

Rezpegaldesleukin Provides Durable and Deepening Improvements in the Signs and Symptoms of Atopic Dermatitis with Monthly and Quarterly Dosing: Results from the Phase 2b REZOLVE-AD Maintenance Part of the Study

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Presenter and Conflicts



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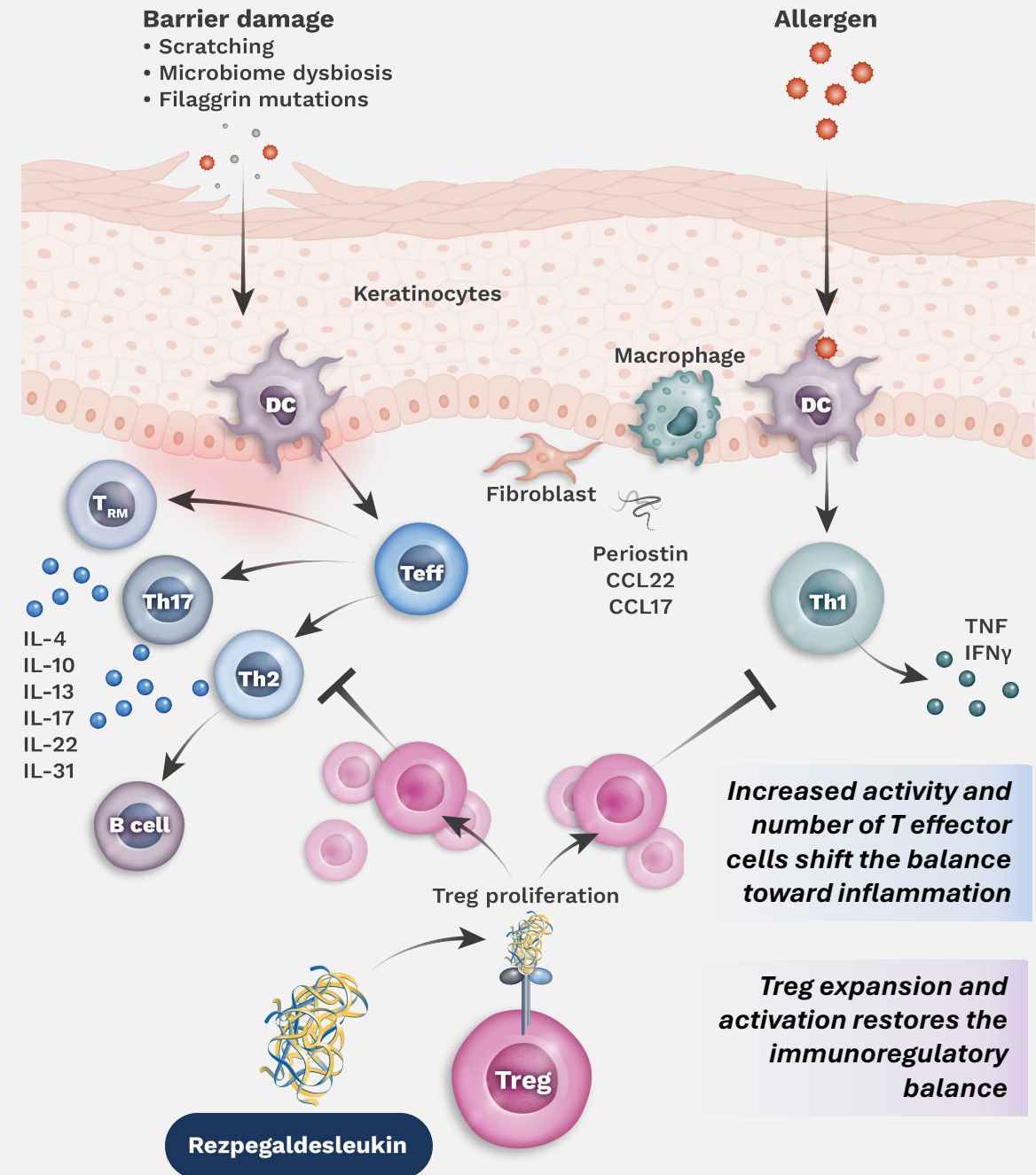
Conflict of Interest Disclosures:

Speaker and/or consultant and/or Investigator for AbbVie, Affibody, Almirall, Amagma/Triveni, AnaptysBio, AOBiom, Anergis, Apogee, Arena, Aristea, Artax, Asana Biosciences, ASLAN pharma, Astria, Attovia, BambusTx, Bayer Health, Belenos, BioVerSys, Böhringer-Ingelheim, Bristol-Myers Squibb, BYOME Labs, Cantargia, CellDex, Connect Pharma, Daichi-Sanyko, Dermavant, DICE Therapeutics, DirigentBio, Domain Therapeutics, DS Pharma, EQRx, EMD Serono, Galderma, Galapagos, Gilead, Glenmark, GSK, Incyte, Innovaderm, Janssen, Kirin, Kymab, LEO, LG Chem, Lilly, Mabylon, MSD, Medac, Micros, Nektar, Nextech, Novartis, Numab, OM-Pharma, Ornavi, Overtone, Pfizer, Pierre Fabre, Protagonist Tx, Q32bio, RAPT, Samsung Bioepis, Sanofi/Regeneron, Scienta Lab, TIRmed, UCB, Union Therapeutics, UPStream Bio, YUHAN. Professor Bieber is founder and chairman of the board of the non-profit biotech “Davos Biosciences AG” within the international Kühne-Foundation and founder of the consulting firm “Bieber Dermatology Consulting”

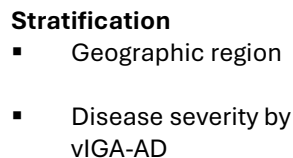
Rezpegaldesleukin (Rezpeg) is a potential first-in-class regulatory T cell mechanism to restore balance in the immune system

- **Tregs play a central role in controlling AD** by dampening inflammatory cytokines and overactive T cells¹
- **Rezpeg** is a potential T-cell balancing therapy that acts on IL-2 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
- **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

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



Patients with Moderate-to-Severe Atopic Dermatitis



- Age: ≥ 18 years
- Moderate/severe AD diagnosis for ≥ 12 months
 - EASI ≥ 16
 - vIGA-AD of 3 or 4
 - BSA $\geq 10\%$

- Biologic-naïve (no prior biologic systemic therapy) and systemic JAKi-naïve
- Failure of prior therapy, including TCS of medium or higher potency, within last 6 months

