

APG777, a half-life-extended mAb targeting IL-13, demonstrates rapid and sustained inhibition of serum TARC levels in patients with moderate-to-severe atopic dermatitis

Emma Guttman-Yassky¹, Sai Thankamony², Melinda Gooderham³, Jonathan I. Silverberg⁴, Andrew Blauvelt⁵, Kristine Nograles², Carl L. Dambkowski², Lukas Dillinger², Kenji Kabashima⁶

¹Icahn School of Medicine at Mount Sinai, New York, NY; ²Apogee Therapeutics, Inc., Waltham, MA; ³SKIN Centre for Dermatology, Peterborough, ON, Canada and Queen's University, Kingston, ON, Canada; ⁴George Washington University School of Medicine and Health Sciences, Washington, DC; ⁵Blauvelt Consulting, LLC, Annapolis, MD; ⁶Kyoto University Graduate School of Medicine, Kyoto, Japan

INTRODUCTION

- IL-13 plays a key role in the pathophysiology of AD, particularly in driving the chronic inflammation, skin barrier dysfunction, and persistence of itch associated with the disease.^{1,2}
- TARC is an IL-13 pathway-dependent biomarker that is known to correlate with AD disease severity.^{3,4}
- APG777 is a first-in-class, extended half-life humanized IgG1 mAb that binds with high affinity to IL-13, preventing formation of the IL-13Rα1/IL-4Rα heterodimer and subsequent IL-13-mediated signaling.⁵
- In a first-in-human phase 1 study, APG777 demonstrated a half-life of 75.3–77.5 days across doses tested and robust and sustained inhibition of key IL-13 biomarkers associated with Type 2 inflammation.⁶
- APEX (APG777-201; NCT06395948), a two-part, randomized, double-blind, placebo-controlled phase 2 study in adults with moderate-to-severe AD, met the primary endpoint at Week 16, demonstrating a 71.0% decrease from baseline in mean EASI at Week 16.⁷
 - APG777 was well tolerated, with a safety profile consistent with other therapies targeting the IL-13 or IL-4/IL-13 pathway.
- Here, we describe the impact of APG777 on TARC from Part A of the APEX study.

CONCLUSIONS

- TARC is a Type 2 biomarker that correlates with disease severity in AD, as confirmed by baseline characteristics and correlation analyses of patients enrolled in APEX Part A.
- Treatment with APG777 induces a rapid and sustained reduction in TARC, with patients approaching normalization of TARC levels (~450 pg/mL)³ by Week 4, demonstrating a robust PD effect.
- Reductions in TARC correlate significantly with reductions in EASI, supporting the clinical relevance of the PD effect observed with APG777.
- Higher APG777 exposures led to greater TARC reductions, supporting evaluation of higher doses in future studies.
- The observed reductions in TARC suggest meaningful modulation of IL-13 signaling by APG777 and support the mechanistic rationale for APG777 as a potent IL-13 inhibitor targeting a pathogenic driver in AD.

STUDY OBJECTIVE

To evaluate the PD effect of APG777 on TARC, a key Type 2 inflammatory biomarker in patients with moderate-to-severe AD.

RESULTS

- Baseline TARC levels were well balanced between APG777 and placebo arms (median APG777: 1047.28 pg/mL; placebo: 769.69 pg/mL).
- Baseline TARC levels correlated with baseline EASI (r=0.44, p<0.0001).

