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APG777, a Novel, Half-Life Extended Anti-IL-13 Antibody, Demonstrates Safety and Efficacy in Moderate-to-Severe Atopic Dermatitis: 16-Week Results From the Phase 2 APEX Study

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Disclosures & Acknowledgements

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- All authors met the ICMJE criteria.
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APG777: the first extended half-life, IL-13-targeting antibody to be evaluated in atopic dermatitis

Mechanism of action

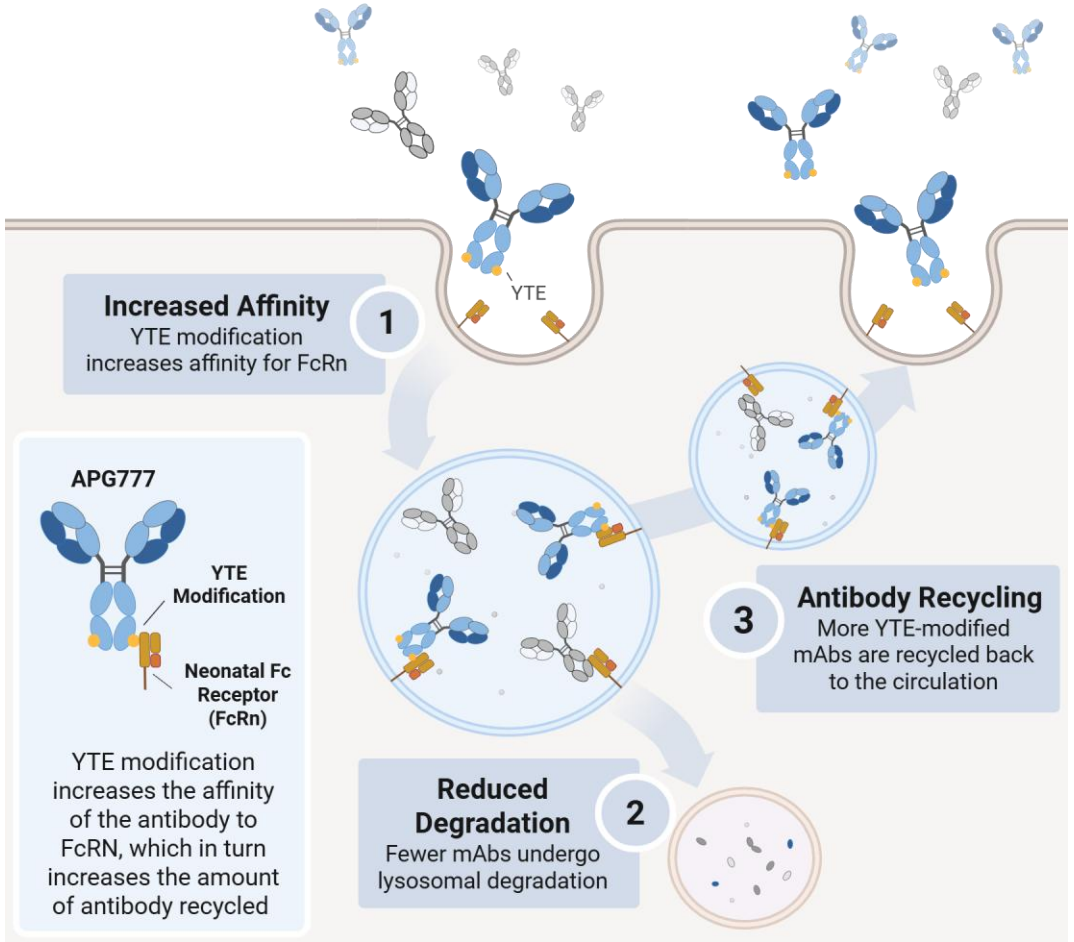
APG777 binds to IL-13 with high affinity, and a similar epitope as lebrikizumab, to block **IL-13-driven type 2 inflammation**

