APEX: An integrated phase 2 program evaluating APG777, a half-life extended anti-IL-13 monoclonal antibody, in atopic dermatitis

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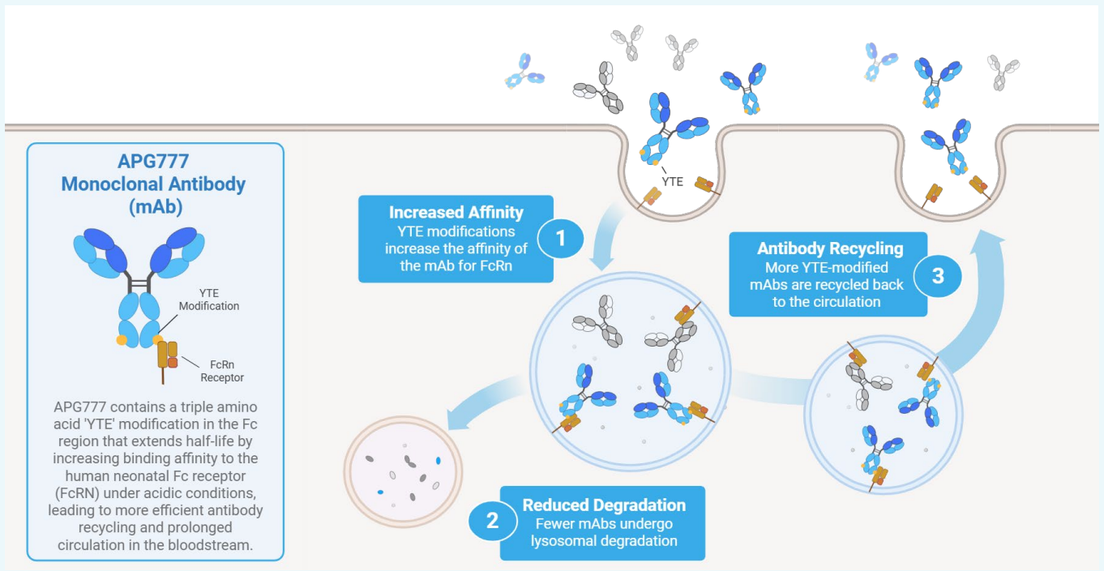
INTRODUCTION

- IL-13 plays a key role in the pathophysiology of atopic dermatitis (AD), particularly in driving the chronic inflammation, skin barrier dysfunction, and persistence of itch associated with the disease.[1,2]
- APG777 is a first-in-class, extended half-life humanized IgG1 monoclonal antibody (mAb) that binds with high affinity to IL-13, preventing formation of the IL-13Rα1/IL-4Rα heterodimer and subsequent IL-13-mediated signaling.
- In a first-in-human phase 1 study, APG777 demonstrated:[3]
  - A half-life of 75.3–77.5 days across doses tested, approximately 3-fold longer than with currently approved anti-IL-13 therapies.
  - Robust and sustained inhibition of key IL-13 biomarkers associated with Type 2 inflammation.

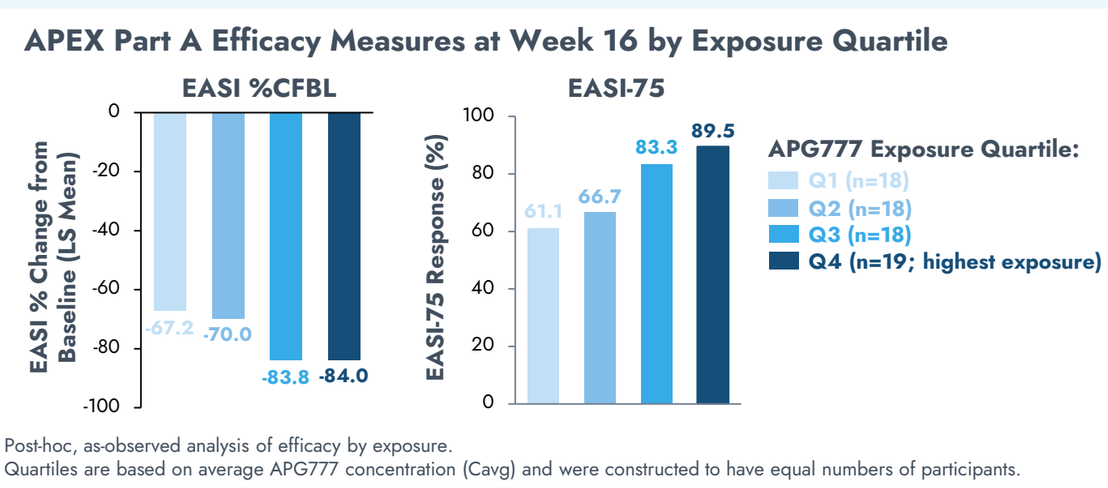
Figure 1: APG777 half-life extension through YTE modification



