Ventyx Biosciences Announces Positive Topline Phase 1 Data for its Peripheral NLRP3 Inhibitor VTX2735

June 29, 2022

Excellent safety, tolerability and pharmacokinetic profile

Robust dose-dependent target engagement as measured by ex vivo IL-1β release assay

Phase 2 trial planned in CAPS patients to efficiently establish clinical proof of concept

Clinical update in Q3 from Phase 1 trial of VTX958, our oral, selective allosteric TYK2 inhibitor

ENCINITAS, Calif., June 29, 2022 (GLOBE NEWSWIRE) -- Ventyx Biosciences, Inc. (Nasdaq: VTYX) ("Ventyx"), a multi-asset, clinical-stage biopharmaceutical company focused on advancing novel oral therapies that address a range of inflammatory diseases with significant unmet medical need, today announced positive data from the company's Phase 1 single ascending dose (SAD) and multiple ascending dose (MAD) trial of VTX2735, a peripheral NLRP3 inhibitor, and the first of two product candidates from its NLRP3 portfolio.

"The Phase 1 study demonstrated an excellent exposure and safety profile and evidence of dose-dependent target engagement and pharmacodynamic activity," said Bill Sandborn, MD, President and Chief Medical Officer. "Inhibition of the NLRP3 inflammasome is emerging as a potent anti-inflammatory mechanism with therapeutic potential in a broad range of indications with high unmet medical need. We look forward to sharing additional details from this trial and a broader discussion of the clinical opportunities available with VTX2735 at an investor event later this year."

The VTX2735 Phase 1 SAD/MAD clinical trial was a two-part, randomized, double-blind, placebo controlled, dose-escalation study designed to evaluate the safety, tolerability and pharmacokinetics of single and multiple ascending doses. The study enrolled 72 adult healthy volunteers in SAD cohorts up to 200 mg and MAD cohorts up to 200 mg daily for 14 days. VTX2735 was well-tolerated across all dose cohorts and all subjects completed the trial.

Drug exposures in both SAD and MAD cohorts increased linearly with dose. All drug-related adverse events (AEs) were considered mild, with no LFT abnormalities and no dose-related trend in the frequency of treatment-emergent AEs was observed. Drug exposures also correlated with markers of target engagement as evidenced by strong pharmacodynamic (PD) activity in *ex vivo* LPS- plus ATP-mediated IL-1β release assays from subject-derived plasma samples from both the SAD and MAD parts of the trial. VTX2735 demonstrated robust dose-related suppression of the induced pro-inflammatory cytokine IL-1β release relative to placebo. VTX2735 also demonstrated reduction from baseline in high sensitivity C-reactive protein (hsCRP) concentrations. Full PD analyses from the Phase 1 trial are ongoing.

The Phase 1 results support progression of VTX2735 into Phase 2 clinical trials. The initial Phase 2 trial is being planned in cryopyrin-associated periodic syndrome (CAPS), a rare autoinflammatory condition characterized by IL-1β-mediated inflammation. This trial is intended to establish that VTX2735 can inhibit IL-1β in a similar fashion as IL-1β-targeted antibody therapy and other related IL-1β-antagonists, which have established clinical efficacy in CAPS and other inflammatory diseases, while further characterizing the profile of VTX2735 and its impact on IL-1□□ and IL-18, along with pyroptosis. It is expected that this trial will initiate in the fourth quarter of 2022. The profile of VTX2735 offers the opportunity to exploit the full therapeutic potential of systemic NLRP3 inhibition across a number of chronic inflammatory conditions, including atherosclerosis and cardiometabolic diseases.

VTX2735 is the first of Ventyx's two NLRP3 development candidates to enter the clinic. The second candidate, VTX3232, is an orally bioavailable, CNS-penetrant NLRP3 inhibitor and belongs to a structurally distinct chemical series than VTX2735. VTX3232 is currently in IND-enabling studies and is expected to start Phase 1 trials in the first quarter of 2023. True CNS-penetrant NLRP3 inhibitors, such as VTX3232, offer potential therapeutic utility in a broad range of neurodegenerative diseases, including Parkinson's disease.