Half-life extension

YTE modification increases antibody recycling, leading to an APG777 **half-life of ~77 days**

Reduced dosing frequency

APG777's improved pharmacokinetics permit evaluation of **4 dosing days** during the first 16 weeks of treatment and 2-4 dosing days per year in maintenance



APG777 half-life extension through YTE modification

YTE, triple amino acid modification in the Fc region of the antibody

Objective

- To evaluate the 16-week efficacy and safety of APG777, administered over 4 dosing days, in patients with moderate-to-severe atopic dermatitis (Phase 2 APEX Part A)

APEX Part A: Study design

Eligibility

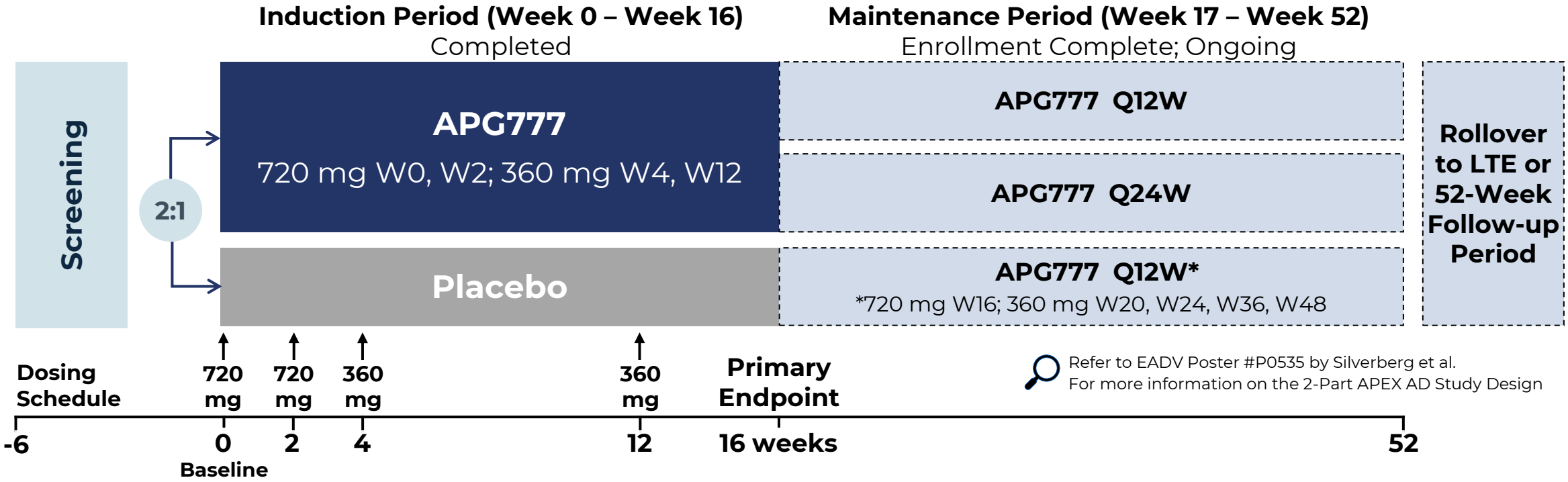
- Adults ≥18 years of age
- Moderate-to-severe atopic dermatitis:
  EASI ≥16, vIGA-AD ≥3, BSA ≥10%

Endpoints (Week 16)