Mean % EASI improvement at Week 16

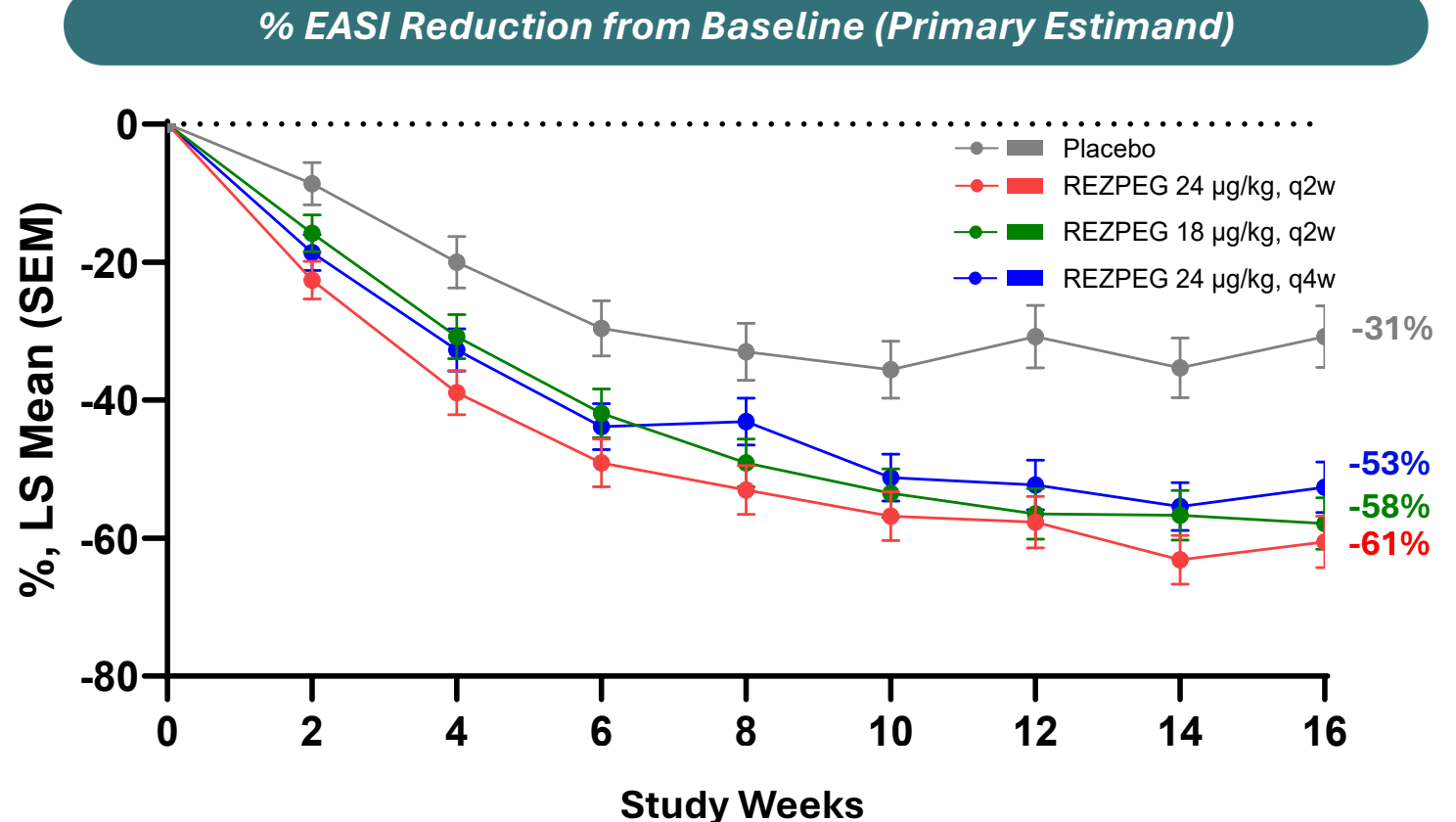
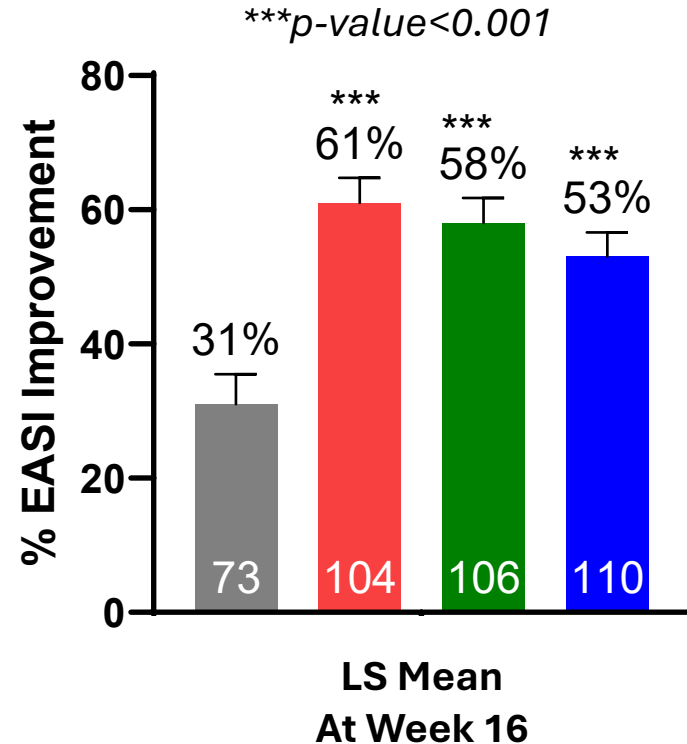
- vIGA-AD of 0 or 1 with ≥ 2 -point reduction from baseline
- EASI-75, EASI-90
- Itch NRS (≥ 4 -point reduction) in patients with baseline score ≥ 4

- Change in ACQ-5 score in patients with self-reported asthma comorbidity with assessment values at baseline and Week 16

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Dose Dependent % EASI Reduction, Clear Separation from Placebo at All Timepoints for Study Treatment Arms (Presented at EADV 2025)

