Annexon Announces Positive Topline Results from Pivotal Phase 3 Trial for First-in-Class C1q Blocking Antibody ANX005 in Guillain-Barré Syndrome

June 4, 2024

Single Infusion of ANX005 30 mg/kg Met Primary Endpoint, Delivering a Highly Statistically Significant and Clinically Meaningful 2.4-fold Improvement in GBS-DS vs. Placebo at Week 8, p=0.0058

ANX005 Demonstrated Early and Sustained Improvements in Key Secondary Endpoints Including Muscle Strength, Nerve Damage and Ventilation

ANX005 Displayed Rapid Target Engagement and was Generally Well-Tolerated Across Doses

Real-World Evidence (RWE) Comparability Data Expected in First Half 2025

Conference call and webcast today at 8:30 a.m. ET

BRISBANE, Calif., June 04, 2024 (GLOBE NEWSWIRE) -- Annexon, Inc. (Nasdaq: ANNX), a biopharmaceutical company advancing a late-stage platform of novel therapies for people living with devastating classical complement-mediated neuroinflammatory diseases of the body, brain, and eye, today announced positive topline results from its randomized placebo-controlled pivotal Phase 3 trial in patients with Guillain-Barré syndrome (GBS). The Phase 3 trial met its primary endpoint, with ANX005 30 mg/kg achieving a highly statistically significant 2.4-fold improvement on the GBS-disability scale (GBS-DS) at week 8 (proportional odds analysis, $p = 0.0058$).

ANX005 30 mg/kg treatment also demonstrated improvements versus placebo on key secondary endpoints, including early gains in muscle strength by Medical Research Council (MRC) sum score at day 8 ($p < 0.0001$*) and at week 8 ($p = 0.0351$*), and a median of 28 fewer days on artificial ventilation through week 26 ($p = 0.0356$*). Additionally, ANX005 30 mg/kg demonstrated a 31-day reduction in the median time to walk independently versus placebo ($p = 0.0211$*) in a prespecified analysis. ANX005 30 mg/kg treated patients got better sooner on each of these assessments, presenting important clinical care outcomes for patients and the healthcare community. ANX005 also provided an early reduction in the prespecified analysis of serum levels of neurofilament light chain (NfL), a biomarker of nerve damage (11.2% reduction relative to placebo between weeks 2–4, $p = 0.03$*). (* nominal)

GBS is a rapid and acute neurological disease with a narrow therapeutic window that results in the hospitalization of over 22,000 people annually in the U.S. and Europe. The significant and long-term disease burden associated with GBS on patients, caregivers, hospitals and payers has led to a multi-billion-dollar annual economic cost to the U.S. healthcare system. Currently, there are no approved treatments for GBS by the U.S. Food and Drug Administration (FDA).

“These data represent an important moment for the GBS community and Annexon,” said Douglas Love, president and chief executive officer of Annexon. “With the potential to be the first targeted treatment for GBS in the U.S., ANX005 demonstrated consistent improvement and functional benefits on key primary and secondary endpoints. Additionally, we observed in our Phase 3 trial that early treatment with ANX005 resulted in rapid neuroprotection that stopped the advancement of disease and helped GBS patients get better sooner. These results reinforce Annexon’s founding thesis that C1q inhibition is a powerful mechanism of action to stop the progression of neuroinflammation and underscore the potential of ANX005 and our classical complement platform to treat GBS and a host of other diseases of the body, brain and eye.”

The randomized, placebo-controlled Phase 3 trial which enrolled 241 subjects in Bangladesh and the Philippines evaluated two doses of ANX005, 30 mg/kg and 75 mg/kg, which both delivered rapid and complete suppression of complement activity but differed in duration of C1q inhibition. The 30 mg/kg dose suppression lasted one week and the 75 mg/kg dose suppression lasted two to three weeks. ANX005 75 mg/kg outperformed placebo on multiple endpoints, however, it was not statistically significant on the primary endpoint of GBS-DS at week 8 ($p = 0.5548$). The two dose levels were evaluated based on findings in the earlier Phase 1b proof-of-concept study, which showed efficacy in pooled analysis of both shorter and longer duration of ANX005 C1q inhibition. Because classical complement drives tissue damage in the early phase of disease, while facilitating nerve repair after acute nerve injury, the strong positive Phase 3 results with the 30 mg/kg dose resulting in one week of C1q inhibition appeared to define the optimal treatment window.

Hugh Willison, MBBS, PhD, Professor Emeritus of Neurology, University of Glasgow said, “In the first placebo-controlled pivotal study in GBS in approximately 40 years, ANX005 demonstrated robust and immediate neuroprotection by inhibiting C1q and suppressing downstream complement components with a single dose during the critical progressive phase of the disease. By directly targeting complement-mediated inflammation, ANX005 has the potential to act early to prevent nerve damage in this acute neurological emergency. The outcomes of this study represent an important breakthrough in effectively tackling GBS and support the potential of ANX005 to address the significant unmet need in this vulnerable patient population.”

