Phase 2b Trial Results of Rezpegaldesleukin: A Novel Treg Inducing Biologic for Atopic Dermatitis

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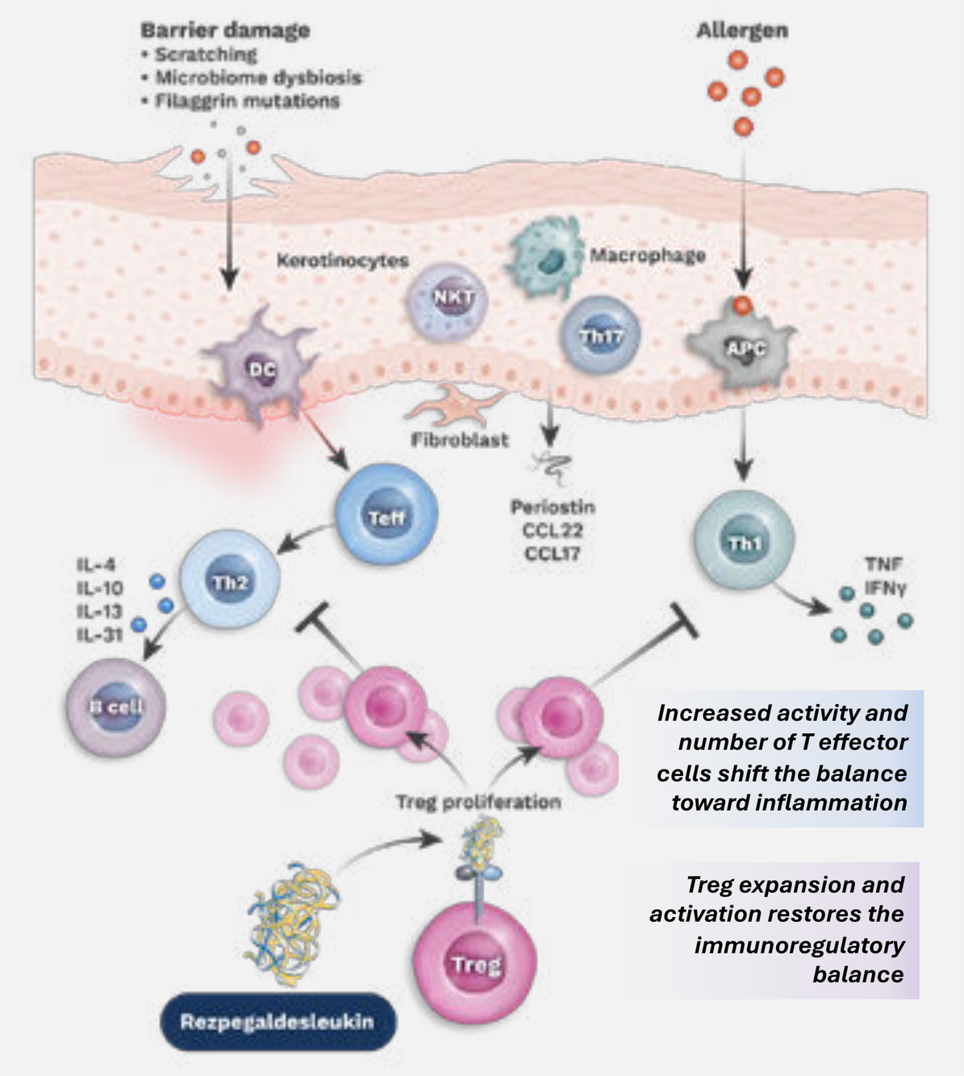
SYNOPSIS

Rezpegaldesleukin (rezpeg) is a Potential First-in-Class Regulatory T Cell (Treg) Inducing Mechanism to Restore Balance in the Immune System

- **Atopic dermatitis (AD) is driven by imbalance in heterogeneous inflammatory T cell subsets,** including T effector cells, that drive inflammation and disease pathology in the skin
- **Tregs play a central role in controlling AD** by dampening inflammatory cytokines and overactive T cells[1]
- **Rezpegaldesleukin** is a potential T cell balancing therapy that acts on Interleukin-2 (IL-2) receptors and has been shown to[2,3]:
  - **Proliferate** Tregs
  - **Restore** their functionality, reducing proinflammatory cytokines
  - **Offer potential long-term control** of overactive immune responses
- **Rezpegaldesleukin was 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



OBJECTIVE

Evaluate the efficacy and safety of rezpegaldesleukin in adult patients with moderate-to-severe atopic dermatitis.