APG777's extended half-life of ~77 days enables evaluation of every 12- and 24-week maintenance dosing in APEX

- Anti-IL-13 mAbs have shown a dose-response relationship during the induction period without an increase in adverse events.[6-8]
- In a post hoc analysis of APEX Part A results, higher exposures to APG777 led to greater mean percent reductions in EASI and higher percentages of participants achieving EASI-75 at week 16 (**Figure 2**).[5]

Figure 2: Exposure-response relationship for APG777 in AD



Post-hoc, as-observed analysis of efficacy by exposure.
Quartiles are based on average APG777 concentration (Cavg) and were constructed to have equal numbers of participants.

Demonstration of an exposure-response relationship supports evaluation of higher doses of APG777 in APEX Part B

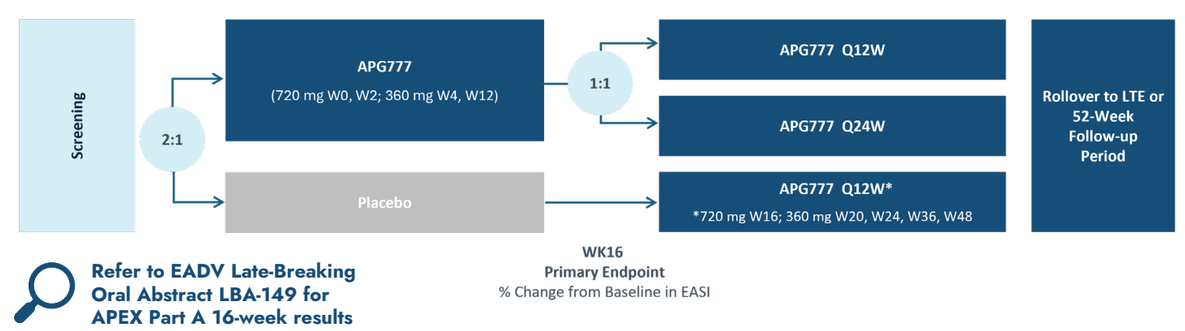
STUDY OBJECTIVE

APEX (APG777-201; NCT06395948) is a two-part, randomized, double-blind, placebo-controlled phase 2 study, evaluating APG777 administered every 12 or 24 weeks in maintenance, in adults with moderate-to-severe AD.

STUDY DESIGN

Figure 3: Design of APEX Part A: Proof of concept (N=123)

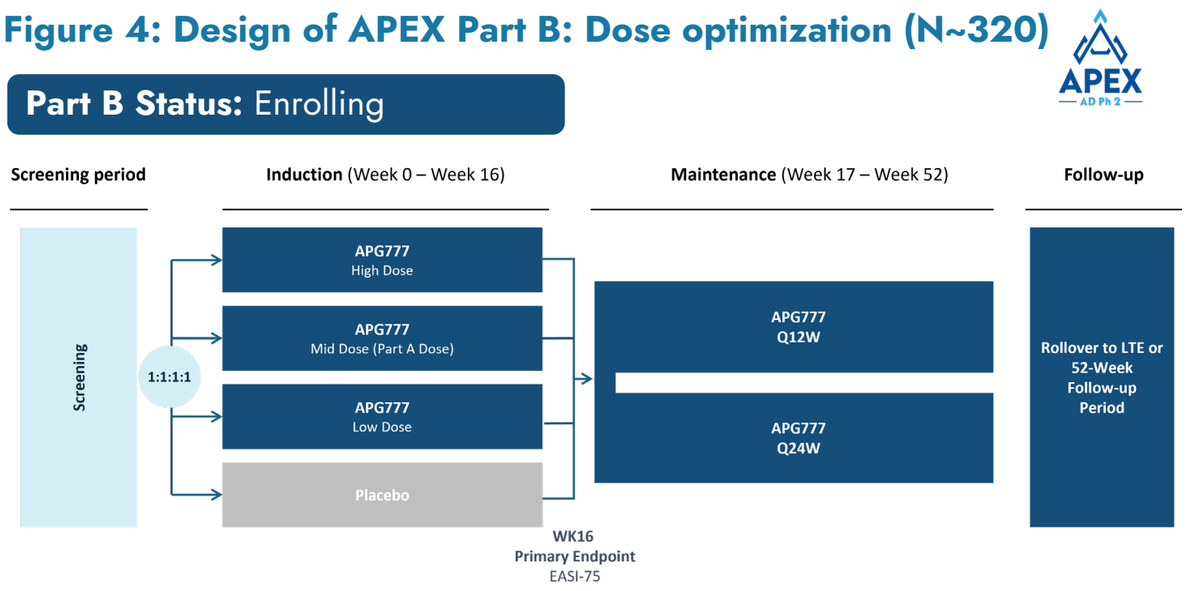
Part A Status: Enrollment complete



Refer to EADV Late-Breaking Oral Abstract LBA-149 for APEX Part A 16-week results