"I am very excited about the progress the Ventyx team has made on our NLRP3 inhibitor portfolio and the emerging clinical profile of VTX2735," said Raju Mohan, PhD, Chief Executive Officer. "Today's update marks the first of two clinical updates expected this summer as we continue to advance our differentiated portfolio of clinical candidates across multiple immune-mediated diseases. We look forward to sharing data from the Phase 1 trial of VTX958, our oral, selective TYK2 inhibitor, in the third quarter."

About the NLRP3 Inflammasome

Activated NLRP3 acts as a 'danger sensor' in the body to release the pro-inflammatory cytokines IL-1β, IL-18 and induce uncontrolled, lytic cell death (pyroptosis). These processes lead to chronic inflammation, and as such, NLRP3 has been implicated in a large number of diseases.

About Cryopyrin-Associated Periodic Syndromes

Cryopyrin-associated periodic syndromes (CAPS), also called cryopyrin-associated autoinflammatory syndromes, are three diseases related to a defect in the NLRP3 gene. CAPS encompasses neonatal onset multisystem inflammatory disease (NOMID), Muckle-Wells syndrome (MWS) and familial cold autoinflammatory syndrome (FCAS). The differences in these diseases lie in their severity and the organs involved.

About Ventyx Biosciences

Ventyx is a clinical-stage biopharmaceutical company focused on developing innovative oral medicines for patients living with autoimmune and inflammatory disorders. We believe our ability to efficiently discover and develop differentiated drug candidates will allow us to address important unmet medical need with novel oral therapies that can shift immunology markets from injectable to oral drugs. Our current pipeline includes three

clinical-stage programs targeting TYK2, S1P1R and NLRP3, positioning us to become a leader in the development of oral immunology therapies. Ventyx is headquartered in Encinitas, California. For more information about Ventyx, please visit www.ventyxbio.com.

Forward-Looking Statements

Ventyx cautions you that statements contained in this press release regarding matters that are not historical facts are forward-looking statements. These statements are based on Ventyx's current beliefs and expectations. Such forward-looking statements include, but are not limited to, statements regarding: the anticipated timing of commencement, enrollment and completion of clinical trials for Ventyx's product candidates; the anticipated timing of releasing data from the Phase 1 trial of VTX958; the potential of Ventyx's product candidates to address a broad range of immune-mediated diseases; the therapeutic potential of inhibition of the NLRP3 inflammasome; plans for advancing VTX2735 into a Phase 2 trial and the anticipated timing for starting such a trial; the therapeutic utility of CNS-penetrant NLRP3 inhibitors, such as VTX3232; and the anticipated timing for starting a Phase 1 trial for VTX3232. The inclusion of forward-looking statements should not be regarded as a representation by Ventyx that any of its plans will be achieved. Actual results may differ from those set forth in this press release due to the risks and uncertainties inherent in Ventyx's business, including, without limitation: potential delays in the commencement, enrollment and completion of clinical trials; disruption to our operations from the ongoing global outbreak of the COVID-19 pandemic, or from the ongoing military conflict in Ukraine, including clinical trial delays; Ventyx's dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the results of preclinical studies and early clinical trials are not necessarily predictive of future results; the success of Ventyx's clinical trials and preclinical studies for its product candidates; interim results not necessarily being predictive of final results; the potential of one or more outcomes to materially change as the trial continues and more patient data becomes available and following more comprehensive audit and verification procedures; regulatory developments in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval and/or commercialization, or may result in recalls or product liability claims; Ventyx's ability to obtain and maintain intellectual property protection for its product candidates; the use of capital resources by Ventyx sooner than expected; and other risks described in Ventyx's prior press releases and Ventyx's filings with the Securities and Exchange Commission (SEC), including in Part II, Item 1A (Risk Factors) of Ventyx's Quarterly Report on Form 10-Q, filed on May 12, 2022, and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Ventyx undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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