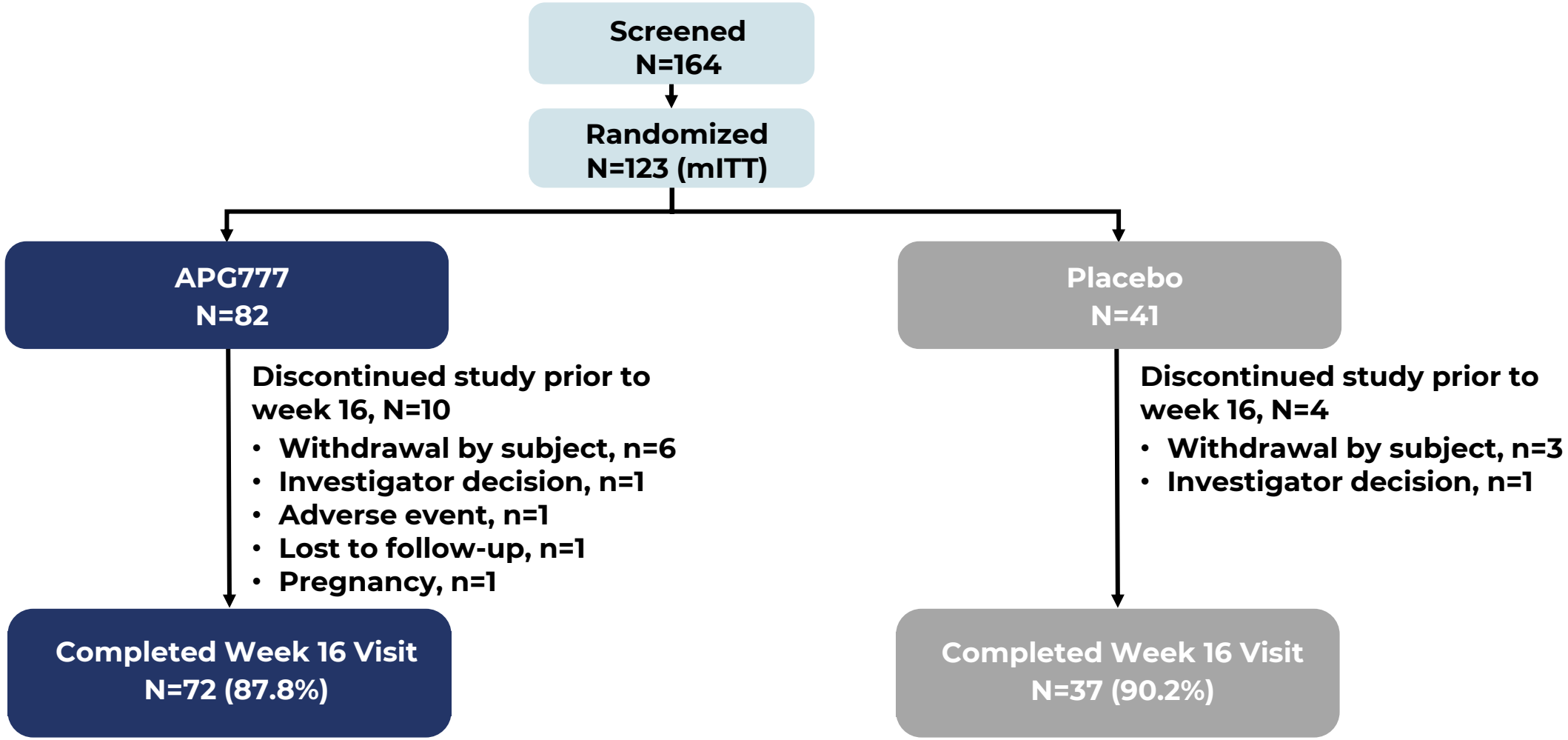
- **Efficacy**
- Primary: EASI % change from baseline
- Secondary: EASI-75, EASI-90, vIGA-AD 0/1 with ≥2-point improvement from baseline, I-NRS % change from baseline

Safety

- Incidence of TEAEs, SAEs



Participant disposition



mITT, modified intent-to-treat population, defined as all randomized participants who received at least 1 dose of study drug during the induction period