METHODS

Figure 1: Study Design for Rezolve AD - Phase 2b Study Evaluating Rezpegaldesleukin in Patients with Moderate-to-Severe AD

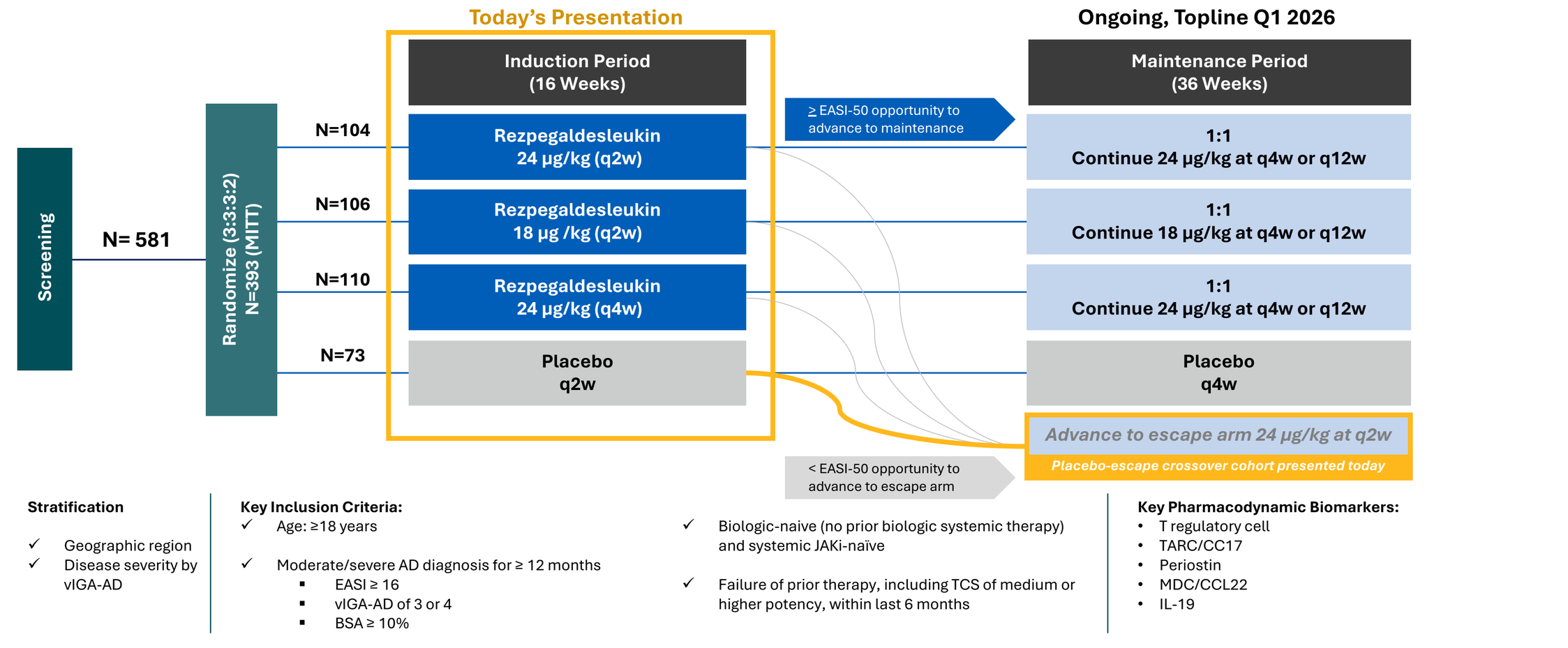


Table 1: Baseline Demographics and Disease Characteristics

	Placebo q2w N = 73	Rezpeg 24 µg/kg q2w N = 104	Rezpeg 18 µg/kg q2w N = 106	Rezpeg 24 µg/kg q4w N = 110
Age, Mean (SD)	37.9 (14.39)	38.0 (13.73)	36.3 (15.41)	36.5 (14.30)
Sex, Female, n (%)	35 (47.9%)	49 (47.1%)	56 (52.8%)	63 (57.3%)
Race, White, n (%)	58 (79.5%)	87 (83.7%)	90 (84.9%)	96 (87.3%)
Region, North America (US/Canada)	21 (28.8%)	27 (26.0%)	29 (27.4%)	31 (28.2%)
vIGA-AD: 4-Severe, n (%)	22 (30.1%)	33 (31.7%)	36 (34.0%)	35 (31.8%)
EASI:				
Mean (SD)	25.2 (8.57)	25.4 (9.14)	27.2 (10.40)	26.1 (10.45)
≥21, n (%)	44 (60.3%)	60 (57.7%)	63 (59.4%)	66 (60.0%)
BSA (%), Mean (SD)	38.2 (19.7)	39.3 (18.8)	40.7 (20.9)	39.6 (20.6)
Itch NRS Score				
Mean (SD)	6.3 (2.2)	6.8 (2.0)	6.7 (1.9)	7.1 (1.8)
≥4, n (%)	63 (86.3%)	95 (91.3%)	92 (86.8%)	102 (92.7%)
Pain NRS Score				
Mean (SD)	5.4 (2.6)	5.9 (2.5)	5.9 (2.5)	6.2 (2.4)
≥4, n (%)	50 (68.5%)	84 (80.8%)	82 (77.4%)	90 (81.8%)
DLQI Score				
Mean (SD)	13.4 (7.1)	14.5 (7.2)	13.8 (7.3)	15.9 (7.1)
≥4, n (%)	65 (89.0%)	100 (96.2%)	102 (96.2%)	107 (97.3%)
ADCT Score				
Mean (SD)	14.5 (5.7)	15.4 (4.9)	15.5 (5.3)	16.3 (5.0)
≥5, n (%)	67 (91.8%)	101 (97.1%)	104 (98.1%)	107 (97.3%)
ADSS Q1 Score				
Mean (SD)	1.8 (1.2)	1.9 (1.1)	2.0 (1.2)	2.1 (1.0)
≥1.25, n (%)	45 (61.6%)	71 (68.3%)	70 (66.0%)	85 (77.3%)

RESULTS

Figure 2: Dose Dependent Improvement in EASI % Change with Clear Separation from Placebo at All Timepoints for Study Treatment Arms