Figure 1: TARC approaches normal levels (~450 pg/mL) by Week 4

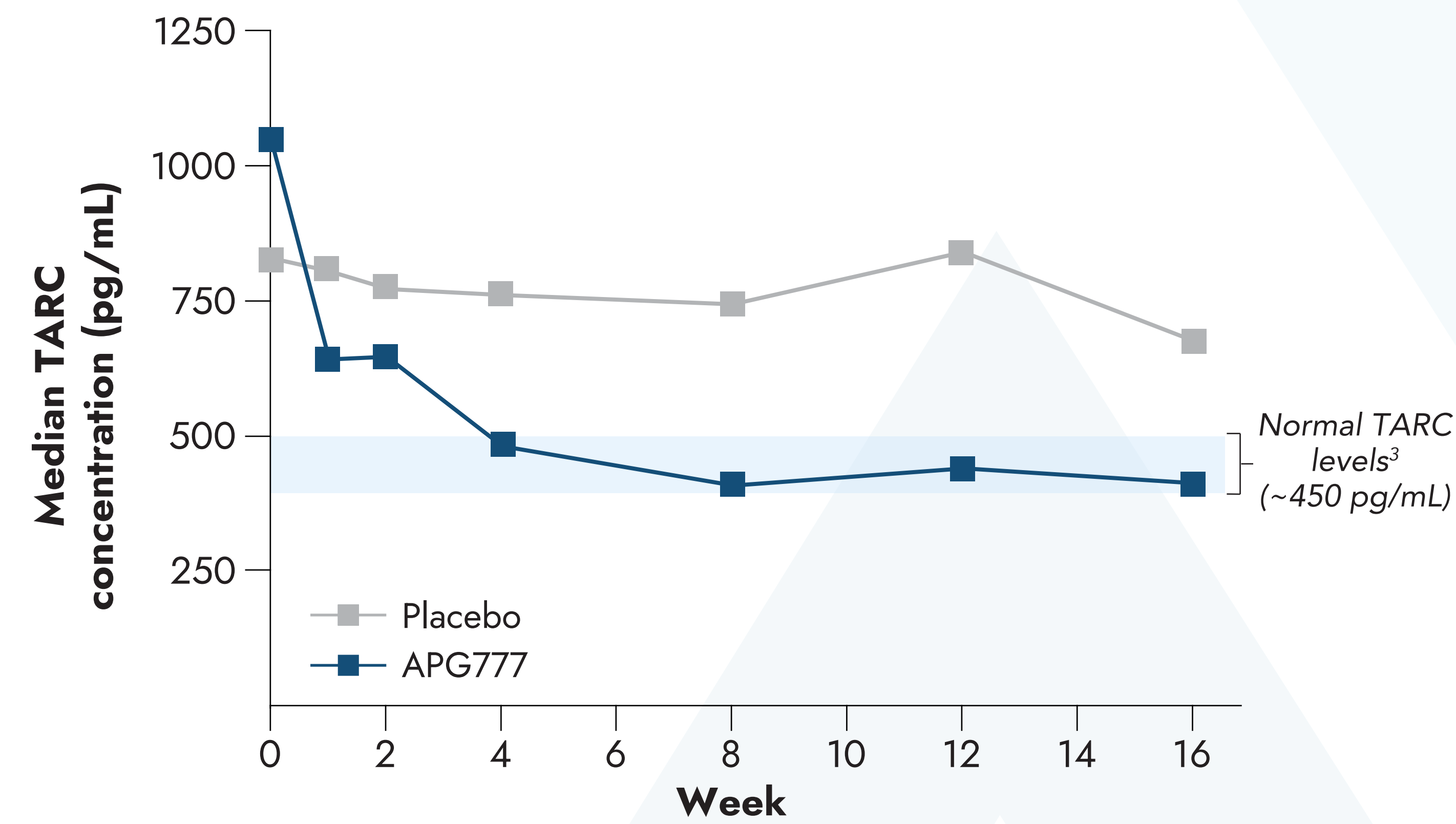
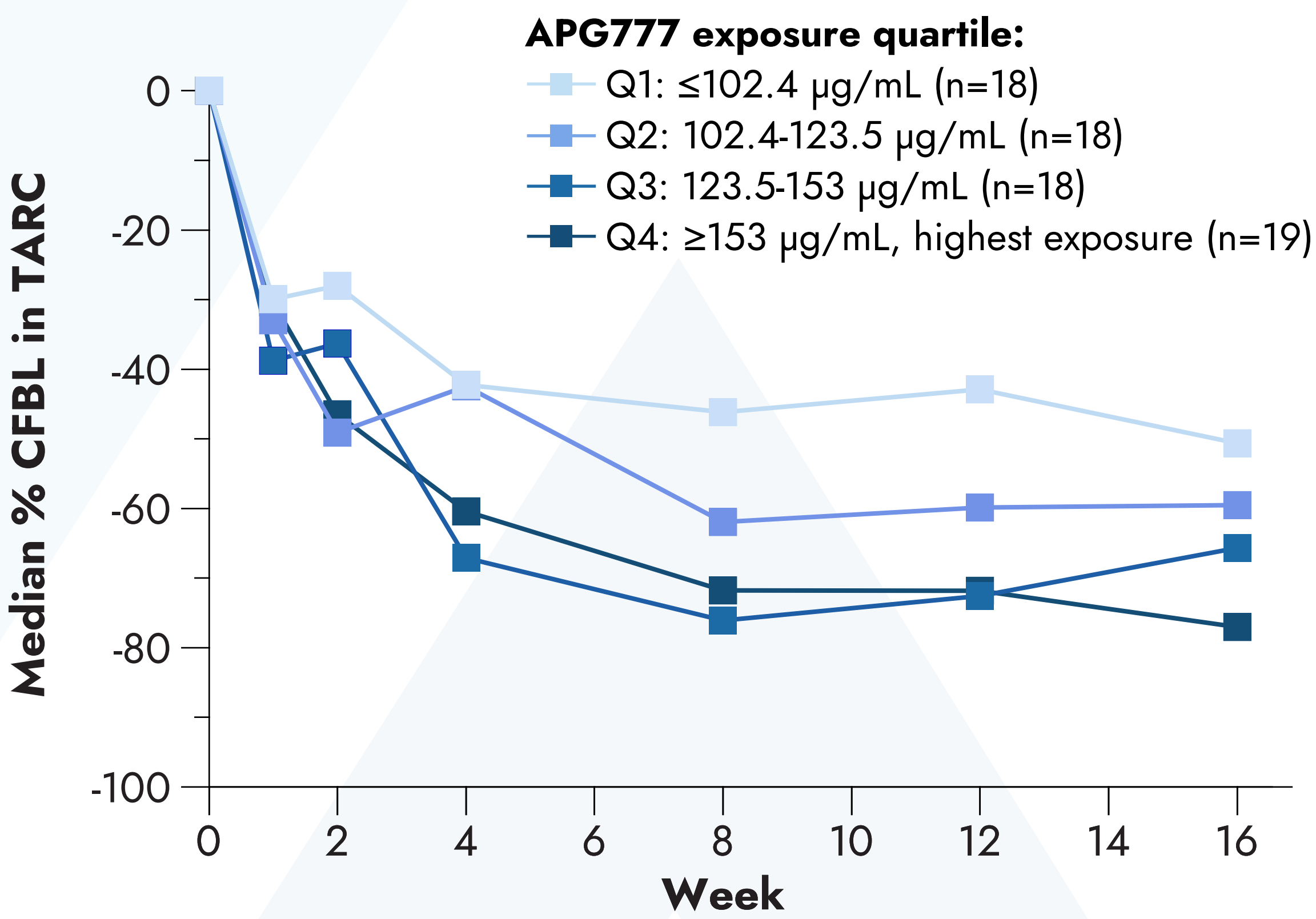


