Annexon Outlines Global Registrational Program for ANX007 in Geographic Atrophy with FDA Alignment on Vision Preservation as Primary Endpoint

December 20, 2023

Alignment with FDA on Best Corrected Visual Acuity ≥ 15-Letter Loss as Primary Outcome Measure - Representing the Highest Value Outcome to Patients and Physicians

ARCHER II, a Global Sham-Controlled Trial Supporting a Potentially Faster Path to Registration, Expected to Initiate in Mid-2024

ARROW, a Head-to-Head Trial using SYFOVRE® as an Injection Comparator to Differentiate Vision Protection from Slowing of Lesion Growth, Expected to Initiate in Late 2024

BRISBANE, Calif., Dec. 20, 2023 (GLOBE NEWSWIRE) -- Annexon, Inc. (Nasdaq: ANNX), a clinical-stage biopharmaceutical company developing a new class of complement-based medicines for people living with devastating inflammation-related diseases, today outlined its global registrational program for ANX007, a first-in-class C1q and classical complement inhibitor, for the treatment of patients with geographic atrophy (GA).

Annexon has gained alignment with the U.S. Food and Drug Administration (FDA) on a Phase 3 registration program that includes using, for the first-time, the prevention of ≥15-letter loss of best corrected visual acuity (BCVA) as the primary outcome measure, as well as conducting a comparison of ANX007 to an injection agent, consistent with requests for trials across ophthalmic indications. Notably, the FDA has not required Annexon to study the slowing of lesion growth as measured by fundus autofluorescence (FAF), an anatomical endpoint used for the approval of other GA programs.

“We are thrilled to have aligned with FDA on vision preservation as the primary endpoint in our Phase 3 GA program, based on the statistically significant and dose-dependent visual protection ANX007 demonstrated in the Phase 2 ARCHER trial,” said Douglas Love, chief executive officer of Annexon. “Blocking C1q with ANX007 is designed to stop classical complement inflammation that drives photoreceptor damage and vision loss. Considering the robust preservation of vision demonstrated by ANX007 in the ARCHER trial, and that current FDA-approved treatments have not shown a meaningful functional benefit after years of treatment, we are encouraged by the potential for ANX007 to demonstrate significant protection against vision loss as measured by BCVA ≥15-letter loss in a head-to-head study. We are excited to embark on this global pivotal program with the aim of providing meaningful functional benefit and offering a new transformative treatment to the patients, and their families, affected by GA.”

Annexon’s registration program will initiate first with ARCHER II, a global sham-controlled trial designed to confirm the results from the Phase 2 ARCHER trial, and potentially expedite the path to regulatory approval in Europe, where there are approximately 2.5 million people living with GA. Given the availability of FDA-approved treatments in the U.S., Annexon plans to conduct its injection-controlled head-to-head study, ARROW, against SYFOVRE® (pegcetacoplan injection), with the potential to underscore ANX007’s unique mechanism of action and critical differentiation on visual function. ARCHER II is expected to begin enrollment in mid-2024, followed by ARROW in late 2024.

“For the millions of patients living with GA, loss of sight is coupled with the loss of independence, leaving a significant impact on quality of life,” said Jeffrey S. Heier, M.D., director of the Retina Service and Retina Research, Ophthalmic Consultants of Boston, and an investigator in ARCHER. “It is every physician’s goal to preserve vision for as long as possible. Based on the outcome of the ARCHER trial, I am excited by the potential of ANX007 and its distinct neuroprotective mechanism of action, and I look forward to further understanding its role in the treatment of GA through its robust Phase 3 program.”

ANX007 Global GA Registrational Program Overview

- ARCHER II Global Sham-Controlled Trial: The Phase 3 ARCHER II trial is designed to enroll approximately 400 patients with GA secondary to age-related macular degeneration (AMD) who will be randomized 1:1 to receive a monthly dose of ANX007 or sham procedure. The primary endpoint will be the prevention of ≥15-letter loss of best corrected visual acuity (BCVA), which represents three lines on the standard ETDRS eye chart, in patients assessed through 12 months. BCVA ≥15-letter loss is a well-established functional endpoint that has served as the basis for numerous ophthalmology drug approvals by the FDA and EMA. Key secondary endpoints in ARCHER II include safety, low-luminance visual acuity (LLVA) and low-luminance visual deficit (LLVD).
- ARROW Head-to-Head Trial: The Phase 3 ARROW trial is designed to enroll approximately 500 patients with GA to evaluate a monthly dose of ANX007 versus SYFOVRE® as an injection comparator, an FDA-approved drug shown to slow lesion growth. The primary endpoint will be the prevention of ≥15-letter loss of BCVA assessed through 12 months and is designed to differentiate vision protection from slowing of lesion growth, offering patients a functional benefit alternative.

Annexon continues to engage with the European Medicines Agency following receipt of PRIME designation and will seek feedback from EMA on the pivotal Phase 3 program in the first half of 2024. ANX007 is the first therapeutic candidate for the treatment of GA to receive PRIME designation, which provides early and proactive support to developers of promising medicines that may offer a major therapeutic advantage over existing treatments or benefit to patients without treatment options.