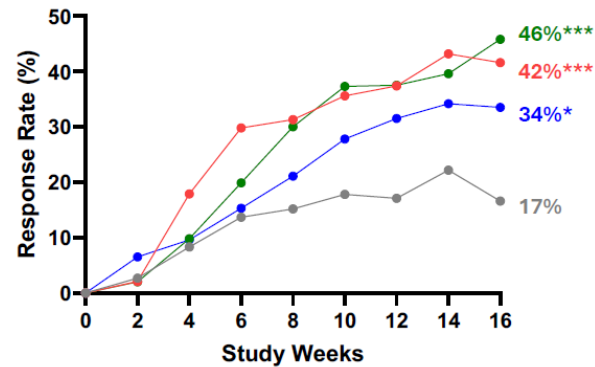
All dose arms met primary endpoint with statistical significance p -value <0.001



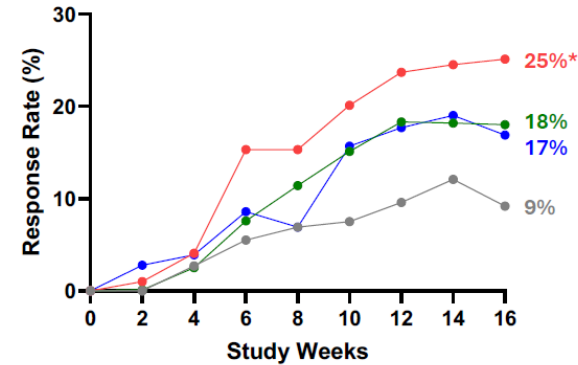
Rezpeg Fast Onset of Action Across All Key Secondary Endpoints (Presented at EADV 2025)

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

EASI-75



EASI-90



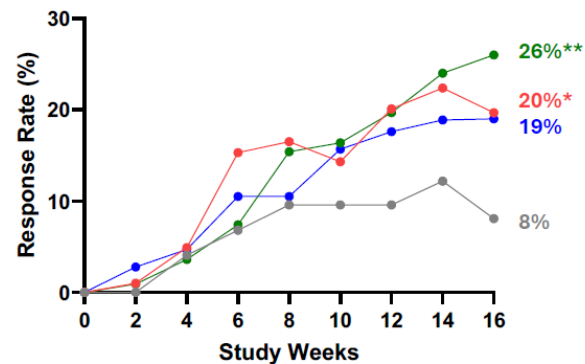
- Placebo
- REZPEG 24 µg/kg, q2w
- REZPEG 18 µg/kg, q2w
- REZPEG 24 µg/kg, q4w

*** p -value < 0.001

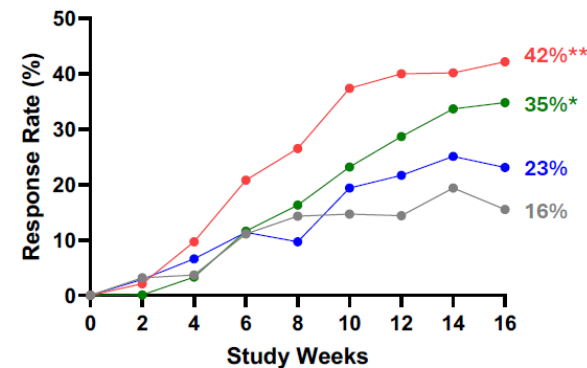
** p -value < 0.01

* p -value < 0.05

vIGA-AD 0/1



Itch NRS

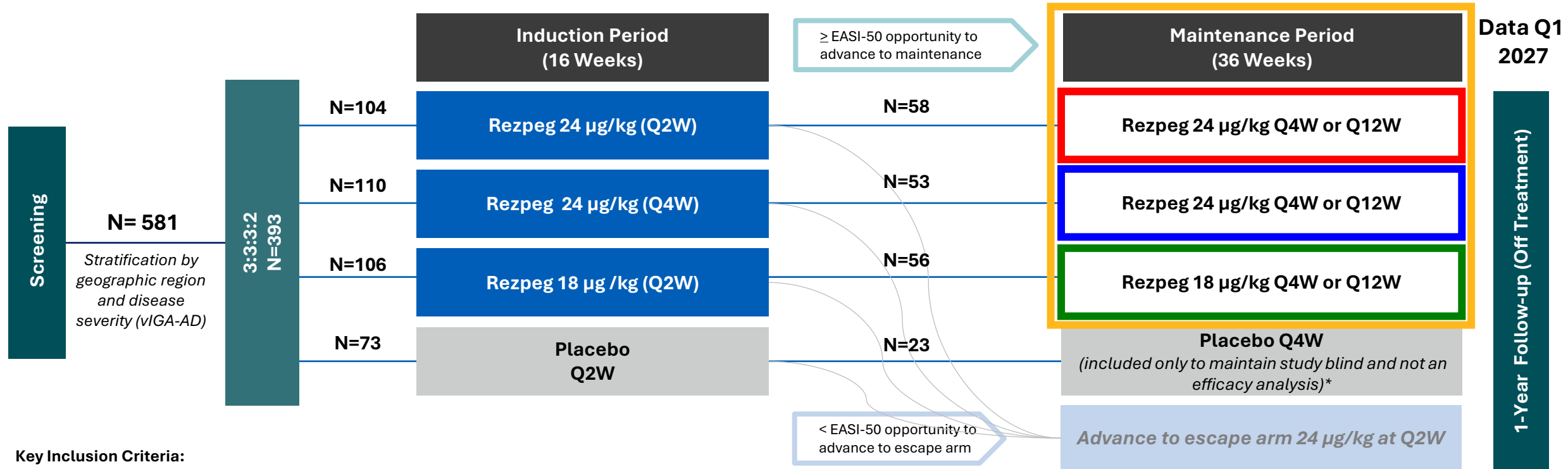


For EASI-75, vIGA-AD 0/1, and EASI-90:
N = 73, 104, 106, and 110 for placebo, 24 µg/kg q2w, 18 µg/kg q2w, and 24 µg/kg q4w

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.