Figure 4: Design of APEX Part B: Dose optimization (N~320)

Part B Status: Enrolling



Design of the 2-part APEX study

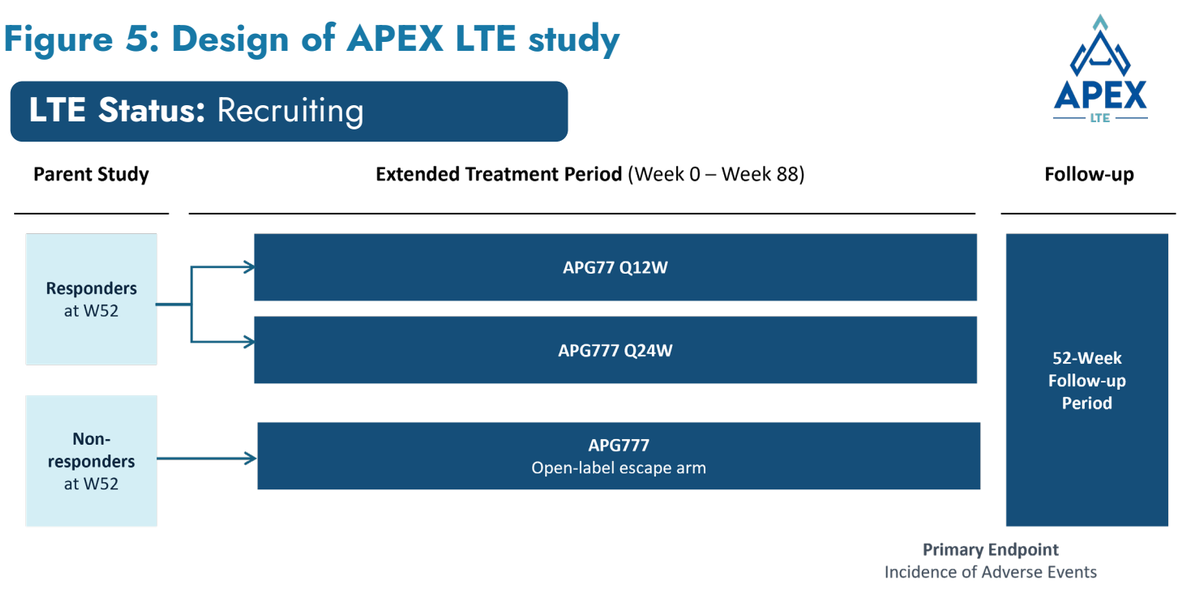
- APEX (APG777-201; NCT06395948) is a phase 2 study evaluating APG777 in adults (≥18 years) with moderate-to-severe atopic dermatitis (EASI ≥16, vIGA-AD score ≥3, BSA ≥10%).
- The study combines typical phases 2a and 2b into a single study:
  - **Part A**, Proof of Concept, consists of a 16-week induction period, followed by a 36-week maintenance period, and then a 52-week follow-up period (**Figure 3**).
  - **Part B**, Dose Optimization, is a global study evaluating 3 doses of APG777 in induction, followed by a 36-week maintenance period, and then a 52-week follow-up period (**Figure 4**).

APEX long-term extension (LTE) study

- Participants who complete the maintenance period may be eligible to participate in a separate long-term extension (LTE) study (APG777-202; NCT06395948).
- APEX LTE consists of a screening visit (coinciding with the last visit of the maintenance period in the parent study), an extended treatment period, and a post-treatment follow-up period (**Figure 5**).

Figure 5: Design of APEX LTE study

LTE Status: Recruiting



ABBREVIATIONS

AD, atopic dermatitis; BSA, body surface area; CFBL, change from baseline; EASI, Eczema Area and Severity Index; EASI-75, 75% improvement in EASI; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; IL, interleukin; LTE, long-term extension; mAb, monoclonal antibody; Q, quartile; Q12W, every 12 weeks; Q24W, every 24 weeks; vIGA-AD, Validated Investigator Global Assessment for AD; W, week; YTE, triple amino acid modification that extends antibody half-life

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ACKNOWLEDGEMENTS AND DISCLOSURES

