Half-life-extended monoclonal antibody APG777 for atopic dermatitis: Design of the phase 2 APEX study

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Introduction

- IL-13 plays a key role in the pathogenesis of atopic dermatitis, asthma, and other inflammatory and immunologic conditions.[1,2]
- APG777 is a humanized, IgG1 monoclonal antibody that potently binds IL-13 and prevents IL-13Rα1/IL-4Rα heterodimer formation (**Figure 1**).
- Interim data from the single-ascending dose portion of a phase 1 study in healthy human volunteers demonstrated that (**Figure 2**):[3,4]
  - APG777 has a half-life of ~75 days and provides strong inhibition of downstream biomarkers pSTAT6 and TARC.
  - APG777 is well tolerated at doses up to 1200 mg.
  - Adverse events were mild and generally considered unrelated to study drug.
- The favorable safety profile and optimized pharmacokinetics of APG777 supported the initiation of a phase 2 study in adults with moderate-to-severe atopic dermatitis where every 3- to 6-month maintenance dosing would be evaluated.

Figure 1. APG777 mechanism of action

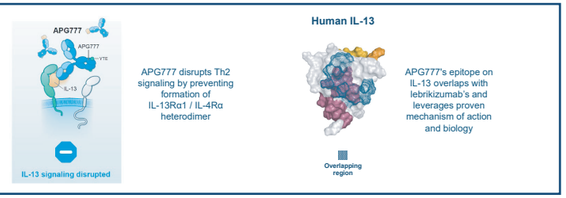
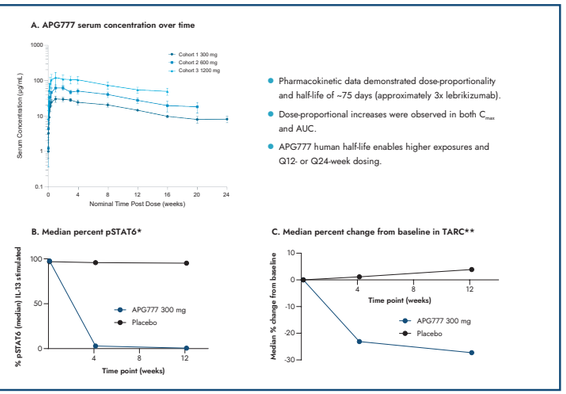


Figure 2. Phase 1 data demonstrate that APG777 has a half-life of ~75 days and provides strong inhibition of downstream biomarkers pSTAT6 and TARC[4]



- Pharmacokinetic data demonstrated dose-proportionality and half-life of ~75 days (approximately 3x lebrikizumab).
- Dose-proportional increases were observed in both C_{max} and AUC.
- APG777 human half-life enables higher exposures and Q12- or Q24-week dosing.

*n=1 in APG777 300 mg group because the pSTAT6 assay was not available when the first participants reached the pre-specified study visits; n=4 in placebo group

**n=5 in APG777 300 mg group, n=6 in placebo group

pSTAT6, phosphorylated Signal Transducer and Activator of Transcription 6; TARC, Thymus and Activation Regulated Chemokine

Study Objective

- APEX (APG777-201; NCT: NCT06395948) is a two-part, randomized, double-blinded, placebo-controlled phase 2 study evaluating APG777 in adults with moderate-to-severe atopic dermatitis.