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-naïve (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, amltelimab Phase 2 STREAM-AD program, and tralokinimab Phase 3 ECZTRA Program)

REZOLVE-AD: Baseline Demographics at Study Entry for the Re-randomized Maintenance Population

Induction regimen	Rezpeg 24 µg/kg Q2W		Rezpeg 24 µg/kg Q4W		Rezpeg 18 µg/kg Q2W		Rezpeg Overall (N=167)
Maintenance regimen	Rezpeg 24 µg/kg Q4W (N=29)	Rezpeg 24 µg/kg Q12W (N=29)	Rezpeg 24 µg/kg Q4W (N=26)	Rezpeg 24 µg/kg Q12W (N=27)	Rezpeg 18 µg/kg Q4W (N=28)	Rezpeg 18 µg/kg Q12W (N=28)	
Age, Mean (SD), years	40.4 (12.8)	38.8 (15.1)	35.5 (14.0)	39.0 (14.4)	33.5 (13.4)	34.2 (14.1)	36.9 (14.0)
< 65 years	28 (96.6)	27 (93.1)	25 (96.2)	25 (92.6)	28 (100.0)	26 (92.9)	159 (95.2)
Sex, Female, no. (%)	14 (48.3)	14 (48.3)	16 (61.5)	11 (40.7)	14 (50.0)	16 (57.1)	85 (50.9)
Race, White, no. (%)	23 (79.3)	24 (82.8)	23 (88.5)	23 (85.2)	25 (89.3)	23 (82.1)	141 (84.4)
Geographic region, no. (%)							
North America	9 (31.0)	6 (20.7)	9 (34.6)	9 (33.3)	8 (28.6)	7 (25.0)	48 (28.7)
Rest of the world	20 (69.0)	23 (79.3)	17 (65.4)	18 (66.7)	20 (71.4)	21 (75.0)	119 (71.3)
Duration since onset, years							
Mean (SD)	27.2 (14.6)	23.0 (16.6)	17.1 (11.1)	16.8 (13.4)	23.0 (13.5)	20.1 (12.9)	21.3 (14.1)
viGA-AD, no. (%)							
3	20 (69.0)	19 (65.5)	19 (73.1)	20 (74.1)	16 (57.1)	20 (71.4)	114 (68.3)
4	9 (31.0)	10 (34.5)	7 (26.9)	7 (25.9)	12 (42.9)	8 (28.6)	53 (31.7)
EASI total score							
Mean (SD)	26.9 (10.7)	25.8 (9.2)	25.9 (11.4)	26.2 (10.4)	30.1 (11.5)	25.5 (9.7)	26.7 (10.5)
BSA (%)							
Mean (SD)	40.5 (22.0)	40.2 (21.8)	35.9 (20.3)	40.1 (19.3)	44.7 (25.5)	39.9 (19.2)	40.3 (21.3)
Itch NRS							
n	29	29	26	26	28	28	166
Mean (SD)	7.0 (1.9)	6.2 (2.2)	7.1 (1.6)	6.9 (2.1)	6.9 (1.4)	6.2 (2.1)	6.7 (1.9)

All Monthly and Quarterly Arms Demonstrated Durability of Responses Over 36 Weeks of Maintenance Dosing Following 16 Weeks of 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)

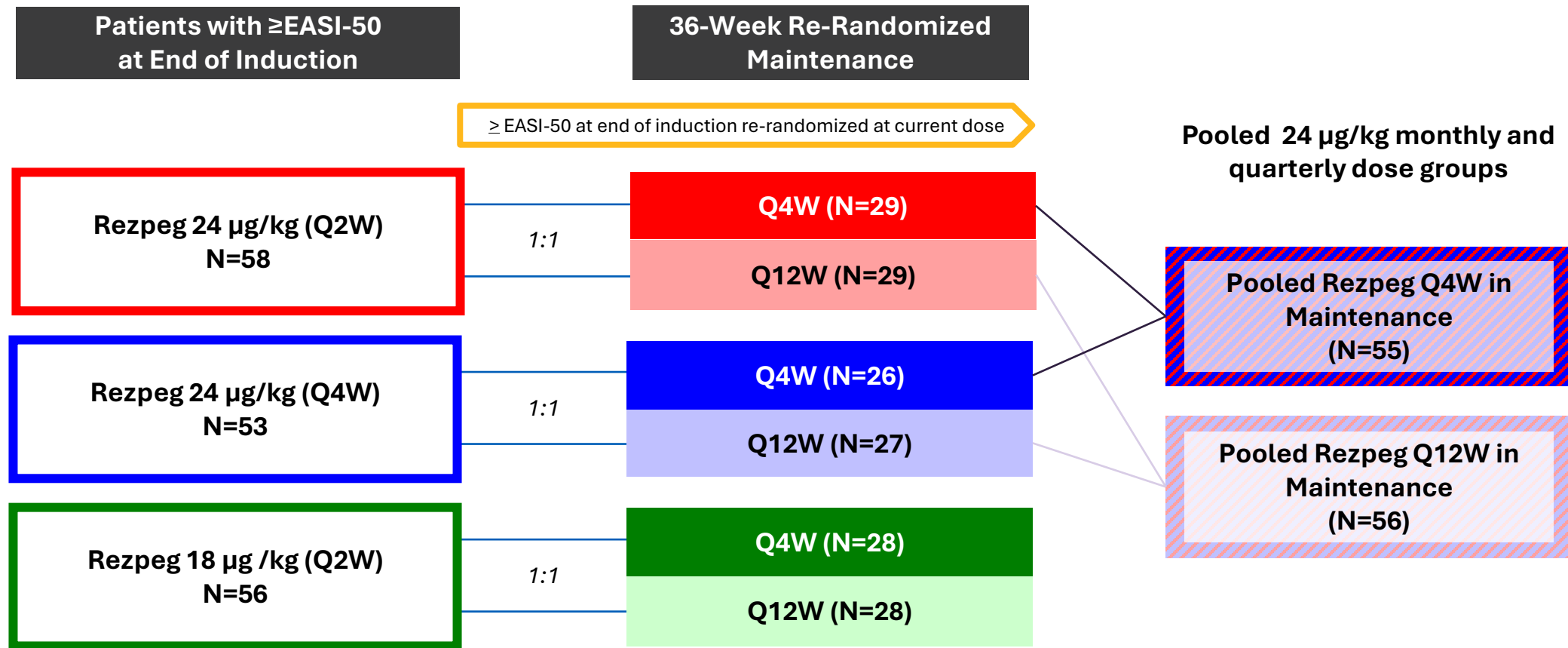
(N=xx) is the entire maintenance population

(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

Multiple Efficacy Endpoints Assessed in Maintenance Portion of Trial (Prespecified Analyses)