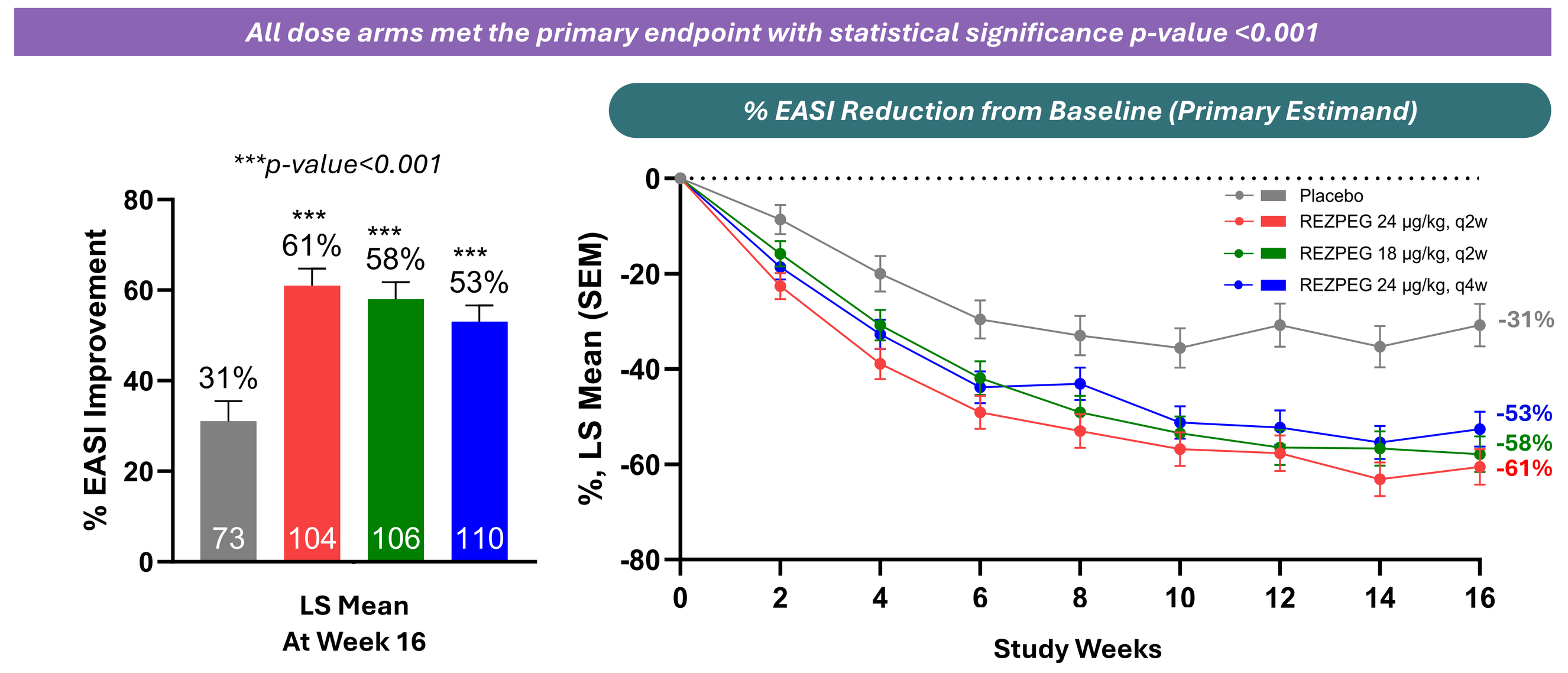