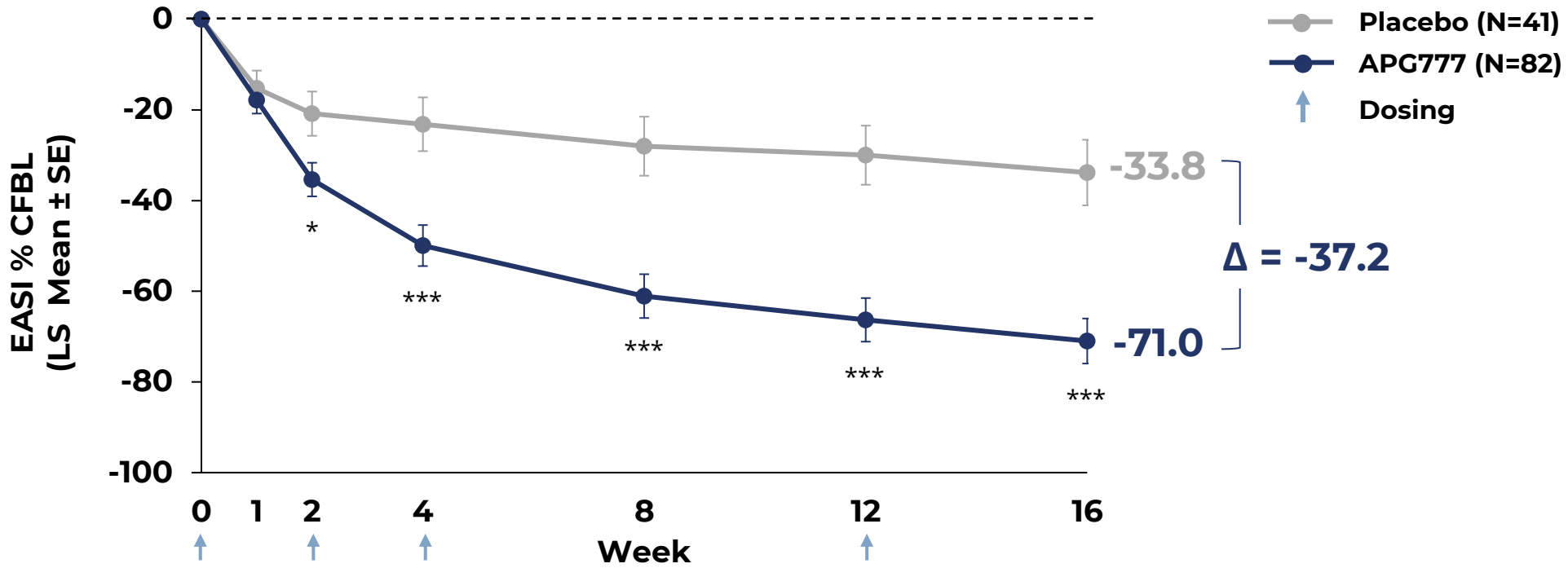
Demographics and baseline characteristics

	Placebo (N=41)	APG777 (N=82)
Age, mean±SD, years	36.0±13.7	38.7±15.6
Female, n (%)	19 (46.3)	41 (50.0)
Race, n (%)[1]		
White	30 (73.2)	54 (65.9)
Black	6 (14.6)	13 (15.9)
Asian	4 (9.8)	12 (14.6)
Other	1 (2.4)	3 (3.7)
Body mass index, mean±SD, kg/m^2	27.7±6.7	30.0±8.4
Geographic region, n (%)		
Canada	16 (39.0)	34 (41.5)
United States	13 (31.7)	25 (30.5)
Europe	12 (29.3)	23 (28.0)
Duration since AD diagnosis, mean±SD, years	24.6±14.1	24.2±14.5
Previous use of systemic treatment, n (%)	11 (26.8)	35 (42.7)
EASI score, mean±SD	25.3±10.8	25.2±10.8
Body surface area affected, mean±SD, %	33.2±22.6	37.2±22.3
vIGA-AD score, n (%)		
3	27 (65.9)	55 (67.1)
4	14 (34.1)	27 (32.9)
I-NRS score, mean±SD	6.7±1.9	6.4±2.1
DLQI, mean±SD	13.3±7.1	14.3±7.0

[1]Race was self-reported. "Other" included American Indian or Alaska Native, Native Hawaiian or Pacific Islander, other, unknown, and not reported.

