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**).
- Results 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 77 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

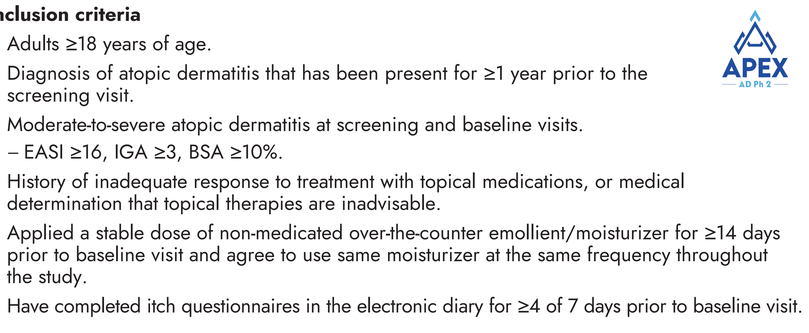
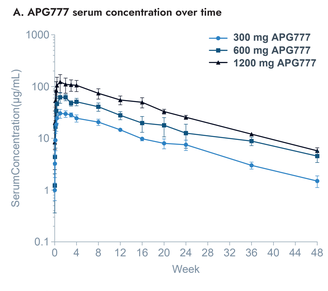
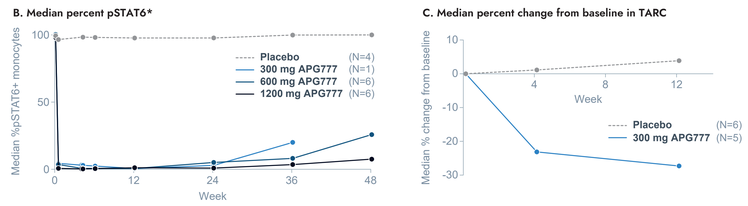


Figure 2. Phase 1 data demonstrate that APG777 has a half-life of 77 days and strongly inhibits downstream biomarkers pSTAT6 and TARC[4]



- Pharmacokinetic data demonstrated dose-proportionality and half-life of 77 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

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

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.

Methods

Figure 3. Design of the 2-part APEX study: Part A Proof of Concept (N~110)

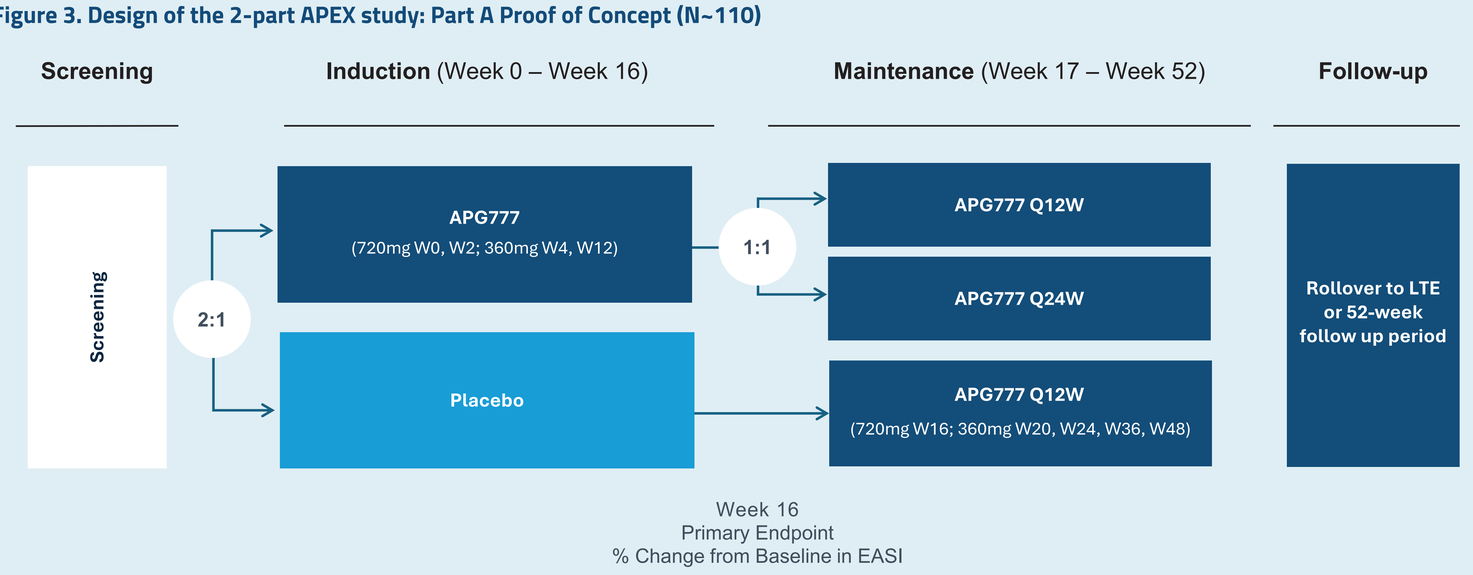
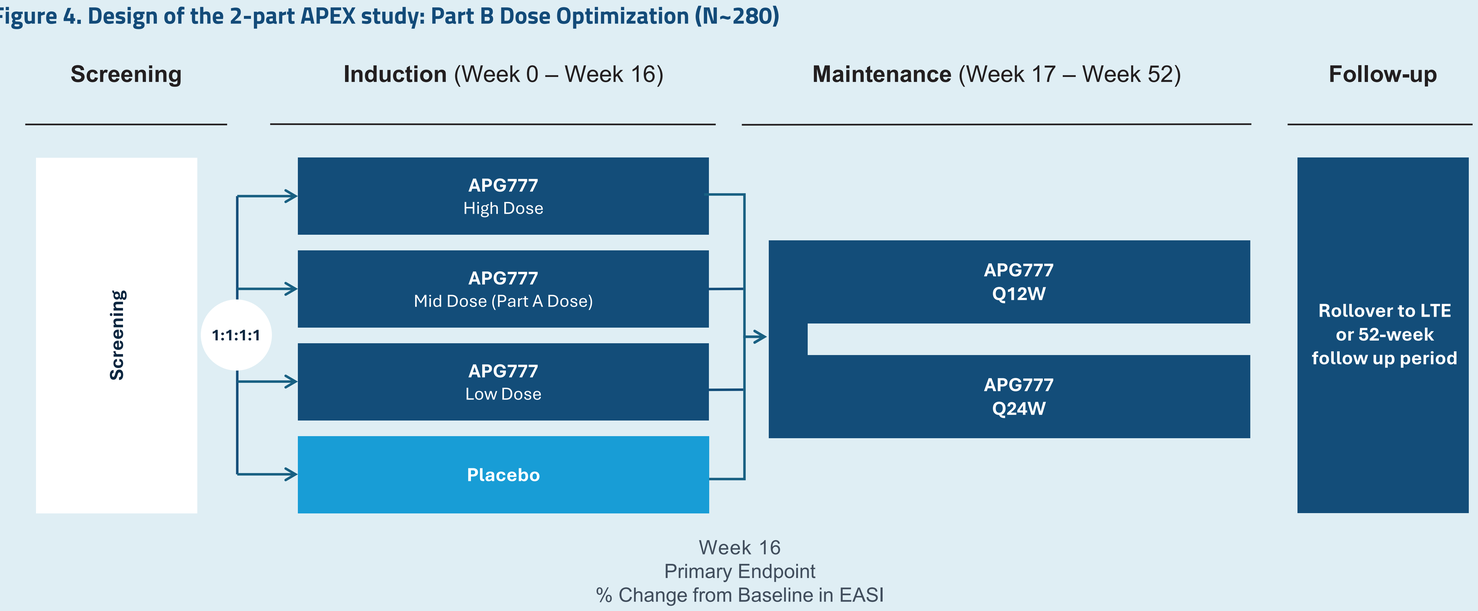


