Apogee Announces Positive Interim Results from Phase 1 Healthy Volunteer Trial for APG777, its Novel Half-Life Extended Anti-IL-13 Antibody for the Treatment for Atopic Dermatitis and Other Inflammatory Diseases, Exceeding its Trial Objectives Ahead of Schedule with Half-Life of Approximately 75 Days

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Pharmacokinetic data support potential best-in-class profile with potential for improved clinical responses from greater exposures in induction than currently available biologic therapies and maintenance dosing of every 3- or 6-months

Single dose showed deep and sustained inhibition of key atopic dermatitis biomarkers pSTAT6 and TARC for ~3 months (longest follow-up available with inhibition still ongoing at time of data cut)

APG777 was well tolerated with a favorable safety profile consistent with the anti-IL-13 class

Company plans to initiate a randomized, placebo-controlled, 16-week Phase 2 clinical trial in patients with moderate-to-severe atopic dermatitis in 1H 2024 with induction regimen designed to exceed lebrikizumab exposures by ~30-40% and every 3- or 6- month maintenance dosing

High dose concentration of 180 mg/mL will enable 44% higher dose than lebrikizumab in the same volume

Management will host a webcast and conference call today at 7:00 a.m. ET

SAN FRANCISCO and WALTHAM, Mass., March 05, 2024 (GLOBE NEWSWIRE) -- Apogee Therapeutics, Inc. (Nasdaq: APGE), a clinical-stage biotechnology company advancing differentiated biologics for the treatment of atopic dermatitis (AD), chronic obstructive pulmonary disease, asthma and other inflammatory and immunology (I&I) indications, today announced positive interim Phase 1 data from its first-in-human study of APG777, one of its lead product candidates being developed as a frontline treatment for moderate-to-severe AD and other inflammatory diseases. Pharmacokinetic (PK) data showed a half-life of approximately 75 days across doses tested and Pharmacodynamic (PD) data showed deep and sustained inhibition of key AD biomarkers pSTAT6 and TARC for ~3 months (longest follow-up available, with inhibition still ongoing at time of the data cut).

Results from the trial exceeded the Company's trial objectives and support the potential for APG777, a novel anti-IL-13 antibody, to optimize exposure levels in 16-week induction and be dosed once every three or six months in maintenance. These findings represent the potential for improved clinical responses from greater exposures in induction and significantly less frequent dosing in maintenance compared to currently approved biologic therapies, which are dosed at every two to four weeks, a potential major advancement for patients with AD and other inflammatory diseases. APG777, in single doses up to 1,200mg and multiple doses of 300mg, was well tolerated and showed a favorable safety profile, in line with the existing body of third-party evidence for the safety of the anti-IL-13 class. Based on these data, the company plans to initiate a randomized, placebo-controlled, Phase 2 clinical trial in patients with moderate-to-severe AD in the first half of 2024 ahead of schedule.

"The positive PK, PD and safety findings from our Phase 1 trial mark the first clinical data ahead of schedule from our portfolio of potentially differentiated biologics and underscore the promising potential of APG777 to offer patients a transformational therapy that could drive improved clinical responses than the current standard of care and extend dosing to every three or six months," said Michael Henderson, M.D., Chief Executive Officer of Apogee. "We are excited to embark on the next phase of development for APG777, with plans to initiate our Phase 2 clinical trial in the first half of this year while rapidly progressing the rest of our pipeline forward. At Apogee, we refuse to stop at good enough and are dedicated to advancing innovative solutions for patients. Today's announcement brings us an important step closer to achieving this goal."

"Currently approved therapies for atopic dermatitis and other immunology indications typically call for injections every two to four weeks, which can lead to poor treatment adherence and long-term disease control," said Jonathan Silverberg, MD, PhD, MPH, Professor of Dermatology at The George Washington University School of Medicine and Health Sciences. "I am very encouraged by the initial data from this study, which demonstrate the potential for APG777 as a well-tolerated treatment with a half-life that would support less frequent injections."

"Significant unmet need remains for patients with moderate-to-severe AD, many of whom continue to have symptomatic disease on current therapies," said Emma Guttman-Yassky, MD, PhD, the Waldman Professor of Dermatology and Immunology and Health System Chair of Dermatology at the Icahn School of Medicine at Mount Sinai in New York City. "APG777's Phase 2 trial will test an important hypothesis, greater inhibition of the pathway during induction, to see if improved clinical responses can be delivered for patients living with AD."