David Cornblath, MD, Professor Emeritus of Neurology, Johns Hopkins University School of Medicine said, “This well designed, rigorous Phase 3 study demonstrated that acute and early intervention with ANX005 can deliver clinical benefits across the entire GBS disease spectrum. These data are consistent with the earlier Phase 1b findings, which showed improvements across multiple supportive functional and prognostic measures important to aid patient recovery. Among other outcomes in the Phase 3 trial, patients dosed with 30 mg/kg were able to walk independently one month earlier and removed off a ventilator one month sooner, which are paramount to getting patients back to normal activities of daily living and represent a potentially transformative advancement for the treatment landscape. I am excited by the potential of ANX005 to be the first FDA approved therapy to treat GBS.”

The clinical safety and tolerability findings of ANX005 at both doses in the Phase 3 study support a generally well-tolerated profile with no new safety signals. The majority of adverse events were mild Grade 1 to moderate Grade 2 events. The most common treatment-related adverse events were infusion related reactions (30.4%) that were mostly mild transient rashes. There were no autoimmune related adverse events, and no drug-related

deaths or serious infections were observed.

The GBS Phase 3 study was conducted in Bangladesh and Philippines due to the high prevalence of GBS and limited access to standard of care intravenous immunoglobulin (IVIg). Based on feedback from the FDA, Annexon has initiated a real-world evidence (RWE) protocol with International Guillain-Barré Syndrome Outcomes Study (IGOS) to establish comparability between Phase 3 participants and Western patients. IGOS is a global, prospective, observational, multicenter cohort study that has enrolled 2,000 patients who were followed for one to three years. Approximately 50% of all Western IGOS patients met the entry criteria for the Annexon GBS Phase 3 trial and, importantly, ANX005 30 mg/kg achieved a robust treatment effect on GBS-DS at week 8 in patients with Western characteristics and milder GBS. In a prespecified subgroup analysis of patients with baseline MRC sum score ≥20, ANX005 30 mg/kg treated patients were three times more likely to be in a better state of health compared to placebo on GBS-DS at week 8 (p = 0.0102*). (* nominal)

RWE data and BLA submission are expected in the first half of 2025. Annexon plans to present Phase 3 data at the 2024 Peripheral Nerve Society Annual Meeting on June 25, 2024.

ANX005 has been granted Fast Track and Orphan Drug Designations from the FDA. ANX005 has also been granted Orphan Drug Designation by the European Medicines Agency (EMA) based on a meta-analysis of past studies with ANX005 and IVIg demonstrating notable, early improvement in muscle strength with ANX005 that translated into observable gains in health status, including a reduction in the need of mechanical ventilation.

Conference Call and Webcast Information
Annexon management will hold a conference call and webcast today at 8:30 a.m. ET to discuss topline results from its Phase 3 trial evaluating ANX005 for patients with GBS. The dial-in number for the conference call is 1-877-407-0784 (U.S./Canada) or 1-201-689-8560 (international). The conference ID for all callers is 13747058. The live webcast and replay may be accessed by visiting Annexon's website at https://ir.annexonbio.com/events-and-presentations/events.

Call me™ Click here. Participants can use guest dial-in numbers above and be answered by an operator or they can click the Call me™ link for instant telephone access to the event (dial-out). The Call me™ link will be made active 15 minutes prior to scheduled start time.

About Guillain-Barré Syndrome (GBS)
GBS is a severe disease resulting from an acute autoantibody attack on peripheral nerves that generally occurs post-infection in otherwise healthy persons following activation of C1q and the classical complement cascade. It is a rapid and acute neurological disease with a narrow therapeutic window that results in hospitalization of over 22,000 people annually in the U.S. and Europe. The peripheral nerve damage progresses rapidly, causing acute neuromuscular paralysis, and may lead to significant morbidity, disability and mortality. Currently, there are no approved treatments for GBS in the U.S. The long-term disease burden associated with GBS has led to a multi-billion-dollar annual economic cost to the U.S. healthcare system alone.

About Annexon
Annexon Biosciences (Nasdaq: ANNX) is a biopharmaceutical company advancing a late-stage clinical platform of novel therapies for people living with devastating classical complement-mediated neuroinflammatory diseases of the body, brain, and eye. Annexon's novel scientific approach targets upstream C1q to block the classical complement inflammatory cascade before it starts, and its therapeutic candidates are designed to provide meaningful benefits across multiple autoimmune, neurodegenerative and ophthalmic diseases. With proof-of concept data in Guillain-Barré syndrome, Huntington's disease 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: ability of ANX005 to stop C1q activity; the clinical and regulatory status of ANX005; the potential of ANX005 to be the first approved treatment for GBS; the potential of the 75mg dose of ANX005 to be used in patients with severe disease; the timing of completion of RWE study and potential submission of a BLA with the FDA; the potential therapeutic benefit of ANX005 or any other product candidates on GBS, Huntington's disease or geographic atrophy; potential benefit of ANX005, if approved, compared to existing therapies; market size; the potential benefits from treatment with anti-C1q therapy; and Annexon's ability to rigorously advance mid-to late-stage clinical trials and continue development 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 potential for any final clinical trial results to differ from preliminary or topline results; 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.

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