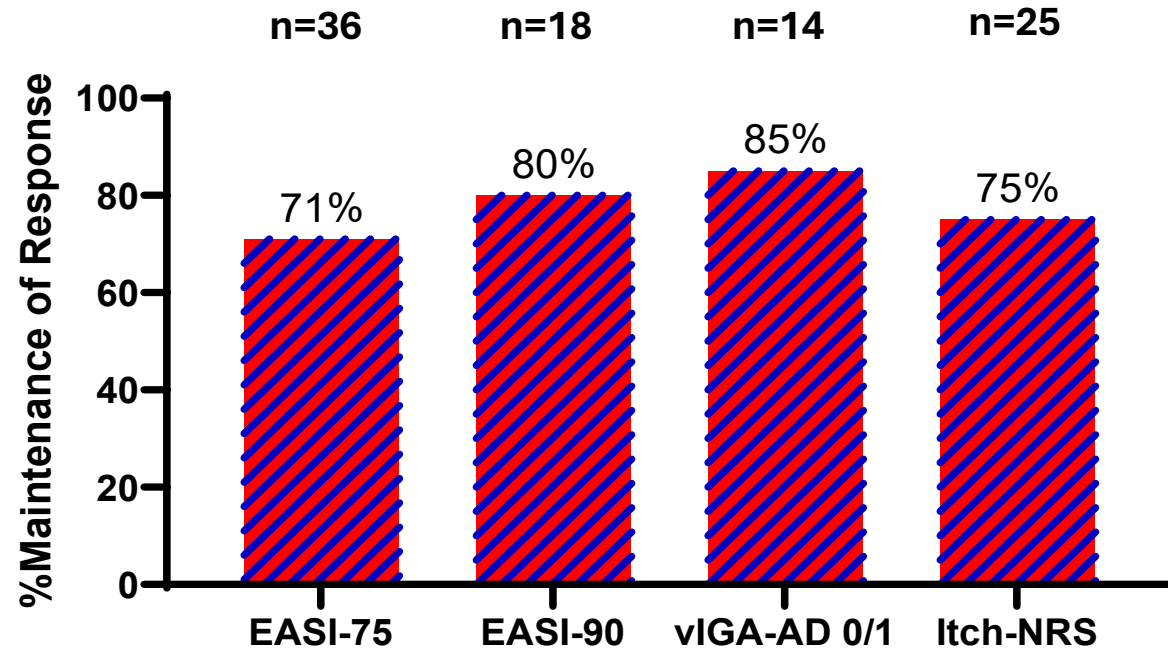


Data after escape are set to be missing. All other data regardless of rescue medication use and/or treatment discontinuation are used as is. Missing data is imputed using multiple imputation.

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

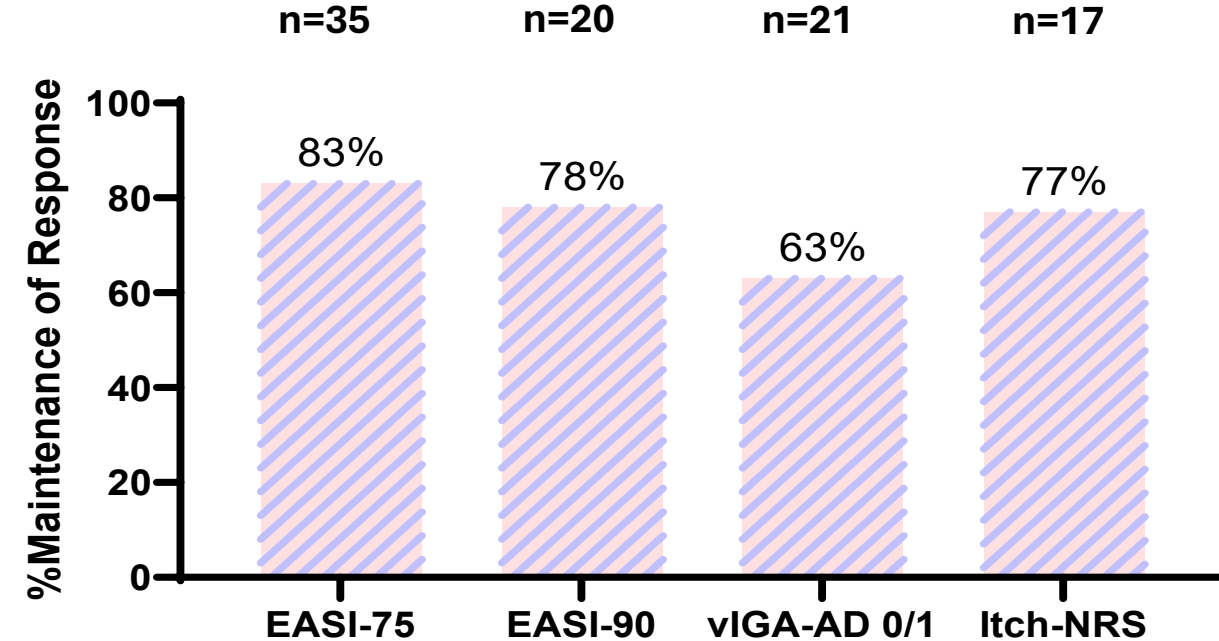
Maintenance at Week 52 in the Q4W Cohorts