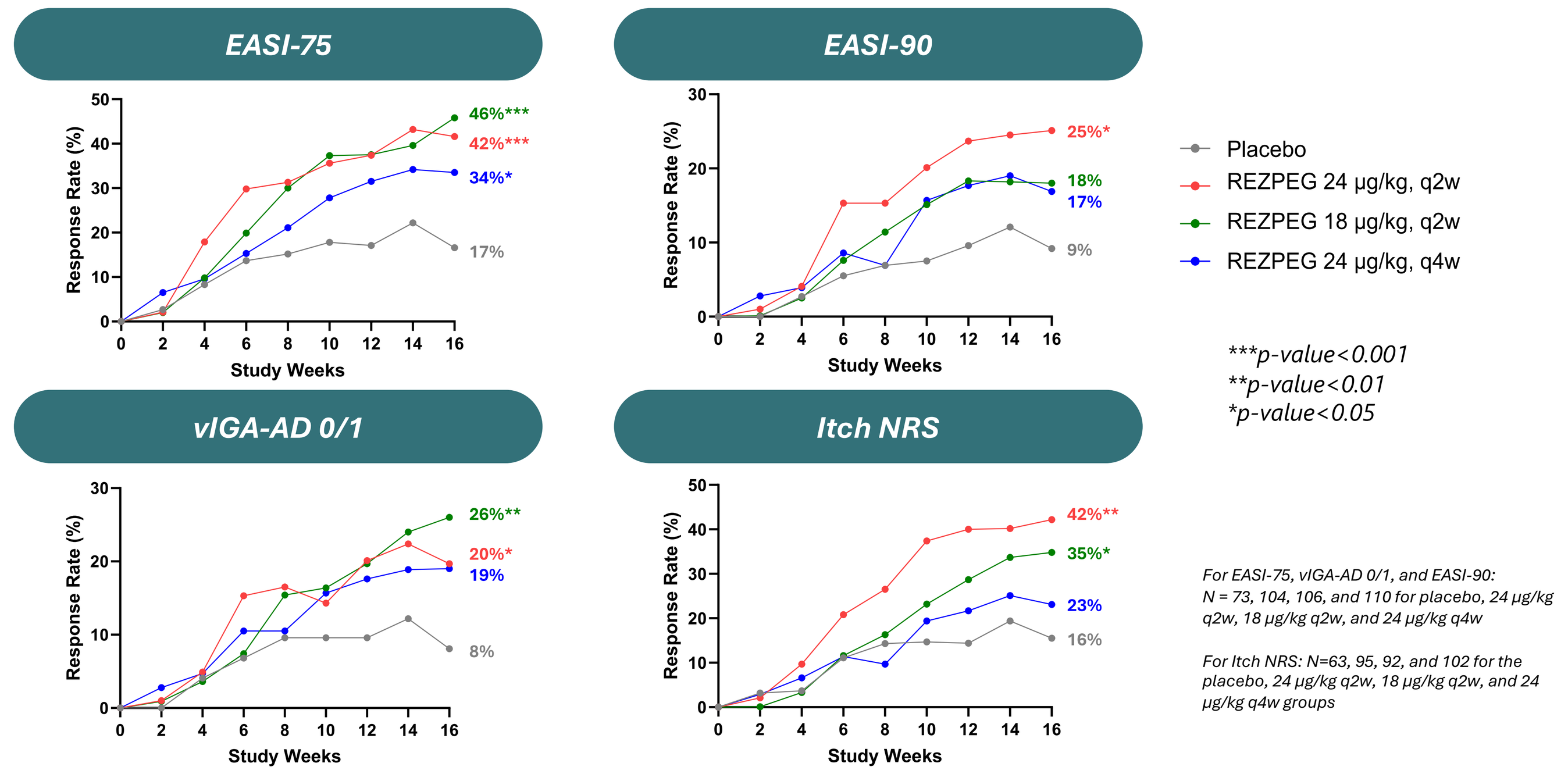