APG777 is a novel, subcutaneous extended half-life monoclonal antibody targeting IL-13 – a critical cytokine in inflammation and a primary driver of AD. In our head-to-head preclinical studies, APG777 demonstrated equivalent or better potency to lebrikizumab in the inhibition of IL-13 signaling. Based on its potentially best-in-class PK profile, APG777 has the potential for improved clinical responses from greater exposures of drug in induction and dosing as infrequently as once every three or six months. AD is a chronic inflammatory skin disorder which can lead to sleep disturbance, psychological distress, elevated infection risk and chronic pain, all of which significantly impact quality of life. Today's treatments are associated with many challenges, including frequent injection regimens that can lead to poor patient compliance. APG777 represents the first clinical-stage product candidate from the company's strategic collaboration with Paragon Therapeutics, Inc., an innovative discovery engine for biologics.

Key Phase 1 Interim Findings

The Phase 1 trial is a first-in-human, randomized, double-blind, placebo-controlled study designed to evaluate safety and PK of APG777 in healthy volunteers. The study enrolled 40 healthy adult participants into three single-ascending dose (SAD) and two multiple-ascending dose (MAD) cohorts. Doses of subcutaneous APG777 evaluated in the study included 300mg, 600mg and 1,200mg. Detailed findings from the SAD portion and interim

results from MAD portion of the Phase 1 trial are as follows:

- **PK differentiation supports further development of APG777 as a treatment for moderate-to-severe AD and other inflammatory diseases**
  - Potentially best-in-class PK profile, including a half-life of approximately 75 days, supporting:
    - Testing higher exposures of drug in induction to potentially achieve improved clinical responses
    - Testing of maintenance dosing of every 3- or 6-months, representing 2-4 injections per year compared to the current treatment paradigm of 13-26 injections per year
  - Dose-proportional increases in serum concentrations and key parameters (e.g., C_{max}, AUC) were observed in the Phase 1 trial
  - PK was consistent across subjects with low variability

- **Single doses of APG777 demonstrated a deep and sustained effect on PD markers for ~3 months (longest follow-up available with inhibition still ongoing at time of data cut)**
  - Single doses of APG777 suppressed pSTAT6, one of the first downstream markers of IL-13 pathway inhibition, with near-complete inhibition for ~3 months
  - Single doses of APG777 suppressed TARC, an inflammatory mediator and the most strongly correlated biomarker to AD severity, with deep and sustained inhibition for ~3 months

- **Well tolerated across all dose groups.** Single doses of APG777 up to 1,200mg and multiple doses of 300 mg were well tolerated with a favorable safety profile consistent with the existing third-party data supporting the safety of the anti-IL-13 class.
  - The most common treatment-emergent adverse events (TEAEs) were vascular access site pain, vessel puncture site bruise, headache, and vascular access bruising
    - 60% of participants observed at least one TEAE; 15% of participants observed at least one drug-related AE
  - There were no Grade 3 TEAEs or severe adverse events (SAEs). No AEs led to study discontinuation

“The interim results from this Phase 1 trial are tremendously encouraging for APG777’s potential to meaningfully improve the standard of care for patients with moderate-to-severe AD. On behalf of the entire Apogee team, I’d like to extend our heartfelt gratitude to the volunteers, investigator, and the study team for their support in the successful execution of this important trial,” said Carl Dambkowski, M.D., Chief Medical Officer of Apogee Therapeutics. “We look forward to rapidly advancing APG777 into Phase 2 clinical trials in AD and other inflammatory conditions.”

Phase 2 trial in AD

Following today’s positive interim results, Apogee plans to advance APG777 into a randomized, placebo-controlled, 16-week Phase 2 clinical trial in patients with moderate-to-severe AD.

- **Phase 2 AD trial is expected to initiate in the 1H of 2024 with 16-week topline data from Part A expected in 2H 2025**
  - Part A is expected to enroll approximately 110 patients randomized 2:1 to APG777 vs placebo with primary endpoint of mean percentage changes in EASI score from baseline to Week 16
  - Part B of the Phase 2 trial is a randomized, placebo-controlled dose optimization with approximately 360 patients randomized 1:1:1:1 to high, medium, or low dose APG777 vs placebo with primary endpoint of mean percentage changes in EASI score from baseline to Week 16
  - All patients benefiting from treatment will continue to APG777 maintenance, which will evaluate 3- to 6-month dosing

- **Integrated design expected to provide for significant timeline acceleration by combining Ph2a and Ph2b elements into a single study protocol**
    - All Part A sites are also expected to participate in Part B, avoiding delays for site startup between the two parts
- **Doses in the Phase 2 trial are enabled by APG777's potentially best-in-class PK profile, extended half-life, and high-concentration formulation**
    - 180 mg/mL formulation enables 44% higher dose of APG777 vs lebrikizumab in the same volume