Methods

Figure 3. Design of the 2-part APEX study: Part A

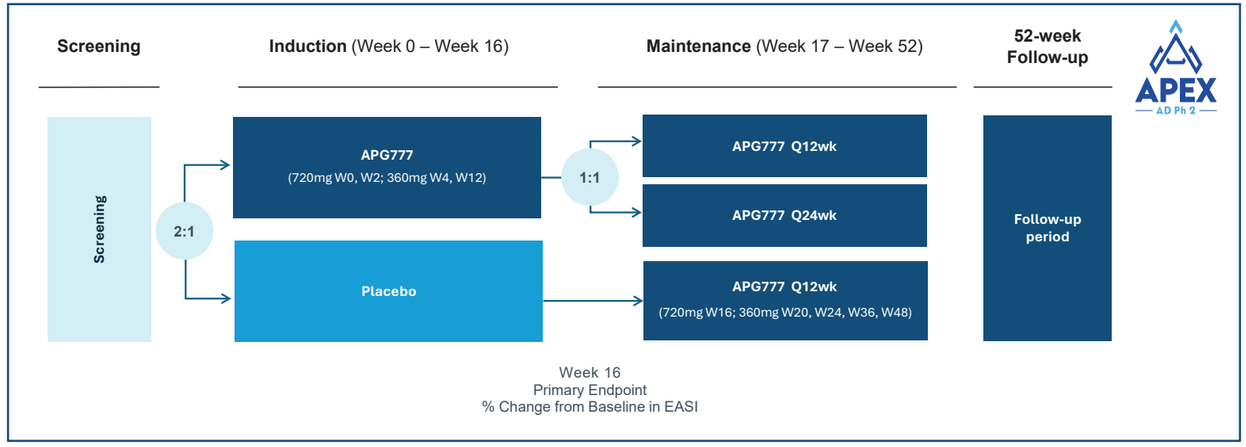
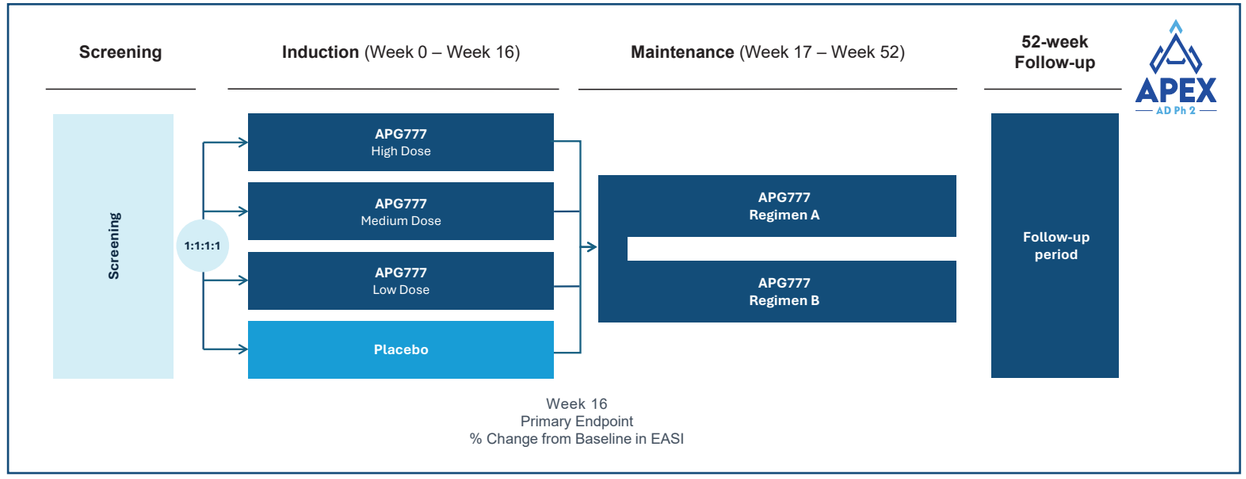


Figure 4. Design of the 2-part APEX study: Part B



Design of the 2-part APEX study

- APEX (APG777-201; NCT: NCT06395948) is a phase 2 study evaluating APG777 in adults with moderate-to-severe atopic dermatitis.
- The study combines typical phases 2a and 2b of a clinical trial into a single study.
  - **Part A:** 16-week proof-of-concept period, followed by a 36-week maintenance period, and then a 52-week follow-up period (**Figure 3**).
  - **Part B:** global 16-week dose-optimization period, followed by a 36-week maintenance period, and then a 52-week follow-up period (**Figure 4**).
- Participants who complete the maintenance treatment period may be eligible to participate in a separate long-term extension (LTE) study.

Inclusion criteria

- Adults ≥18 years of age.
- Diagnosis of atopic dermatitis that has been present for ≥1 year prior to the screening visit.
- Moderate-to-severe atopic dermatitis at screening and baseline visits.
  - EASI ≥16, IGA ≥3, BSA ≥10%.
- History of inadequate response to treatment with topical medications, or medical determination that topical therapies are inadvisable.
- Applied a stable dose of non-medicated over-the-counter emollient/moisturizer for ≥14 days prior to baseline visit and agree to use same moisturizer at the same frequency throughout the study.
- Have completed itch questionnaires in the electronic diary for ≥4 of 7 days prior to baseline visit.

Exclusion criteria

- Participation in a prior study with APG777.
- Prior treatment with protocol-specified monoclonal antibodies.
- Use of any atopic dermatitis-related topical medications within 7 days prior to baseline visit.
- Use of systemic treatments (other than biologics) and/or phototherapies and/or laser therapy that could affect atopic dermatitis within 4 weeks prior to baseline visit.

Study Endpoints

Objectives	Endpoints
Efficacy	**Primary endpoint:** Percentage change in **EASI** from baseline at Week 16. **Secondary endpoints:** ● **EASI** 50, 75, 90, and 100. ● **vIGA** 0 (clear) or 1 (almost clear) and a 2-point reduction from baseline. ● Change in **BSA**. ● 4-point responder analysis in **Itch NRS**.
Safety	Safety evaluations, including TEAEs.

BSA, Body Surface Area; EASI, Eczema Area and Sensitivity Index; vIGA, validated Investigator Global Assessment; NRS, Numerical Rating Scale

Study Status

- The APEX study (NCT06395948) is currently enrolling.

For further information please contact ClinicalTrials@apogeetherapeutics.com

References

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