Figure 3: Fast Onset of Action Across All Key Secondary Endpoints



Key Endpoints and Statistical Analysis Methodology

Primary Endpoint:
- Mean % EASI improvement at Week 16

Key Secondary Endpoints at Week 16:
- vIGA-AD of 0 or 1 with ≥ 2-point reduction from baseline (vIGA-AD 0/1)
- EASI-75, -90, -50
- Itch NRS, Pain NRS, DLQI response defined as ≥ 4-point reduction from baseline
- ADCT response defined as ≥ 5-point reduction from baseline
- ADSS Q1 response defined as ≥ 1.25-point reduction in weekly average score from baseline
- Mean % Body Surface Area (BSA) improvement

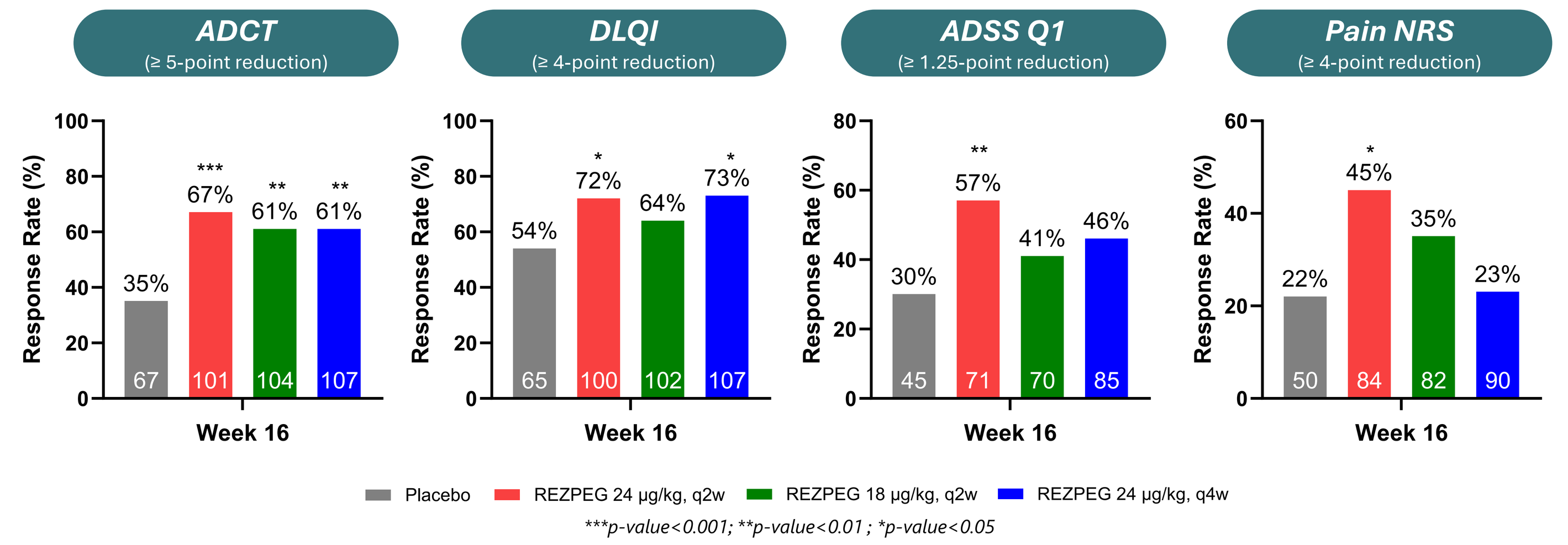
- MITT is defined as patients who were randomized and received at least one dose of study treatment or placebo.
- **Primary Estimand Analysis:** MITT patients who used rescue therapy outside protocol specifications or who discontinued treatment due to lack of efficacy were considered **NONRESPONDERS** (using baseline observation carry forward (BLOCF) for continuous endpoints, and non responder imputation for binary endpoints), regardless of observed clinical response; data after patients who discontinued due to other reasons are set to missing and all missing data are imputed using the multiple imputation method.