Primary endpoint of EASI % CFBL at Week 16 was achieved

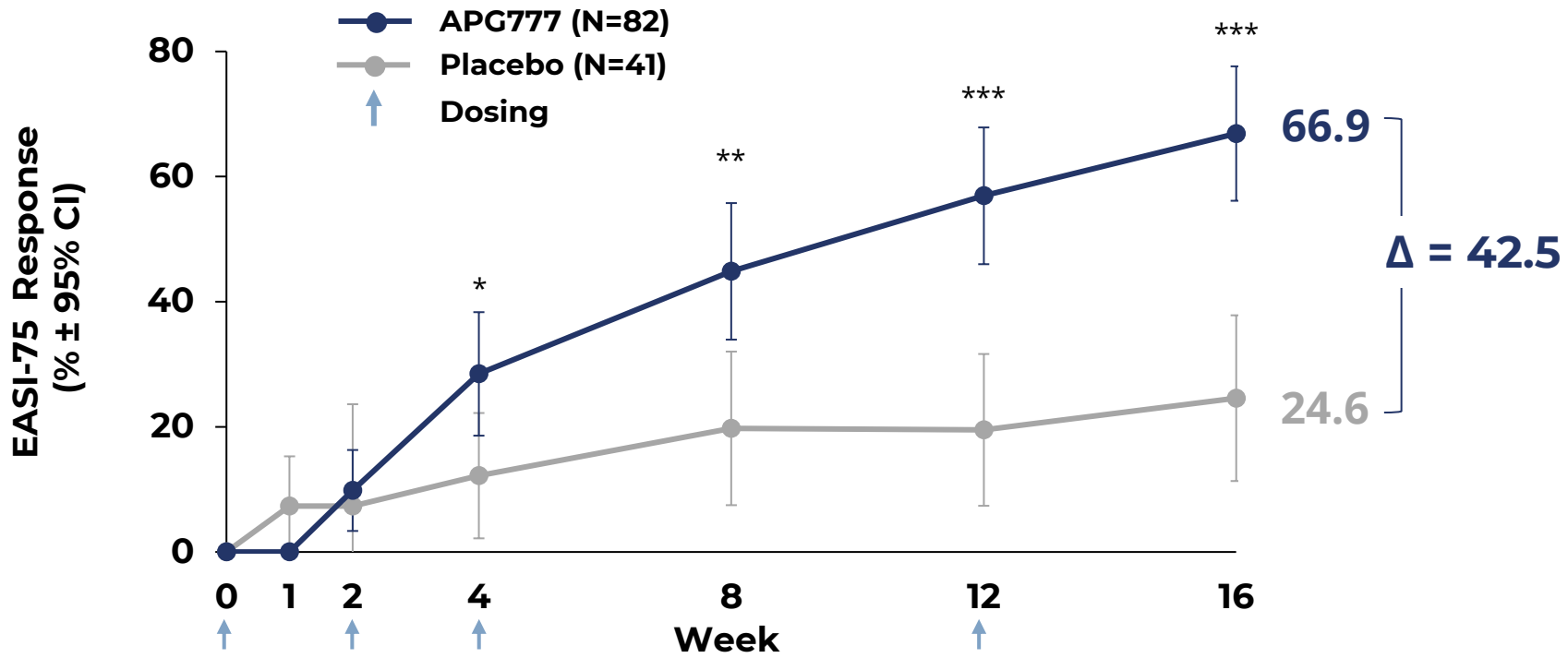
Reduction in EASI was significantly greater than placebo at Week 2 and all subsequent timepoints through Week 16



*p<0.05; ***p<0.001 vs placebo.
Arrows indicate dosing schedule. CFBL, change from baseline.
Missing data were imputed with Markov Chain Monte Carlo Multiple Imputation, including the data set to missing after rescue or study treatment discontinuation.

