Annexon Biosciences Reports Phase 2 Clinical Trial Results Demonstrating Upstream Classical Complement Inhibition Associated with Clinical Benefit in Huntington's Disease

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ANX005 Demonstrated Full C1q Target Inhibition and Was Generally Well-Tolerated

Disease Progression Stabilized in Overall Patient Population Through the Nine-month Study

Rapid Improvement in Clinical Outcome Measures Maintained in Patients with High Baseline Complement Activity Through the Nine-month Study

Company to Host Conference Call Today at 8:00 a.m. ET

BRISBANE, Calif., June 07, 2022 (GLOBE NEWSWIRE) -- Annexon, Inc. (Nasdaq: ANNX), a clinical-stage biopharmaceutical company developing a new class of complement medicines for patients with classical complement-mediated autoimmune, neurodegenerative and ophthalmic disorders, today announced promising, final data from its open-label Phase 2 clinical trial of ANX005 in patients with Huntington's disease (HD).

HD is a fatal, progressive movement disorder that affects approximately 80,000 people globally, with about 300,000 people who are at-risk of inheriting the disease-causing gene. Annexon's unique approach to tackle HD targets C1q, the initiating molecule of the classical complement pathway, to slow or halt classical complement diseases. In neurodegenerative diseases like HD, C1q inappropriately recognizes and tags functioning synapses necessary for normal brain health by activating and amplifying complement components that cause neuroinflammation, synapse damage and ultimately synapse loss. ANX005 is designed to fully block C1q and the entire classical complement pathway with the aim of preserving functioning synapses to slow or halt neurodegeneration.

"Huntington's disease is a devastating condition, with no cure or approved disease-modifying treatments available," said Edward Wild, FRCP, Ph.D., professor of neurology at University College London, consultant neurologist at the National Hospital for Neurology and Neurosurgery in London's Queen Square, and associate director of UCL Huntington's Disease Centre. "The apparent continued stabilization of clinical function over nine months is notable, and generally not expected in a progressive disease like HD. Moreover, the evidence of sustained improvement observed in patients with elevated baseline complement activity coupled with the benefit-risk profile demonstrated by ANX005 through the nine-month study underscore the potential of complement inhibition as a promising therapeutic mechanism for this difficult disease."

ANX005 Phase 2 Target Engagement, Efficacy and Biomarker Results
The Phase 2 multi-center, open-label clinical trial evaluated ANX005 administered intravenously for a six-month dosing period in patients with, or at risk for, early manifest HD, followed by a three-month follow-up period. The primary outcome measures of the study were the safety and tolerability of ANX005; the pharmacokinetics (PK) of ANX005, as measured by serum and CSF concentrations; and pharmacodynamics (PD) effects, as measured by C1q, C4a and NfL serum and CSF concentrations. The study enrolled a total of 28 patients, of whom 23 completed both six-months of treatment and subsequent three-month follow-up period. The Phase 2 results reported today include efficacy data as measured by Composite Unified Huntington's Disease Rating Scale (cUHDRS) and Total Functional Capacity (TFC), PK and PD data and NfL for those 23 patients, and safety data for all 28 patients enrolled.

Final data showed:

- Treatment with ANX005 led to complete and durable target engagement of C1q in both serum and CSF throughout the treatment period and well into the follow-up period
- Disease progression was stabilized in the overall HD patient population for the entire nine months of the study, as assessed by both cUHDRS and TFC, the two primary clinical measurement scales for HD
    - In contrast, published natural history data show that HD patients are expected to experience decline over nine months as their disease progresses
- HD patients with higher baseline complement activity, as measured by elevated levels of C4a in CSF, demonstrated a rapid clinical benefit, as assessed by both cUHDRS and TFC, that was sustained over the entire nine months of the study
    - Improvement in cUHDRS and TFC in HD patients with higher baseline complement was evident six weeks after dosing initiation and was maintained over nine months through the on-treatment and follow-up periods
- Plasma and CSF NfL levels remained generally consistent through the nine-month study, and were comparable to NfL levels described in published natural history data for HD patients[1]
    - Published data suggest that in slowly progressive neurodegenerative diseases like HD, synapse loss is associated with progressive functional decline, and precedes the loss of neurons[2] and increase in NfL, a biomarker of neuronal loss[3]