As Observed Analysis: Data from patients treated with placebo during Induction that moved to the Open-label Escape arm at Week 16 (REZPEG 24 µg/kg q2w) are summarized using observed data.

Statistical Analysis Methods
- The Primary Estimand analysis for continuous endpoints of % EASI improvement and % BSA improvement use a mixed model for repeated measures (MMRM) to estimate the treatment difference between dose arms and placebo
- The Primary Estimand analysis for binary endpoints (vIGA-AD 0/1, EASI-75, EASI-90, EASI-50, Itch NRS, Pain NRS, DLQI, ADCT, ADSS Q1 response) use a logistic regression model to estimate the treatment difference between dose arms and placebo

Figure 4: High Dose Met All Key Patient-Reported Outcomes at Week 16

Multiple endpoints met for 2 additional dose arms



Sample size for ADCT response is based on patients with baseline ADCT ≥ 5; Sample size for DLQI response is based on patients with baseline DLQI ≥ 4. Sample size for ADSS Q1 response is based on patients with baseline ADSS Q1 ≥ 1.25; Sample size for Pain NRS response is based on patients with baseline Pain NRS ≥ 4.

Table 2: Overall Summary of Treatment Emergent Adverse Events (TEAE)

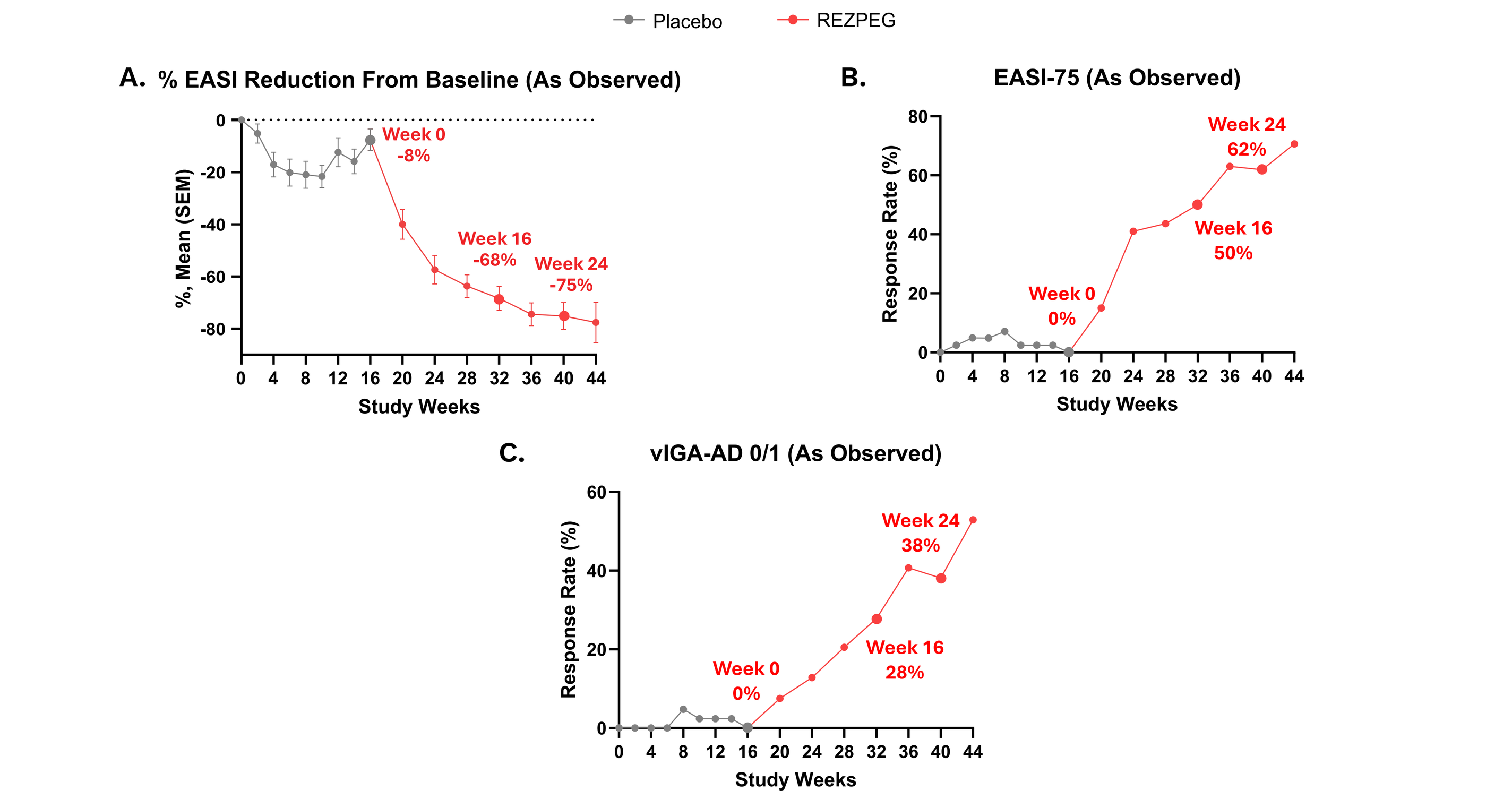
16-Week Induction Period

	Placebo q2w N = 73	Rezpeg 24 µg/kg q2w N = 104	Rezpeg 18 µg/kg q2w N = 106	Rezpeg 24 µg/kg q4w N = 110	Rezpeg Total N = 320
Patients With at Least One TEAE	42 (57.5%)	89 (85.6%)	78 (73.6%)	90 (81.8%)	257 (80.3%)
Patients With at Least One TEAE (Excluding ISRs)	42 (57.5%)	69 (66.3%)	60 (56.6%)	64 (58.2%)	193 (60.3%)
Patients With at Least One Serious TEAE	0	1 (1.0%)	4 (3.8%)	0	5 (1.6%)
Patients With at Least One Severe TEAE	1 (1.4%)	3 (2.9%)	6 (5.7%)	1 (0.9%)	10 (3.1%)
