Ventyx Biosciences Announces Positive Topline Phase 1 Data for Its Selective Allosteric TYK2 Inhibitor VTX958

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VTX958 was well-tolerated across all SAD and MAD cohorts with an excellent safety profile

Class-leading target coverage, with TYK2 IC_{50} and IC_{90} coverage up to 24 hours

Robust dose-dependent pharmacodynamic activity and evidence of target engagement as measured by in vivo IFNα challenge and ex vivo IL-12/IL-18 stimulation assays

Ventyx to host conference call and webcast today at 4:30 PM ET to discuss VTX958 results

ENCINITAS, Calif., Aug. 15, 2022 (GLOBE NEWSWIRE) -- Ventyx Biosciences, Inc. (Nasdaq: VTYX), ("Ventyx"), a 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 VTX958, a novel and selective allosteric TYK2 inhibitor.

The VTX958 Phase 1 SAD/MAD clinical trial was a two-part, randomized, double-blind, placebo-controlled dose-escalation study designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple ascending doses. The study enrolled 96 adult healthy volunteers.

VTX958 Was Well Tolerated Across All Dose Groups

VTX958 was well tolerated across all 7 cohorts in the SAD portion and all 5 cohorts in the MAD portion of the Phase 1 trial with no discontinuations due to adverse events. No drug-related serious adverse events (SAEs) were reported. All treatment emergent adverse events (TEAEs) were classified as mild. No dose-limiting toxicities were identified and no dose-dependent trend in the frequency of TEAEs was observed. Additionally, there were no significant effects on hematological parameters, lipids/triglycerides and CPK laboratory values.

VTX958 Demonstrated a Dose-Dependent Increase in Exposure and Target Coverage

In both the SAD and the MAD portions of the trial, a dose-dependent increase in exposure was observed through all cohorts. In the MAD portion of the trial, VTX958 achieved TYK2 IC_{50} and IC_{90} coverage up to 24 hours. The exposures achieved by VTX958 demonstrated class-leading coverage of TYK2 IC_{50} and IC_{90} and its target cytokines, IL-12, IL-23 and IFNα.

VTX958 Demonstrated Dose-Dependent Pharmacodynamic Effects

In the MAD portion of the trial, pharmacodynamic (PD) activity was measured by the impact on TYK2-mediated target genes following an *in vivo* IFNα challenge, and by the IFNγ response to *ex vivo* IL-12/IL-18 stimulation of blood samples derived from all dosing cohorts. In both the *in vivo* IFNα challenge PD assay, as well as the *ex vivo* IFNγ response assay, VTX958 demonstrated robust dose-dependent PD, thereby confirming its impact on TYK2-mediated pathways and providing direct *in vivo* evidence of target engagement.

Planned Phase 2 Trials

"Data from the Phase 1 trial of VTX958 demonstrate an excellent safety profile and class-leading TYK2 inhibition as measured by IC_{50} and IC_{90} coverage," said William Sandborn, MD, President and Chief Medical Officer. "We believe these data will allow us to explore high levels of target inhibition in future clinical studies, which may support clinical differentiation in relevant disease populations, such as psoriasis, psoriatic arthritis and lupus. Additionally, we believe that our ability to achieve TYK2 target coverage throughout the day at levels typically associated with biologic therapies, may position VTX958 for success in disease indications that are expected to require higher therapeutic doses, such as Crohn's disease. We look forward to advancing VTX958 into multiple Phase 2 trials, including psoriasis, Crohn's disease and psoriatic arthritis, beginning in the fourth quarter of 2022."

Conference Call Information

Ventyx will host a conference call today at 4:30 p.m. ET to discuss topline results from the Phase 1 trial of VTX958. Investors and the general public may access the live webcast here, or register for the teleconference here. A live audio webcast will be available in the Investors section of the Company's website at www.ventyxbio.com. A recording of the webcast will be available following the call.

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 internally discovered 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.

About VTX958 and TYK2 Inhibition

VTX958 is an oral, selective allosteric inhibitor of tyrosine kinase 2 (TYK2). TYK2 regulates both innate and adaptive immunity by mediating IFNα,

IL-12 and IL-23 signaling. These targets have been clinically validated as relevant in the treatment of a broad range of immune-mediated diseases, including psoriasis, psoriatic arthritis, Crohn's disease, ulcerative colitis and lupus. Selectively targeting inhibition of TYK2 without inhibition of other JAK family enzymes may reduce inflammation while preserving protective immune function. VTX958 was internally discovered and all commercial rights to the compound are owned by Ventyx.

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 coverage profile of VTX958 potentially enabling clinical differentiation in disease indications where TYK2 has already been validated, including psoriasis, psoriatic arthritis and lupus; the broad therapeutic window of VTX958 potentially positioning VTX958 for success in inflammatory bowel disease, in particular Crohn's disease; Phase 1 data for VTX958 potentially allowing the exploration of high levels of target inhibition in future clinical studies; and the anticipated timing of advancing VTX958 into Phase 2 trials in psoriasis, psoriatic arthritis and Crohn's disease. 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; the potential of one or more outcomes to materially change as the trial continues and more patient data become 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 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 the date hereof, 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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