Figure 4. Design of the 2-part APEX study: Part B Dose Optimization (N~280)



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.

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; TEAE, Treatment Emergent Adverse Event

Study Status

- The APEX study (NCT06395948) is currently enrolling.

For further information please contact ClinicalTrials@apogeetherapeutics.com

Acknowledgments and Disclosures

- Apogee Therapeutics supports the APEX study and provided support for the development of this poster.
- Medical writing and editorial support was provided by Annalise M. Nawrocki, PhD, of Apogee Therapeutics. Further editing and layout support was provided by Lee Miller of Miller Medical Communications (funded by Apogee Therapeutics).
- **EG-Y** has received research grants from and/or is a consultant for: Research Grants (paid to the institution): Leo Pharma, Pfizer, Amgen, GSK, Incyte, Sanofi, Bristol Meyers Squibb, Aslan, Regeneron, Anaptysbio, Concert, Janssen, Q32Bio, Abbvie, Eli-Lilly, Arcutis, Inmagene Bio. Consultant: Abbvie, Arcutis , Almirall, Amgen, AnaptysBio, Apogee Therapeutics, Apollo Therapeutics Limited, Artax Biopharma Inc., Astria, Bristol Meyers Squibb, Boerhinger-Ingelhiem, Callidita, Cara Therapeutics, Celldex, Centrexion Therapeutics Corporation, Connect Biopharm, Coty, DBV Technologies, Eli Lilly, Enveda Biosciences, Escient Pharmaceuticals, Inc., Fairmount Funds Management LLC, FL2022-001, Inc., Galderma, Gate Bio, Google Ventures (GV), GSK Immunology, Incyte, Inmagene, Janssen Biotech, Jasper Therapeutics, Kymera Therapeutics, Kyowa Kirin, Leo Pharma, Matchpoint Therapeutics, Merck, Nektar Therapeutics, Novartis Pharmaceuticals, NUMAB Therapeutics AG, Nuvig, OrbiMed Advisors LLC, OTSUKA, Pfizer, Pharmaxis Ltd, Pioneering Medicine VII, Inc., Proteologix US Inc, RAPT, RayThera, Inc, Regeneron Pharmaceuticals, RibonTherapeutics, Inc., Rocatinlimab, SAGIMET Biosciences, Sanofi, SATO, Schrödinger, Inc., Sityx, Sun Pharma Advanced Research Company (SPARC), Takeda, Teva Branded Pharmaceutical Products R&D, Inc, TRex, UCB, Ventyx Biosyences. **KK** has received consulting fees, honoraria, grant support, and/or lecture fees from AbbVie, Amgen, Eli Lilly, Kyowa Kirin, Japan Tobacco, LEO Pharma, Maruho, Mitsubishi Tanabe, Ono Pharmaceutical, Pfizer, Procter & Gamble, Sanofi, Taiho, and Torii Pharmaceutical. **AB**, **JS**, and **MG** have no disclosures to report. **MO**, **LX**, **AW**, **CD**, and **KN** are employees of Apogee Therapeutics and own Apogee stock/stock options.

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