- **APG777 Phase 2 induction regimen is designed to exceed lebrikizumab (an IL-13 inhibitor with an overlapping epitope with APG777) exposures by ~30 to 40% with potential for improved clinical responses and maintenance regimen is designed to equal lebrikizumab's exposures**
    - In Phase 3 studies, ~30% higher exposure seen in lebrikizumab low bodyweight group resulted in numerically higher efficacy than the overall study population across all key endpoints, including EASI-75 and more stringent endpoints such as EASI-90 and IGA 0/1
    - ~30-40% higher induction exposures for APG777 than lebrikizumab are based on a planned six injection induction regimen given in the first sixteen weeks of APG777 treatment. This is approximately half as many of the 11 injections of lebrikizumab given during the same period
    - At 52 weeks, exposures of APG777 dosed every three months are designed to exceed those of lebrikizumab and exposures of APG777 dosed every six months are designed to equal those of lebrikizumab

Conference Call and Webcast

Apogee will host a conference call and webcast today, March 5, 2024, at 7:00 a.m. ET to discuss the APG777 Phase 1 interim results. A live webcast of the call will be available on the Investor Relations page of Apogee's website at https://investors.apogeetherapeutics.com/news-events/events. The webcast will be made available for replay on the company's website following completion of the event.

About APG777

APG777 is a novel, subcutaneous extended half-life monoclonal antibody targeting IL-13 for the potential treatment of atopic dermatitis (AD). In head-to-head preclinical studies, APG777 showed equivalent or better potency to lebrikizumab in the inhibition of IL-13 signaling. AD is a chronic inflammatory skin disorder that affects approximately 40 million adults and 18 million children in the United States, France, Germany, Italy, Japan, Spain and the United Kingdom, 40 percent of which have moderate-to-severe disease. Based on initial clinical data, the company may initiate a Phase 2 trial in asthma and plans to further evaluate opportunities to develop APG777 for other I&I indications, including alopecia areata, chronic rhinosinusitis with nasal polyps, chronic spontaneous urticaria, eosinophilic esophagitis and prurigo nodularis.

About Apogee

Apogee Therapeutics is a clinical-stage biotechnology company seeking to develop differentiated biologics for the treatment of atopic dermatitis (AD), chronic obstructive pulmonary disease (COPD), asthma and other inflammatory and immunology indications with high unmet need. Apogee's antibody programs are designed to overcome limitations of existing therapies by targeting well-established mechanisms of action and incorporating advanced antibody engineering to optimize half-life and other properties. The company's two most advanced programs are APG777 and APG808, which are being initially developed for the treatment of AD and COPD, respectively. Based on a broad pipeline and depth of expertise, the company believes it can deliver value and meaningful benefit to patients underserved by today's standard of care. For more information, please visit www.apogeetherapeutics.com.

Financial Disclosures
Dr. Silverberg and Dr. Guttman- Yassky receive financial compensation as a scientific advisor for Apogee.

Forward Looking Statements

Certain statements in this press release may constitute "forward-looking statements" within the meaning of the federal securities laws, including, but not limited to, statements regarding: the efficacy, safety, tolerability, PK and PD profile of APG777, the potential dosing regimen of APG777, the potential superiority of APG777 compared to current therapies, our expectations regarding plans for our current and future product candidates and programs, our plans for our current and future clinical trials, including a Phase 2 trial for APG777, our plans for clinical trial design, the anticipated timing of the initiation of and results from our clinical trials, including data from our Phase 2 trial of AP777, and the potential clinical benefit and half-life of APG777. Words such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "design," "estimate," "predict," "potential," "develop," "plan" or the negative of these terms, and similar expressions, or statements regarding intent, belief, or current expectations, are forward-looking statements. While Apogee believes these forward-looking statements are reasonable, undue reliance should not be placed on any such forward-looking statements, which are based on information available to the company on the date of this release. These forward-looking statements are based upon current estimates and assumptions and are subject to various risks and uncertainties (including, without limitation, those set forth in Apogee's filings with the U.S. Securities and Exchange Commission (the SEC)), many of which are beyond the company's control

and subject to change. Actual results could be materially different. Risks and uncertainties include: global macroeconomic conditions and related volatility, expectations regarding the initiation, progress, and expected results of our preclinical studies, clinical trials and research and development programs; expectations regarding the timing, completion and outcome of our clinical trials; the unpredictable relationship between preclinical study results and clinical study results; the timing or likelihood of regulatory filings and approvals; liquidity and capital resources; and other risks and uncertainties identified in our Quarterly Report on 10-Q for the quarterly period ended September 30, 2023, filed with the SEC on November 13, 2023 , and subsequent disclosure documents we may file with the SEC. Apogee claims the protection of the Safe Harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. Apogee expressly disclaims any obligation to update or alter any statements whether as a result of new information, future events or otherwise, except as required by law.

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