Figure 2: Reduction in TARC follows an exposure-response relationship



- The median TARC levels in the APG777 group approached the reported normal level of ~450 pg/mL³ by Week 4 (Figure 1).
- Reduction in TARC levels correlated significantly with % CFBL in EASI (pooled Weeks 4, 12, and 16; r=0.37, p<0.001).

- Higher serum concentration of APG777 led to a greater reduction in serum TARC (Figure 2), supporting the need for further dose optimization and evaluation of higher doses of APG777 in APEX Part B.

METHODS

- Serum samples were collected from Part A of the APEX phase 2 study, a multicenter, placebo-controlled, double-blind, randomized study of APG777 in moderate-to-severe AD (NCT06395948).
- A total of 123 adult patients were randomized 2:1 to receive a 720 mg loading dose of APG777 or matching placebo subcutaneously on Day 1 and Week 2, followed by 360 mg at Weeks 4 and 12.
- Time points for serum collection included pretreatment/baseline and posttreatment time points (Weeks 1, 2, 4, 8, 12, and 16).
- To evaluate the PD response of APG777 on TARC, samples were analyzed using a validated TARC immunoassay based on an electrochemiluminescence platform (Mesoscale Discovery).
- Serum concentrations of TARC were calculated by interpolation from the run-defined calibration curve and adjusted for 2-fold sample dilution for reporting the final concentration.
- Serum concentration of TARC is reported in pg/mL for baseline and at specified time points.
- Spearman correlation was calculated for baseline TARC and EASI and for % CFBL in TARC and % CFBL in EASI (Weeks 2, 4, 12, and 16).
- In a post hoc analysis, exposure-response relationship between TARC levels and serum exposures to APG777 was determined. Quartiles are based on average APG777 concentration and were constructed to have equal numbers of participants in each quartile.
- In a post hoc analysis, to understand the change in TARC during the study, median serum protein levels were plotted for both the APG777 and placebo groups at Weeks 0, 1, 2, 4, 8, 12, and 16.

ABBREVIATIONS
AD, atopic dermatitis; CFBL, change from baseline; EASI, Eczema Area and Severity Index; Ig, immunoglobulin; IL, interleukin; IL-13Rα1, interleukin 13 receptor alpha 1; IL-4Rα, interleukin 4 receptor alpha; mAb, monoclonal antibody; PBO, placebo; PD, pharmacodynamic; Q, quartile; TARC, thymus and activation-regulated chemokine.