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

New and Deepening Responses with Monthly and Quarterly Rezpeg Dosing

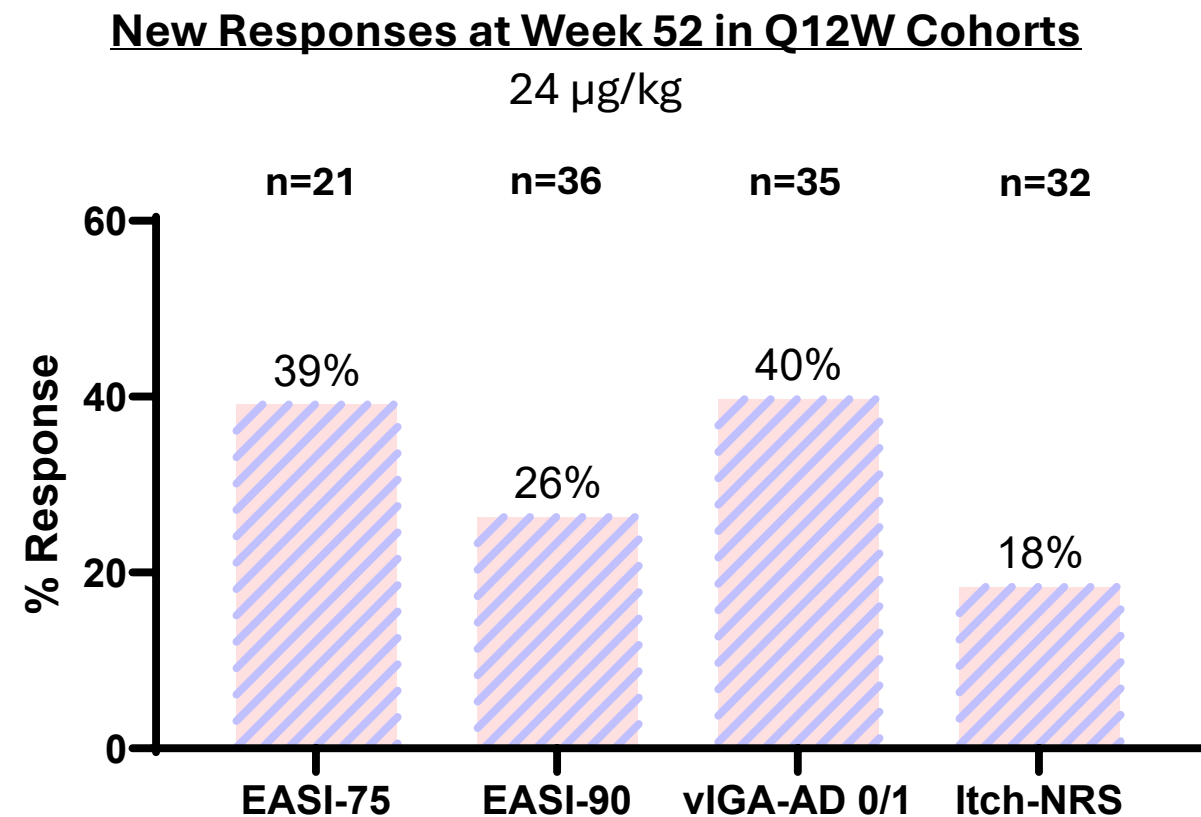
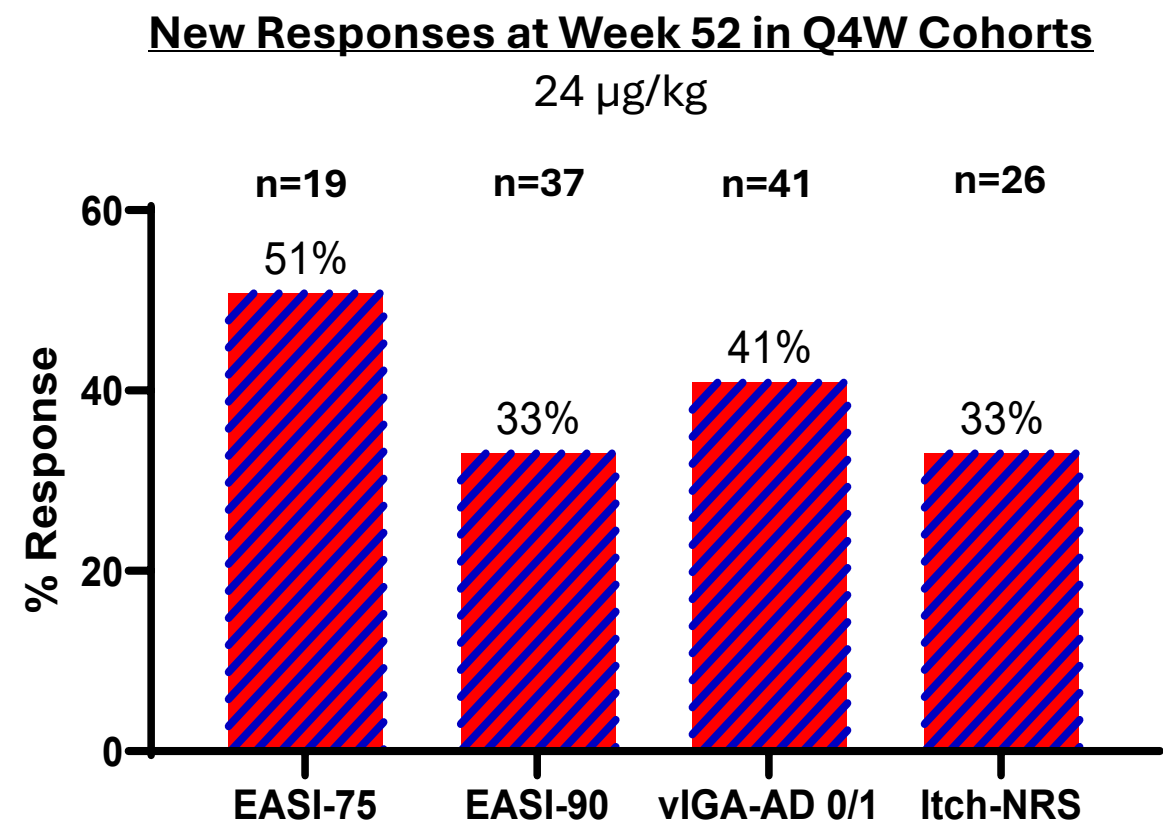
At Week 52

	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 Rezpeg (High Dose) Maintenance Arms



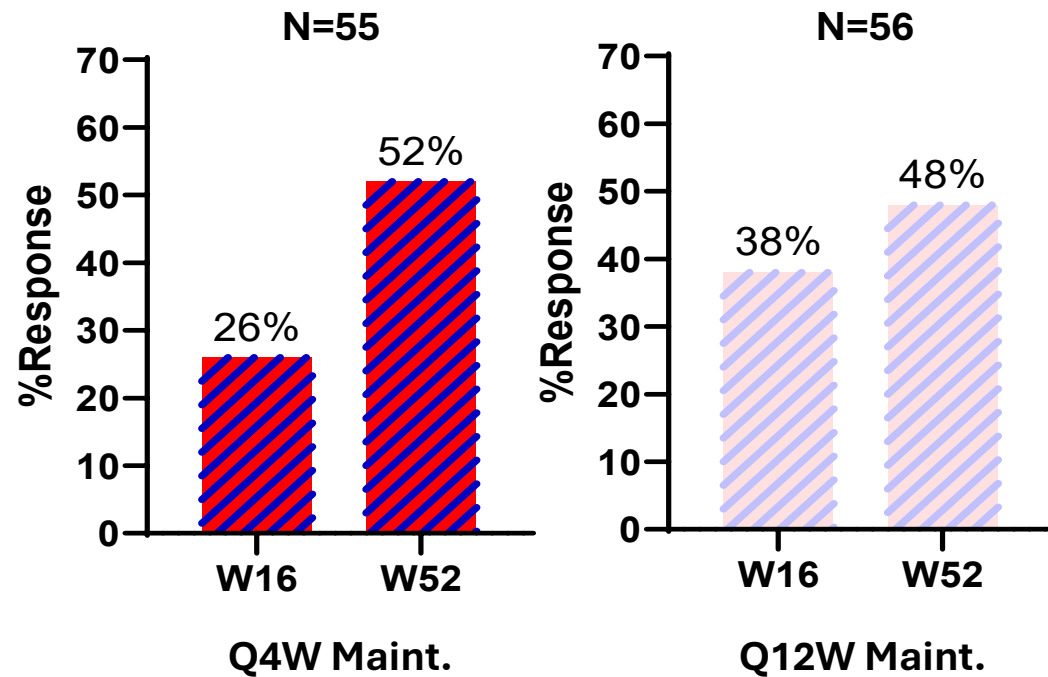
New and deepening responses among re-randomized patients achieving EASI-50 in 16-week induction