Significant EASI-75 response with APG777 as early as Week 4

Two-thirds of participants treated with APG777 achieved EASI-75 response at Week 16



*p<0.05; **p<0.01; ***p<0.001 vs placebo.
Arrows indicate dosing schedule.
Missing data were imputed with Markov Chain Monte Carlo Multiple Imputation.
Rescue medication use or treatment discontinuation due to lack of efficacy was imputed as non-responder for all subsequent timepoints.

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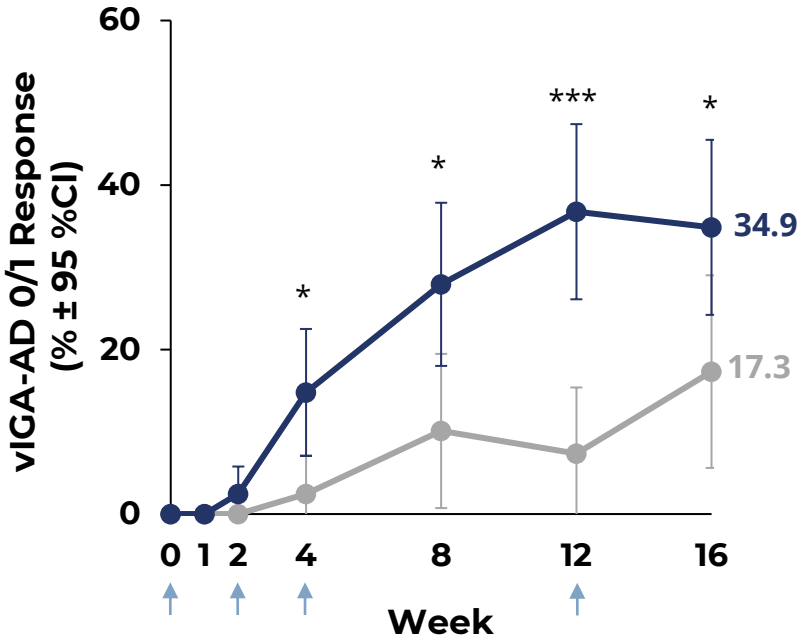
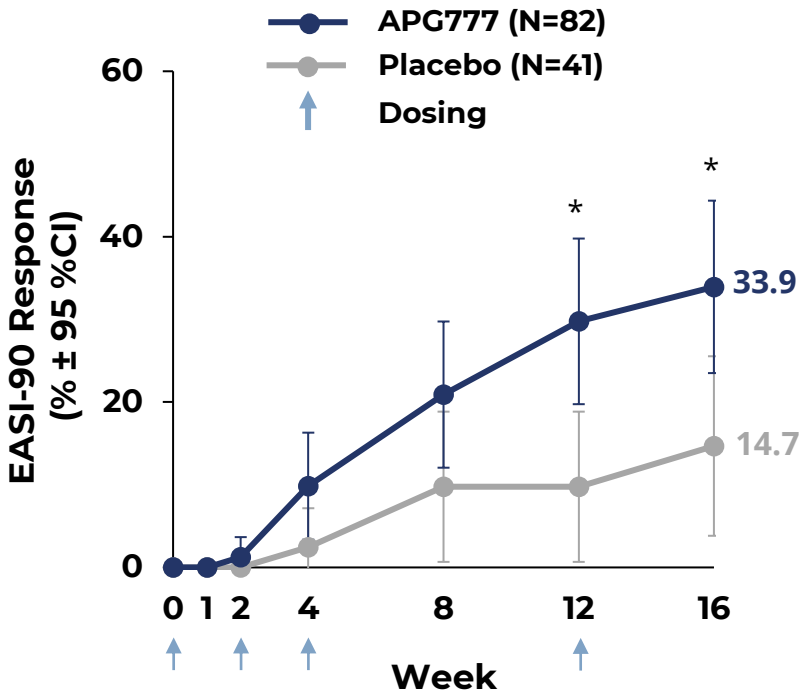
Treatment with APG777 resulted in significant improvements in secondary endpoints vs. placebo