REFERENCES
1. Gorelick J, et al. *Am J Clin Dermatol*. 2025;26(2):199-211.
2. Miron Y, et al. *J Allergy Clin Immunol*. 2022;150(3):690-700.
3. Hijnen D, et al. *J Allergy Clin Immunol*. 2004;113(2):334-340.
4. Furue M, et al. *J Derm Science*. 2012;66(1):60-63.
5. Zhu E, et al. *J Allergy Clin Immunol Global*. 2025;4(4):1-8.
6. Lim X-Q, et al. Presented at: WSAAI 2025; Feb 9-13, 2025; Waimea, HI.
7. Guttman E, et al. Presented at: EADV 2025; Sep 17-20, 2025; Paris, France.

ACKNOWLEDGMENTS AND DISCLOSURES
• Apogee Therapeutics, Inc. sponsored the studies reported in this poster.
• Medical writing and editorial support for this poster were provided by Namita Gandhi of Apogee Therapeutics, Inc. and Aidan Moriarty, PhD, and Paula Stuckart of Apollo Medical Communications, on behalf of Apogee Therapeutics, Inc.
• Author disclosures: **EGY** is an employee of Mount Sinai and has received research grants (paid to the institution) from and/or is a consultant for: AbbVie, Actavis Therapeutics, Almirall, Alkermes, Amgen, AnaptysBio, Apogee Therapeutics, Apollo Therapeutics, Arcutis, Artax Biopharma, Astra, Boehringer-Ingelheim, Bristol Myers Squibb, Celldex, Centexon Therapeutics, Connect BioPharm, Concerto Biosciences, Cytex, DBV, Dualitas Therapeutics, Eli Lilly, Enveda Biosciences, Escent Pharmaceuticals, Galderma, Gilead, GSK, GSK Immunology, Incyte, Immagine, Janssen Biotech, Jaxx Therapeutics, Kymira Therapeutics, Kyowa Kirin, LEO Pharma, Matchpoint Therapeutics, Merck, Nektar Therapeutics, NIMAB Therapeutics, Obisidlo, OTSUKA, Pfizer, Pharmaxis, Proteologix, Q32 Bio, RAPT, RayThera, Regeneron, Ribon Therapeutics, Sanofi, SATO, Schrödinger, Sitryx, Sun Pharma, Takeda, Teva, TReX Bio, UCB, VRG Therapeutics, Xenor. **MG** has served as an investigator, speaker and/or advisor for: AbbVie, Acetylin, Alkermes, Amgen, Akros, Arcutis, Arista, AnaptysBio, Apogee, Bausch Health, BMS, Boehringer Ingelheim, Dermira, Dermavant, Eli Lilly, Galderma, GSK, Incyte, Immagine, JAMP Pharma, Janssen, LEO Pharma, L'Oréal, MedImmune, Meiji, Moonlake, Nektar, Nimbus, Novartis, Organon, Orluma, Pfizer, Q32 Bio, Regeneron, Sanofi Genzyme, Sun Pharma, Takeda, UCB, Union, Ventyx and Vyne. **JIS** has received honoraria as a consultant and/or advisory board member for AbbVie, Aldena, Amgen, AOBio, Apollo, Arcutis, Arena, Atova, Boehringer-Ingelheim, Bristol Myers Squibb, Castle Biosciences, Connect BioPharma, Corevix, Dermavant, Eli Lilly, FIDE, Forman Bio, Galderma, GlaxoSmithKline, Immunocore, Incyte, Immagine, Invea, Leo Pharma, Merck, Nektar, Novartis, Pfizer, RAPT, Reclutix, 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, and Pfizer. **AB** has served as a speaker (received honoraria) for Almirall, Eli Lilly and Company, and UCB; has served as a scientific advisor (received honoraria) for AbbVie, Almirall, Alkermes, Amgen, AnaptysBio, Apogee, Arcutis, Astra, Boehringer-Ingelheim, Bristol Myers Squibb, Celltrion, Corvus, Dermavant, Eli Lilly and Company, Galderma, GlaxoSmithKline, Immunovant, Incyte, IQVIA, Janssen, Leo, Lipidix, Merck, Novartis, Orluma, Paragon, Pfizer, Rati Therapeutics, Regeneron, Sanofi, Spharix 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, Acetylin, Almirall, Alkermes, 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 Lipidix and Orluma. **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. **CLD** is an employee of Apogee Therapeutics, Inc. and holds company stock/stock options; serves on the board of directors of Junevity, Orluma Therapeutics, Inc.; and holds stock/stock options in Orluma, Spyre, and Junevity. **ST, KN**, and **LD** are employees of Apogee Therapeutics, Inc. and hold company stock/stock options.

Scan to access digital poster



For questions, please contact MedAffairs@apogee therapeutics.com