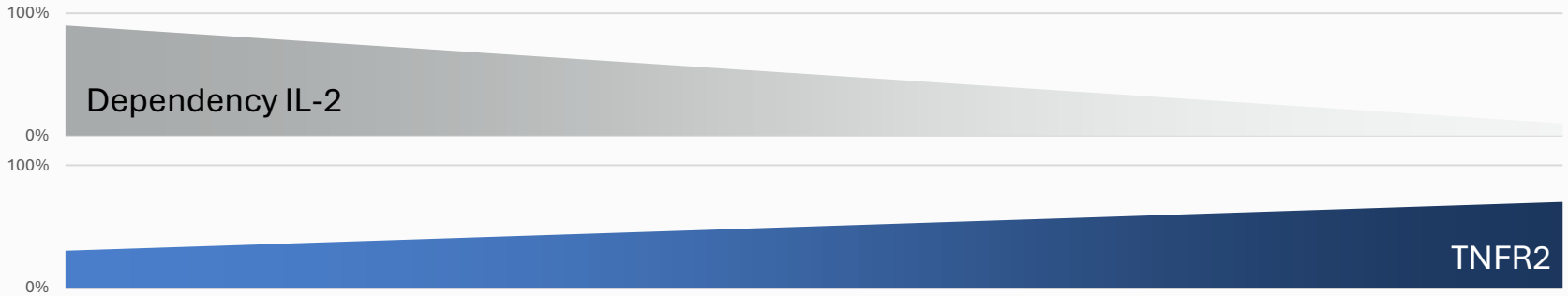
- TNFR2 signaling drives immunoregulatory function could provide direct protective effect for tissue cells
- Unique Nektar antibody candidates show selective T regulatory cell binding and signaling profiles enabling it to be developed for the treatment of autoimmune conditions
- Program targets multiple MOAs including suppression of inflammation, regrowth of myelin after demyelination (MS) and promotion of immune resolution.

TNFR2/NF-kB Axis is critical to maintain effector and tissue regulatory T cells

Rezpegaldesleukin (IL-2 T Regulatory Cell Stimulator)



NKTR-0166 (Bispecific Antibody Incorporating TNFR Agonist)



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