- Apogee Therapeutics, Inc. sponsored the study reported in this poster.
- Medical writing and editorial support for this poster was provided by Kate Smigiel, PhD, of Apogee Therapeutics, Inc. and Apollo Medical Communications on behalf of Apogee Therapeutics, Inc.
- Author disclosures: **JS** has received honoraria as a consultant and/or advisory board member for Abbvie, Aldena, Amgen, AObiome, Apollo, Arcutis, Arena, Attovia, Boehringer-Ingelheim, Bristell-Meyers Squibb, Castle Biosciences, Connect Biopharma, Corevitas, Dermavant, Eli Lilly, FIDE, Formation Bio, Galderma, GlaxoSmithKline, Immunocore, Incyte, Inmagene, Invea, Leo Pharma, Merck, Nektar, Novartis, Pfizer, RAPT, Recludix, Regeneron, Sandoz, Sanofi-Genzyme, Shaperon, TARGET-RWE, Teva, Triveni, UCB, Union, UpToDate; speaker for Abbvie, Arcutis, Dermavant, Eli Lilly, Galderma, Leo Pharma, Pfizer, Regeneron, Sanofi-Genzyme; institution received grants from Galderma, Incyte, Pfizer; **MG** has served as an investigator, speaker and/or advisor for: AbbVie, Acelyrin, Alumis, Amgen, Akros, Arcutis, Aristea, AnaptysBio, Apogee, Bausch Health, BMS, Boehringer Ingelheim, Dermira, Dermavant, Eli Lilly, Galderma, GSK, Incyte, Inmagene, JAMP Pharma, Janssen, LEO Pharma, L'Oreal, MedImmune, Meiji, Moonlake, Nektar, Nimbus, Novartis, Organon, Oruka, Pfizer, Q32 Bio, Regeneron, Sanofi Genzyme, Sun Pharma, Tarsus, Takeda, UCB, Union, Ventyx and Vyne; **KE** is an advisory board member and/or speaker for AbbVie, Almirall, Apogee, BMS, Boehringer Ingelheim, Leo, Lilly, Janssen, Novartis, Pfizer, Sanofi, Sitryx, and UCB and co-founder and shareholder of Dermagnostix and Dermagnostix R&D; **AB** has served as a speaker (received honoraria) for Almirall, Eli Lilly and Company, and UCB; has served as a scientific adviser (received honoraria) for AbbVie, Almirall, Alumis, Amgen, Anaptysbio, Apogee, Arcutis, Astria, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Corvus, Dermavant, Eli Lilly and Company, Galderma, GlaxoSmithKline, Immunovant, Incyte, IQVIA, Janssen, Leo, Lipidio, Merck, Novartis, Oruka, Paragon, Pfizer, Rani Therapeutics, Regeneron, Sanofi, Spherix Global Insights, Sun Pharma, Syncona, Takeda, UCB, Union, and Zai Lab; has acted as a clinical study investigator (institution has received clinical study funds) for AbbVie, Acelyrin, Almirall, Alumis, Amgen, Arcutis, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Galderma, Incyte, Janssen, Leo, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, Takeda, and UCB; and owns stock in Lipidio and Oruka; **KK** has received consulting fees, honoraria, grant support, and/or lecture fees from AbbVie, Amgen, Apogee Therapeutics, Inc., Eli Lilly, Kyowa Kirin, Japan Tobacco, LEO Pharma, Maruho, Mitsubishi Tanabe, Ono Pharmaceutical, Pfizer, Procter & Gamble, Sanofi, Taiho, and Torii Pharmaceutical; **E-GY** is an employee of Mount Sinai and has received research grants (paid to the institution) from and/or is a consultant for: Abbvie, Aclaris Therapeutics, Almirall, Alumis, Amgen, AnaptysBio, Apogee Therapeutics, Apollo Therapeutics, Arcutis, Artax Biopharma, Astria, Boerhinger-Ingelheim, Bristol Meyers Squibb, Celldex, Centrexion Therapeutics, Connect Biopharm, Concerto Biosciences, Coty, DBV, Dualitas Therapeutics, Eli Lilly, Enveda Biosciences, Escient Pharmaceuticals, Galderma, Gate Bio, GSK, GSK Immunology, Incyte, Inmagene, Janssen Biotech, Jasper Therapeutics, Kymera Therapeutics, Kyowa Kirin, LEO Pharma, Matchpoint Therapeutics, Merck, Nektar Therapeutics, NUMAB Therapeutics, Obsidio, OTSUKA, Pfizer, Pharmaxis, Proteologix, Q32 Bio, RAPT, RayThera, Regeneron, Ribon Therapeutics, Sanofi, SATO, Schrödinger, Sitryx, Sun Pharma, Takeda, Teva, TRex Bio, UCB, VRG Therapeutics, Xencor; **SW**, **LX**, **AW**, **CD**, and **KN** are employees of Apogee Therapeutics, Inc. and own Apogee stock/stock options.

Poster number: P0535

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Presented at the European Academy of Dermatology and Venereology (EADV) Congress, Paris, France, September 17 – 20, 2025