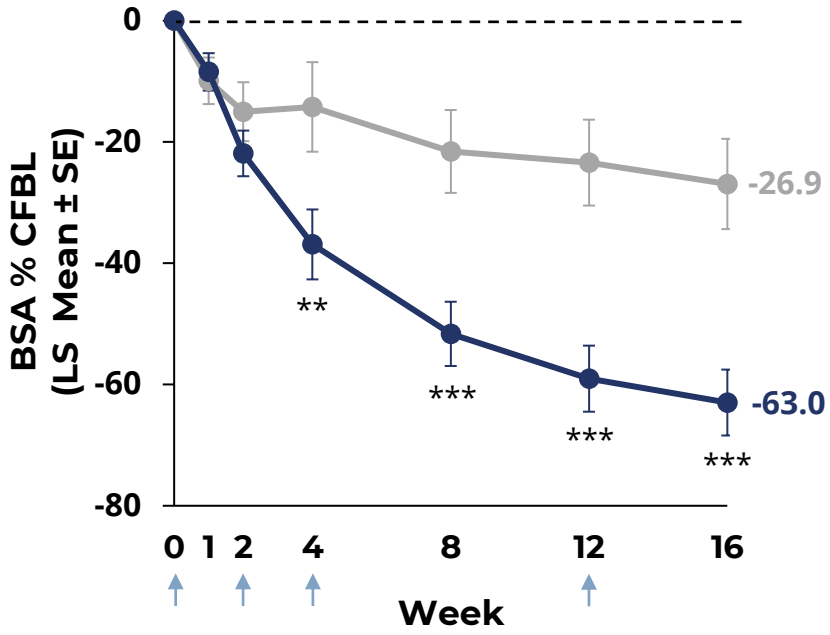
vIGA-AD score of 0/1 with ≥2-point reduction from baseline



EASI-90 response



% CFBL in affected body surface area (BSA)



*p<0.05; **p<0.01; ***p<0.001 vs placebo.
Arrows indicate dosing schedule. CFBL, change from baseline.
Missing data were imputed with Markov Chain Monte Carlo Multiple Imputation, including the data set to missing after rescue or study treatment discontinuation.
For vIGA and EASI-90 responder analyses, rescue medication use or treatment discontinuation due to lack of efficacy was imputed as non-responder for all subsequent timepoints.

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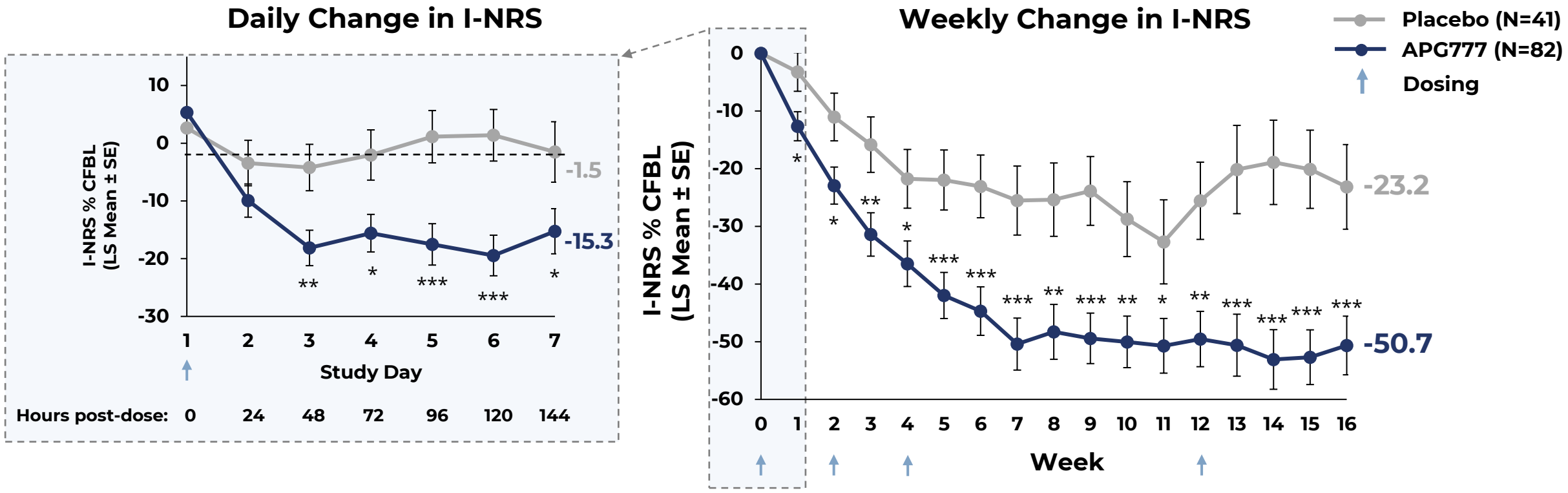
Treatment with APG777 led to rapid itch relief

