

Annexon Biosciences Reports Promising Interim Phase 2 Data Showing Improvement in Clinical Measures with ANX005 in Huntington's Disease Following Six-Month Treatment

ANX005 Has Been Generally Well-Tolerated and Has Shown Full Target Engagement of C1q in the CSF

Improvements in Clinical Outcome Measures Observed in Greater than 50% of All Evaluable Patients and 75% of Evaluable Patients with Excess Baseline Complement Activity

NfL Levels Remained Consistent and Were Comparable to Published Natural History Data for HD Patients

Phase 2 Trial Ongoing with Full Data Expected in the Second Quarter of 2022

Company to Host Conference Call Today at 4:30 p.m. ET

BRISBANE, Calif., January 4, 2022 - [Annexon, Inc.](#) (Nasdaq: ANNX), a clinical-stage biopharmaceutical company developing medicines that stop destructive immune activity in complement-mediated autoimmune, neurodegenerative and ophthalmic disorders, today announced interim data from its ongoing, open-label Phase 2 clinical trial of ANX005 in patients with Huntington's disease (HD) who completed the 24-week treatment period. Annexon is developing ANX005, its lead monoclonal antibody candidate, for the treatment of a range of complement-mediated disorders, including HD.

HD is a fatal, progressive movement disorder involving the activation of the classical complement pathway. C1q, the initiator of the classical pathway, is recognized as a major driver of a destructive immune response that leads to synapse loss and neurodegeneration. ANX005 is designed to disrupt the disease course, stopping the start of damaging complement activation by blocking C1q and the entire classical complement pathway.

Interim data from the ongoing Phase 2 trial show that treatment with ANX005 has been generally well-tolerated, with full target engagement of C1q in both serum and cerebrospinal fluid (CSF) observed in evaluable patients through the dosing period. Evaluable patients maintained clinical function, as measured by changes in mean Composite Unified Huntington's Disease Rating Scale (cUHDRS), relative to baseline after six months of treatment, and improvement in cUHDRS was observed in more than half of all evaluable patients and in 75% of evaluable patients who showed excess complement activity at baseline. NfL levels observed after six months of treatment remained generally consistent and were comparable to NfL levels described in published natural history data for HD patients. Overall, these interim findings appear to build on the scientific hypothesis of Annexon scientific founder, the late Ben Barres, who believed that blocking C1q protects synaptic loss and can lead to rapid functional impact on clinical outcomes in neurodegenerative diseases.

"People with HD face a devastating condition, with no cure or approved disease-modifying treatments available," said Edward Wild, FRCP, Ph.D., consultant neurologist, NHNN Queen Square and associate director, UCL Huntington's Disease Centre. "I believe the interim data from this open-label trial of ANX005 are encouraging, showing complete CSF target engagement and that ANX005 has been generally well-tolerated, with no concern regarding the NfL levels seen in this early readout. The apparent stabilization of cUHDRS observed relative to normal disease progression, together with the potential improvement seen in patients with elevated baseline C4a, supports the hypothesis that protecting synapses via C1q inhibition could produce meaningful functional benefit in HD, and justifies the continued development of ANX005 for this indication."

ANX005 Interim Safety and Target Engagement Data

ANX005 has been generally well-tolerated in the study (n=28). As of the data cutoff date of October 17, 2021, the most common adverse events (AEs) reported were first dose-associated infusion-related reactions, including transient skin rash, consistent with the experience observed in the company's Phase 1b trial of ANX005 in patients with Guillain-Barré Syndrome (GBS). In the HD trial, five patients discontinued ANX005 treatment, three of whom discontinued due to a drug-related AE. Two patients experienced a drug-related serious adverse event, including one event of systemic lupus erythematosus (mucocutaneous), whose symptoms resolved post-study drug discontinuation, and one event of idiopathic pneumonitis, which stabilized post-study drug discontinuation. Of note, no cases of serious infection were identified, and no deaths were reported.

Interim data show that treatment with ANX005 has led to full target engagement of C1q in both serum and CSF through the dosing period in patients who were evaluable as of the cutoff date of October 17, 2021 (n=13).