About ANX007 and Phase 2 ARCHER Trial
ANX007 is a fragment antigen-binding (Fab) antibody designed as a first-in-kind therapeutic to selectively inhibit C1q, the initiating molecule of the classical complement pathway, and a key driver of neurodegeneration. In GA, C1q binds to photoreceptor synapses early in the disease process,

causing aberrant activation of the classical pathway with synapse loss, inflammation and neuronal damage that results in vision loss. Intravitreal administration of ANX007 stops C1q and activation of the entire downstream classical pathway to protect photoreceptor synapses and cells essential for vision.

In the randomized, multi-center, double-masked, sham-controlled Phase 2 ARCHER clinical trial, ANX007 demonstrated consistent protection against vision loss in a broad population of patients with GA. Specifically, topline data reported in May 2023 and presented at the American Society of Retina Specialists (ASRS) Annual Meeting in July 2023 showed that ANX007 provided statistically significant, time and dose-dependent protection from vision loss in patients with GA, measured by BCVA ≥ 15-letter loss, the widely accepted and clinically meaningful functional endpoint assessing visual acuity. Protection from vision loss was also shown in multiple additional prespecified measures of BCVA and visual function, including LLVA and LLVD. ANX007's treatment effect increased over the course of the on-treatment portion of the study, suggesting that ANX007 may provide a growing and durable treatment effect over time. While benefit gained against vision lost was maintained during the subsequent six-month off-treatment period, the rate of decline for BCVA ≥ 15-letter vision began to parallel that of sham, providing additional support for the observed on-treatment protection. ANX007 treatment was generally well-tolerated, with no increase in choroidal neovascularization (CNV) rates between the treated and sham arms and no events of retinal vasculitis reported.

About Geographic Atrophy
Geographic atrophy (GA) is an advanced form of dry age-related macular degeneration (AMD), an eye disease that is the leading cause of blindness in the elderly. GA is a chronic progressive neurodegenerative disorder of the retina involving the loss of photoreceptor synapses and cells in the outer retina. GA affects an estimated one million people in the United States and eight million people globally, severely limiting their independence and causing frustration, anxiety and emotional hardship. Effective treatments that preserve vision are still needed, as no currently approved therapies have been shown in clinical trials to significantly prevent vision loss.

About Annexon
Annexon Biosciences (Nasdaq: ANNX) is a clinical-stage biopharmaceutical company utilizing a distinct scientific approach to stop C1q and all inflammatory aspects of classical complement pathway activation before it starts. As the only company solely focused on shutting down the early classical cascade, Annexon is developing a fit-for-purpose pipeline of therapeutics designed to provide meaningful benefits across multiple diseases of the body, brain and eye. With proof-of concept data in both Guillain-Barré syndrome and geographic atrophy, Annexon is rigorously advancing its mid-to late-stage clinical trials to bring their potential treatments to patients as quickly as possible. To learn more visit annexonbio.com.

Forward Looking Statements
This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "positioned," "potential," "predict," "seek," "should," "suggest," "target," "on track," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. All statements other than statements of historical facts contained in this press release are forward-looking statements. These forward-looking statements include, but are not limited to, statements about: timing of initiation of the ARCHER II and ARROW trials; ANX007's distinct potential neuroprotective mechanism of action and potential to provide protection from vision loss; the potential for robust, dose and time dependent preservation of vision loss in the broad patient population; continued development of ANX007; market size; meeting with regulators to determine the optimal path forward; expected superiority on BCVA ≥ 15-letter loss in a head-to-head study with SYFOVRE®; anticipated growing and durable treatment effect over time of ANX007; plans to report final results following study conclusion; ability to achieve regulatory approval in the United States, Europe and other large jurisdictions; potential for a global sham-controlled trial to support a faster path to regulatory approval; the potential benefits from treatment with anti-C1q therapy; and continuing advancement of the company's portfolio. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, risks and uncertainties related to: the ongoing off-treatment follow-up portion of the ARCHER trial and final results from the ARCHER trial; the company's history of net operating losses; the company's ability to obtain necessary capital to fund its clinical programs; the early stages of clinical development of the company's product candidates; the effects of public health crises on the company's clinical programs and business operations; the company's ability to obtain regulatory approval of and successfully commercialize its product candidates; any undesirable side effects or other properties of the company's product candidates; the company's reliance on third-party suppliers and manufacturers; the outcomes of any future collaboration agreements; and the company's ability to adequately maintain intellectual property rights for its product candidates. These and other risks are described in greater detail under the section titled "Risk Factors" contained in the company's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q and the company's other filings with the SEC. Any forward-looking statements that the company makes in this press release are made pursuant to the Private Securities Litigation Reform Act of 1995, as amended, and speak only as of the date of this press release. Except as required by law, the company undertakes no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

Investor Contact:
Monique Allaire
THRUST Strategic Communications
monique@thrustsc.com

Media Contact:
Sheryl Seapy
Real Chemistry
949-903-4750
sseapy@realchemistry.com