Patients With at Least One TEAE Leading to Death†	0	0	0	0	0
TEAEs by System Organ Class and Preferred Term Over ≥ 5% in Any Arm					
General disorders and administration site conditions	7 (9.6%)	80 (76.9%)	67 (63.2%)	78 (70.9%)	225 (70.3%)
Injection site reaction	3 (4.1%)	79 (76.0%)	66 (62.3%)	78 (70.9%)	223 (69.7%)
Proportion of ISR events-mild (%)	100%	65.5%	70.7%	69.9%	68.3%
Proportion of ISR events-moderate (%)	0%	33.9%	28.9%	30.1%	31.3%
Proportion of ISR events-severe (%)	0%	0.6%	0.4%	0%	0.4%
Pyrexia	2 (2.7%)	11 (10.6%)	5 (4.7%)	4 (3.6%)	20 (6.3%)
Infections and infestations	25 (34.2%)	29 (27.9%)	39 (36.8%)	32 (29.1%)	100 (31.3%)
Nasopharyngitis	10 (13.7%)	10 (9.6%)	14 (13.2%)	14 (12.7%)	38 (11.9%)
Upper respiratory tract infection	4 (5.5%)	7 (6.7%)	8 (7.5%)	4 (3.6%)	19 (5.9%)
Blood and lymphatic system disorders	3 (4.1%)	29 (27.9%)	6 (5.7%)	11 (10.0%)	46 (14.4%)
Eosinophilia‡	2 (2.7%)	17 (16.3%)	4 (3.8%)	4 (3.6%)	25 (7.8%)
Lymphadenopathy	0	7 (6.7%)	1 (0.9%)	3 (2.7%)	11 (3.4%)
Musculoskeletal and connective tissue disorders	3 (4.1%)	19 (18.3%)	5 (4.7%)	11 (10.0%)	35 (10.9%)
Arthralgia	1 (1.4%)	10 (9.6%)	2 (1.9%)	4 (3.6%)	16 (5.0%)
Skin and subcutaneous tissue disorders	8 (11.0%)	12 (11.5%)	10 (9.4%)	13 (11.8%)	35 (10.9%)
Worsening atopic dermatitis	7 (9.6%)	2 (1.9%)	5 (4.7%)	6 (5.5%)	13 (4.1%)
Nervous system disorders	6 (8.2%)	10 (9.6%)	10 (9.4%)	9 (8.2%)	29 (9.1%)
Headache	3 (4.1%)	8 (7.7%)	6 (5.7%)	6 (5.5%)	20 (6.3%)
Gastrointestinal disorders	3 (4.1%)	8 (7.7%)	7 (6.6%)	11 (10.0%)	26 (8.1%)
Respiratory, thoracic and mediastinal disorders	1 (1.4%)	6 (5.8%)	5 (4.7%)	5 (4.5%)	16 (5.0%)
Investigations	1 (1.4%)	6 (5.8%)	4 (3.8%)	3 (2.7%)	13 (4.1%)