Significant improvement in itch was observed 48 hours after the first dose of APG777



*p<0.05, **p<0.01, ***p<0.001 vs placebo.
Arrows indicate dosing days. CFBL, change from baseline. I-NRS, Itch Numeric Rating Scale
Baseline is defined as the weekly average of the I-NRS score on the 7 days prior to the first dose.
Daily change in I-NRS in Week 1 was evaluated as-observed without imputation for missing data.
For the weekly change in I-NRS through Week 16, missing data were imputed with Markov Chain Monte Carlo Multiple Imputation, including the data set to missing after rescue or study treatment discontinuation

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Summary of safety through Week 16

Event, n (%)	Placebo (N=41)	APG777 (N=82)
≥1 adverse event	26 (63.4)	46 (56.1)
≥1 serious adverse event	1 (2.4)	1 (1.2)
Adverse events leading to discontinuation	0	2 (2.4)[1]
Deaths	0	0
Severity of adverse events		
Mild	10 (24.4)	15 (18.3)
Moderate	14 (34.1)	29 (35.4)
Severe	2 (4.9)	2 (2.4)
Most common adverse events (in ≥5% of APG777-treated participants)		
Noninfectious conjunctivitis[2]	1 (2.4)	12 (14.6)
Upper respiratory tract infection	5 (12.2)	7 (8.5)

- The total conjunctivitis rate was 18.3%[3].
- Conjunctivitis was transient and led to no discontinuations, dose interruptions, or dose adjustments

[1]Includes one participant who discontinued due to Sézary syndrome and one participant who discontinued due to a positive pregnancy test.
[2]MedDRA preferred term is noninfective conjunctivitis.
[3]Combined rate for all conjunctivitis-related MedDRA preferred terms including: allergic conjunctivitis, atopic keratoconjunctivitis, bacterial conjunctivitis, conjunctivitis, noninfective conjunctivitis, and viral conjunctivitis.
Safety data are summarized for all randomized participants who received at least one dose of study drug during the 16-week induction period.

Conclusions

- The improved pharmacokinetics of APG777 allow for a reduced injection frequency of only **4 dosing days** during the first 16 weeks of treatment
- APEX Part A met the primary endpoint, resulting in a **71.0% decrease** from baseline in EASI at Week 16 (-37.2% placebo-adjusted)
- **Two-thirds (66.9%)** of participants treated with APG777 achieved EASI-75 at Week 16 (42.5% placebo-adjusted)
- Statistically significant reductions in itch were observed **48 hours** after the first dose of APG777, with progressive improvement through Week 16
- APG777 was well tolerated, with a safety profile consistent with other therapies targeting the IL-13 or IL-4/IL-13 pathway
- Every **12- and 24-week maintenance dosing** is being evaluated in the ongoing APEX Part A, while a higher dose regimen of APG777 is currently being explored in APEX Part B

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Thank you

- We thank the trial participants and study investigators involved in APEX Part A.

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The End

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