(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 Rezpeg (High Dose) Maintenance Arms

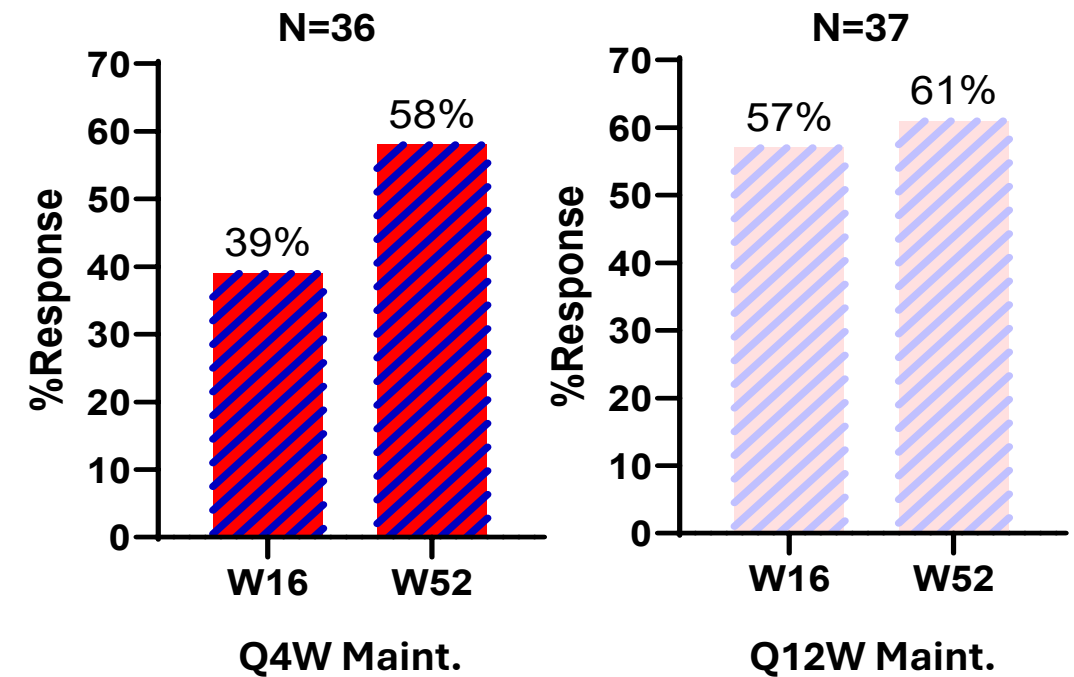
vIGA-AD 0/1 Response Rate at Week 52 Among
≥ EASI-50 Responders
at Re-Randomization