†Following 16-week induction, one death in a 38 y/o female occurred in the escape arm due to coronary thrombosis/heart failure. Patient had multiple, overlapping pre-existing cardiovascular risk factors. The death was assessed as unrelated to study treatment by the Sponsor Drug Safety Committee and independent external experts; ‡Eosinophilia was reported by the investigator based on the laboratory value being above the upper limit of normal. Only one patient discontinued in the study (at the mid-dose of 18 µg/kg q2w) due to meeting protocol specified stopping criteria for an asymptomatic increase in eosinophil count.

No increased risk of conjunctivitis, facial swelling or erythema, oral ulcers, asthma, myocardial infarction, pulmonary embolus (PE), deep venous thrombosis (DVT), malignancy, depression / suicidality, infections or MACE

Figure 5: Treatment Effect Amongst Crossover Cohort from Placebo to 24 µg/kg q2w Rezpegaldesleukin at Week 16



																Crossover
Weeks	0	2	4	6	8	10	12	14	16	20	24	28	32	36	40	44
EASI-75 Response, n	0	1	2	2	3	1	1	1	0	6	16	17	18	17	13	12
vIGA-AD Response, n	0	0	0	0	2	1	1	1	0	3	5	8	10	11	8	9
Observations, N	42	42	41	42	42	42	42	42	42	40	39	39	36	27	21	17

Interim analysis (18Aug2025 data cut), dosing up to study week 52 is ongoing.

Increased clinical benefit observed with extended dosing beyond 16 weeks of rezpegaldesleukin 24 µg/kg q2w

As of 18Aug2025 data cut, 8 patients have discontinued up to week 44 (patient decision most common reason) and 16 patients have not yet reached week 44. Note 1 patient had missing data at week 44 but is ongoing and has data at later timepoints.

CONCLUSIONS

- First large study to validate the Treg MOA and therapeutic potential of rezpegaldesleukin, an IL-2 agonist, in moderate-to-severe atopic dermatitis
  - High dose rezpegaldesleukin demonstrated significant improvement over placebo during the 16-Week induction in:
    - Primary: EASI LS Mean Percent Change (p<0.001)
    - Key Secondary: EASI-75 (p<0.001), vIGA-AD 0/1 (p<0.05), Itch NRS (p<0.01), EASI-90 (p<0.05), BSA (p<0.01)
    - Additional PROs: ADCT response (p<0.001), DLQI response (p<0.05), ADSS Q1 response (p<0.01), Pain NRS response (p<0.05)
  - Other dose levels demonstrated significant improvement in multiple endpoints
  - Substantial improvement in primary and key secondary endpoints with 24-weeks of open label escape therapy, as compared to 16-weeks with rezpegaldesleukin 24 µg/kg after therapy
  - The data is consistent with the previously-reported safety profile with no new safety signals reported in the study treatment arms
    - No increased risk of conjunctivitis, oral ulcers, or infections, including oral herpes
    - Most frequent AEs were mild injection site reactions (ISRs) that were self-resolving (<1% discontinuations due to ISRs)
- Upcoming data readouts from this ongoing AD study:
  - Maintenance data (comparing q4w vs. q12w regimens) is expected 1Q2026
  - 1-year off-treatment data is expected 1Q2027
- Additional data readouts from the rezpegaldesleukin clinical program:
  - Phase 2b 36-week treatment data in severe alopecia areata is expected in December 2025
- **Next steps: Phase 3 planning for moderate-to-severe atopic dermatitis is underway**

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ABBREVIATIONS

AD: atopic dermatitis; IL-2: interleukin 2; Treg: regulatory T cells; TEAE: treatment emergent adverse events; DVT: deep vein thrombosis; MOA: mechanism of action; ISR: injection site reaction; LS mean: least-squares mean; EASI: Eczema Area and Severity Index; vIGA-AD: Validated Investigators Global Assessment for Atopic Dermatitis; NRS: Numerical Rating Scale; DLQI: Dermatology Life Quality Index; ADCT: Atopic Dermatitis Control Tool; ADSS: Atopic Dermatitis Sleep Scale; Pulmonary embolus: PE

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AUTHOR DISCLOSURE INFORMATION