ANX005 Interim Efficacy and Biomarker Data

Patients evaluable as of the cutoff date of December 14, 2021 (n=23) experienced improvements in clinical measures, assessed by cUHDRS, a clinical rating scale with four domains measuring the progression of HD consisting of motor, cognitive and functional capacity. Overall, patients maintained clinical function relative to baseline in cUHDRS after six months of treatment. Published natural history data show that HD patients typically experienced a decline of approximately 1 point over one year¹, or 0.5 points over six months. Additionally, as of the cutoff date, 56% of patients showed improvement from baseline in cUHDRS and several subdomains of cUHDRS over six months of treatment. Moreover, in a sub-analysis of patients assessed according to baseline complement activity (C4a), 75% of patients with excess baseline complement activity demonstrated a statistical improvement in cUHDRS over six months of treatment versus 36% with low baseline complement activity, consistent with the scientific hypothesis of rapid response to anti-C1q therapy via enhanced synapse function. Elevated C4a is an objective measurement of excess complement activity in CSF that has been found to correlate with disease progression and multiple clinical endpoints in HD.² These findings suggest that patients with excess complement activity may be more likely to respond to anti-C1q therapy in future clinical trials and may inform future trial designs.

NfL, a protein component of the neuronal cytoskeleton, has been shown to increase in the CSF with disease severity in HD patients. Interim data assessing NfL from patients evaluable as of the cutoff date of October 17, 2021 (n=16) who completed 24 weeks of treatment showed that mean plasma and CSF NfL levels remained generally consistent and were comparable to NfL levels described in published natural history data for HD patients.³ Published data suggest that in slowly progressive neurodegenerative diseases like HD, synapse loss is associated with progressive functional decline, preceding the loss of neurons⁴ and NfL changes. As such, changes in NfL may require treatment durations longer than six months and Annexon will continue to assess NfL levels in patients over the three-month follow-up period.

“We are quite encouraged by the interim data generated with ANX005 in HD. We are particularly excited to see a heightened clinical response in patients with excess baseline complement activity, suggesting that

¹ Schobel 2017

² Suri, et al., HSG conference 2021

³ Tabrizi 2019 and Rodrigues 2020

⁴ Delva, et al., Neurology, 2021; Albin, et al., Ann Neurol, 1991; Gomez-Tortosa, Ann Neurol, 1991

the classical complement pathway plays a key role in the neurodegenerative disease process and that ANX005 has the potential to provide meaningful benefit to HD patients,” remarked Douglas Love, Esq., president and chief executive officer of Annexon. “These early data in HD patients, coupled with prior proof-of-concept data in GBS, provide a growing body of evidence for the potential role of anti-C1q in treating complement mediated neurodegenerative and autoimmune diseases, and we look forward to continuing to assess the full potential of our approach in several ongoing trials in diseases of high unmet need.”

The Phase 2 trial remains ongoing, and Annexon anticipates reporting full data from all patients enrolled, including data from the three-month follow-up period, in the second quarter of 2022. Pending results from the full dataset, Annexon plans to evaluate the opportunity for a Phase 3 trial of ANX005 in HD patients.

Conference Call Information

Annexon management will host a conference call today at 4:30 p.m. ET. To participate in the conference call, please dial (833) 649-1187 (domestic) or (281) 206-0036 (international) and refer to conference ID 6297344. 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 the Phase 2 Trial (ANX005-HD-01)

The Phase 2 multi-center, open-label trial is evaluating ANX005 administered intravenously for a 24-week (six-month) dosing period in patients with, or at risk for, early manifest HD. The study enrolled a total of 28 patients in May of 2021, and 23 patients completed the 24-week treatment period. The interim data reported today include safety data for all 28 patients enrolled, efficacy data as measured by UHDRS in all 23 evaluable patients, pharmacokinetics (PK) and pharmacodynamics (PD) data for the first 13 patients, and NfL for the first 16 patients who completed the 24-week treatment period based on cutoff dates required to obtain data for this interim analysis.

About Annexon

Annexon (Nasdaq: ANNX) is a clinical-stage biopharmaceutical company developing a new class of complement medicines for patients with classical complement-mediated autoimmune, neurodegenerative, and ophthalmic disorders of the body, brain and eye. The company’s pipeline is based on its platform technology addressing a broad spectrum of well-researched classical complement-mediated autoimmune and neurodegenerative diseases triggered by aberrant activation of C1q, the initiating molecule of the classical complement pathway. Annexon is advancing a portfolio of innovative product candidates designed to block the activity of C1q and the entire classical complement pathway: ANX005 (intravenous administration), ANX007 (intravitreal administration), and ANX009 (subcutaneous administration). Annexon is deploying a disciplined, biomarker-driven strategy designed to improve the probability of technical success of its portfolio. 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: initial findings and observations related to the interim data from the company’s

ongoing, open-label Phase 2 clinical trial of ANX005 in patients with HD; the potential benefits from treatment with anti-C1q therapy; timing of full data from the Phase 2 trial of ANX005 in HD patients; plans to evaluate the opportunity for a Phase 3 trial of ANX005 in HD patients; and continuing advancement of the company's innovative 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 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.

Investor Contact:

Chelcie Lister
THRUST Strategic Communications
chelcie@thrustsc.com

Media Contact:

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