ANX005 Phase 2 Safety Results
ANX005 was generally well-tolerated throughout the trial, with no change in safety results from the interim findings previously reported. To date, ANX005 has been evaluated and generally well-tolerated in trials that have enrolled more than 170 patients across multiple indications.

Findings from the Phase 2 clinical trial in HD showed (n=28):

- Transient first dose-associated infusion-related reactions were the most common adverse events (AEs) reported
- No cases of serious infection were observed, and there were no deaths during study
- Five patients discontinued ANX005 treatment, two of which were unrelated to treatment. Three discontinuations were determined to be potentially drug-related, and all three cases improved or resolved after ANX005 treatment was discontinued:
    - A total of two drug-related SAEs were reported: one event of systemic lupus erythematosus, which completely resolved with dosing cessation, and one event of idiopathic pneumonitis (noninfectious), which improved after dosing cessation
    - One patient experienced an AE of hemolytic anemia that remained asymptomatic and completely resolved after dosing cessation
    - All three cases were observed in patients with elevated antinuclear antibody (ANA) titers at baseline. No patient with normal ANA titers at baseline developed a SAE, experienced autoimmune-associated complications or discontinued the study

“We are very encouraged by these final data with ANX005, which provide significant insights into our mechanism of action for a chronic neurodegenerative disease where the role of classical complement has been well-characterized,” remarked Douglas Love, Esq., president and chief executive officer of Annexon. “The totality of the data, including robust and sustained C1q inhibition, clear impact on clinical outcomes, and favorable safety results observed, strongly support the potential for ANX005 to treat patients with HD. We are particularly encouraged that patients with higher complement activity may be more likely to respond to anti-C1q therapy. Based on these results, we look forward to engaging with regulatory authorities to assess the opportunity for a well-controlled trial in HD leveraging a mechanistically compelling precision medicine approach. Our mission is to deliver game-changing treatments to patients, and these data bring us an important step closer to achieving our objective.”

Conference Call Information
Annexon management will host a conference call today at 8:00 a.m. ET. To participate in the conference call, please dial (833) 649-1187 (domestic) or (281) 206-0036 (international) and refer to conference ID 7693725. The webcast and accompanying slides can be accessed under the ‘Events & Presentations’ section on the Investors page at www.annexonbio.com. A replay of the webcast will be archived on the Annexon website for 30 days.

About Annexon
Annexon (Nasdaq: ANNX) is a clinical-stage biopharmaceutical company that aims to bring game-changing medicines to patients with classical complement-mediated diseases of the body, brain and eye. The classical complement cascade is a seminal pathway within the immune system that anchors and drives a host of autoimmune, neurodegenerative and ophthalmic diseases. Annexon is advancing a new class of complement medicines targeting the early classical cascade and all downstream pathway components that contribute to disease, while selectively preserving the beneficial immune functions of other complement pathways. Annexon is rigorously developing a pipeline of diversified product candidates across multiple mid- to late-stage clinical trials, with several clinical data sets anticipated throughout 2022 and 2023. For more information, visit www.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: the potential benefits from treatment with anti-C1q therapy; the company’s plans to continue development of ANX005 as a potential treatment for HD; continuing development of the company’s pipeline of product candidates; and timing of clinical data. 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 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 COVID-19 or other 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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[1] Tabrizi 2019 and Rodrigues 2020

[2] Delva, et al., Neurology, 2021; Albin, et al., Ann Neurol, 1991; Gomez-Tortosa, Ann Neurol, 1991

[3] Rodrigues et al., Sci. Transl. Med. 12, eabc2888 (2020)