24 µg/kg



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

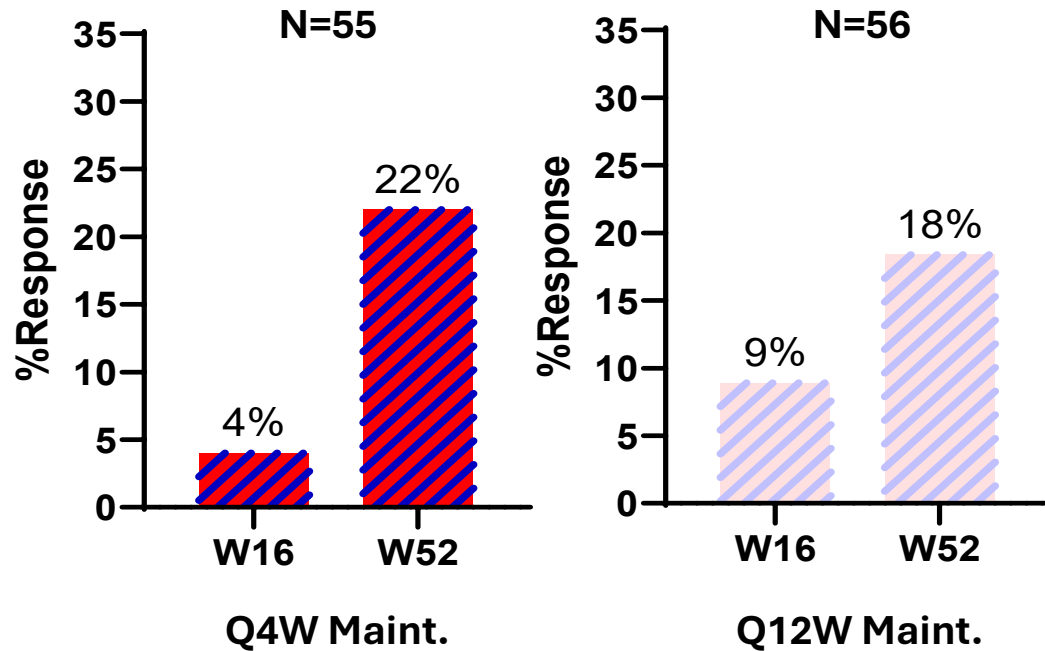
24 µg/kg



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

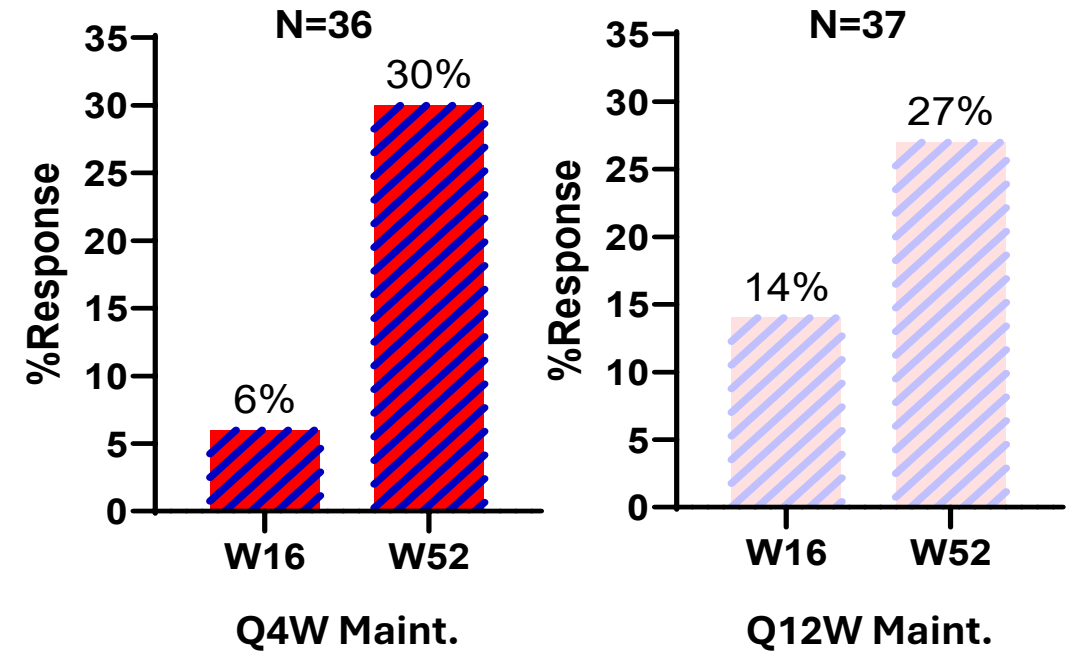
**EASI-100 Rate at Week 52 Among
≥ EASI-50 Responders
at Re-Randomization**

24 µg/kg



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

24 µg/kg



Overall Summary of Treatment Emergent Adverse Events

36-Week Maintenance Treatment Period: $\geq 5\%$ Rezpeg Overall or Placebo Arm

	Placebo	Rezpeg 24 µg/kg Q4W	Rezpeg 24 µg/kg Q12W	Rezpeg 18 µg/kg Q4W	Rezpeg 18 µg/kg Q12W	Rezpeg Overall
	(N=23)	(N=55)	(N=56)	(N=28)	(N=28)	(N=167)
Patients With at Least One TEAE	15 (65%)	38 (69%)	42 (75%)	22 (79%)	18 (64%)	120 (72%)
Patients With at Least One TEAE (Excluding ISRs)	15 (65%)	28 (51%)	37 (66%)	17 (61%)	15 (54%)	97 (58%)
Patients With at Least One Serious TEAE (<i>not treatment related</i>)	0	1 (2%)	4 (7%)	2 (7%)	0	7 (4%)
Patients With at Least One Severe TEAE (<i>not treatment related</i>)	1 (4%)	1 (2%)	1 (2%)	0	1 (4%)	3 (2%)
Patients With at Least One TEAE Leading to Death	0	0	0	0	0	0
Patients With at Least One TEAE Leading to Discontinuation*	0	1 (2%)	0	0	0	1 (1%)
TEAEs by System Organ Class and Preferred Term Over $\geq 5\%$ in Rezpeg Overall or Placebo Arm						
General disorders and administration site conditions	1 (4%)	28 (51%)	33 (59%)	18 (64%)	12 (43%)	91 (55%)
Proportion of patients with at least one Injection Site Reaction (ISR)	1 (4%)	28 (51%)	32 (57%)	17 (61%)	12 (43%)	89 (53%)
Injection site reaction (ISR) by Number of Events						
Proportion of ISR events-mild (%)	100%	61%	72%	78%	76%	69%
Proportion of ISR events-moderate (%)	0	39%	28%	22%	24%	31%
Proportion of ISR events-severe (%)	0	0	0	0	0	0
Infections and infestations	7 (30%)	9 (16%)	19 (34%)	7 (25%)	7 (25%)	42 (25%)
Nasopharyngitis	3 (13%)	7 (13%)	6 (11%)	1 (4%)	2 (7%)	16 (10%)
Upper respiratory tract infection	1 (4%)	0	8 (14%)	2 (7%)	1 (4%)	11 (7%)
Blood and lymphatic system disorders	1 (4%)	3 (6%)	5 (9%)	1 (4%)	2 (7%)	11 (7%)
Musculoskeletal and connective tissue disorders	2 (9%)	3 (6%)	5 (9%)	0	0	8 (5%)
Skin and subcutaneous tissue disorders	7 (30%)	10 (18%)	15 (27%)	5 (18%)	8 (29%)	38 (23%)
Worsening atopic dermatitis	5 (22%)	7 (13%)	11 (20%)	4 (14%)	8 (29%)	30 (18%)
Nervous system disorders	2 (9%)	3 (6%)	1 (2%)	2 (7%)	0	6 (4%)
Gastrointestinal disorders	2 (9%)	2 (4%)	3 (5%)	1 (4%)	1 (4%)	7 (4%)
Investigations	2 (9%)	1 (2%)	5 (9%)	2 (7%)	0	8 (5%)

All serious and severe TEAEs deemed unrelated to study treatment and none led to discontinuation of treatment

*Treatment related AE that led to discontinuation was atopic dermatitis

Safety Profile at 52-Weeks Consistent with Previously Reported Results

- ✓ **52-week safety of Rezpeg 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 Rezpeg exposed patients
 - Lower frequency of ISRs observed over longer dosing duration in maintenance

Key Takeaways from REZOLVE-AD Maintenance Part of Study

- **Treg MoA validated** for deep and durable efficacy in patients with moderate-to-severe atopic dermatitis with extended dosing out to 52 weeks
- **Both Rezpeg Q4W and Q12W maintenance regimens achieved durability and demonstrated a deepening of responses**
 - Supports evaluation of both regimens in Phase 3
- **Extended dosing regimens with Rezpeg compare favorably** to historically reported longer term maintenance data across Phase 2/Phase 3 trials
- **Extended dosing regimens with Rezpeg 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
 - Over 1,000 subjects treated with Rezpeg to date (= 381 patient-years of exposure)
- **52 week off treatment follow up data planned for Q1 2027**
- **Three Phase 3 studies in the ZENITH-AD program have been initiated**

Acknowledgements

- **Thank you to:**
 - The patients and their families
 - The investigators and their study teams
- This study was sponsored by Nektar Therapeutics
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