Ventyx Biosciences Reports Clinical Data for its NLRP3 Inhibitor Portfolio and Provides Pipeline Updates at Virtual Investor Event

March 11, 2024

VTX3232 was well-tolerated in the Phase 1 trial with robust target coverage achieved in both plasma and CSF; Ventyx is planning to initiate Phase 2a trials in Parkinson's disease and obesity in H2 2024

Topline Phase 2 data for VTX2735 in CAPS patients establish clinical proof of concept; Ventyx is planning to evaluate VTX2735 in cardiovascular diseases

Early Phase 2 open-label extension data continue to support the clinical profile of VTX002 in ulcerative colitis; Ventyx is planning to seek a partner or other nondilutive financing for pivotal Phase 3 trial

Based on pipeline reprioritization and recent PIPE financing, Ventyx expects its current cash, cash equivalents and marketable securities to fund planned operations into at least H2 2026

SAN DIEGO, March 11, 2024 (GLOBE NEWSWIRE) -- Ventyx Biosciences, Inc. (Nasdaq: VTYX) ("Ventyx"), a clinical-stage biopharmaceutical company focused on advancing novel oral therapies that address a broad range of inflammatory diseases with significant unmet medical need, will provide clinical and pipeline updates today during its virtual investor event.

"We are excited to announce clinical updates from our novel NLRP3 inhibitor portfolio, including topline results from the Phase 1 trial of VTX3232 in healthy volunteers and topline results from the Phase 2 trial of VTX2735 in CAPS patients," said Raju Mohan, Chief Executive Officer. "With these compelling clinical results and support from our recent PIPE financing, we are announcing a pipeline reprioritization, with internal resources to be focused on advancing our portfolio of potential best-in-class NLRP3 inhibitors in high value indications with substantial unmet medical need."

Pipeline Updates

- **VTX3232 (CNS-penetrant NLRP3 Inhibitor):** We completed a Phase 1 single- and multiple-ascending dose trial of VTX3232 in adult healthy volunteers to assess the safety, pharmacokinetics and pharmacodynamics of VTX3232. Separate cohorts were included in this trial in which serial cerebrospinal fluid (CSF) sampling was conducted to assess drug exposure and target engagement in the CSF.

  VTX3232 was well-tolerated with no dose-limiting toxicities identified. All treatment-emergent adverse events were graded mild or moderate. VTX3232 exhibited a dose-dependent and dose-linear pharmacokinetic profile. Repeat doses of 3 mg QD maintained steady-state IL-1β IC_{50} coverage in both plasma and CSF over 24 hours. Repeat doses of 40 mg QD exceeded steady-state IL-1β IC_{90} coverage in both plasma and CSF over 24 hours. Robust, dose-dependent pharmacodynamic effects were observed in a whole blood *ex vivo* IL-1β stimulation assay. Additionally, reductions in inflammatory biomarkers were observed in plasma and CSF samples. We believe these data support the potential for VTX3232 to emerge as a best-in-class CNS-penetrant NLRP3 inhibitor for the treatment of neuroinflammatory diseases.

  We expect to initiate a Phase 2a trial of VTX3232 in patients with early Parkinson's disease during the second half of 2024. We also expect to initiate a Phase 2a trial of VTX3232 in subjects with obesity and certain additional risk factors for cardiovascular disease during the second half of 2024.

- **VTX2735 (Peripheral NLRP3 Inhibitor):** We completed a Phase 2 trial of VTX2735 in patients with cryopyrin-associated periodic syndromes, or CAPS, a group of rare autoinflammatory conditions caused by gain-of-function mutations in the NLRP3 gene. This trial enrolled 7 patients with familial cold autoinflammatory syndrome (FCAS), the most common subset of CAPS. Treatment with VTX2735 demonstrated clinically meaningful improvements in disease activity, including an 85% mean reduction in the Key Symptom Score during Treatment Period 1. Reductions in inflammatory biomarkers were also observed, consistent with improvements in disease activity. VTX2735 was well-tolerated and all drug-related adverse events were graded mild. We believe these data establish compelling clinical proof of concept for our peripheral NLRP3 inhibitor VTX2735.

  We plan to evaluate VTX2735 in cardiovascular diseases with an initial focus on the secondary prevention of major adverse cardiovascular events (MACE) and recurrent pericarditis.

- **VTX002 (S1P1R Modulator):** In October 2023, we announced positive results from the Phase 2 trial of VTX002 in patients with moderately to severely active ulcerative colitis (UC). We believe these results establish VTX002 as a potential best-in-disease oral agent in UC based on its differentiated efficacy profile, including a high rate of complete endoscopic remission, and its potential best-in-class safety profile.

At our virtual investor event, we will present data from the ongoing Phase 2 open-label extension. We believe these data continue to support the potentially differentiated profile of VTX002 in ulcerative colitis, with robust rates of clinical remission and endoscopic remission observed among participants completing 52 weeks of treatment with VTX002. At least half of the patients in the 60 mg treat-through group achieved clinical remission or endoscopic remission at Week 52. Activities are underway to prepare for a Phase 3 trial. We intend to identify a partner or other source of non-dilutive financing to support the pivotal Phase 3 trial of VTX002 in ulcerative colitis.

- **VTX958 (TYK2 Inhibitor):** We are evaluating VTX958 in a Phase 2 trial in patients with moderately to severely active Crohn's disease. We recently implemented a protocol amendment for the ongoing Phase 2 trial to streamline trial design and accelerate the detection of an efficacy signal. As a result of the protocol amendment, target enrollment in the trial was revised from approximately 132 patients to approximately 93 patients. The trial's sole primary endpoint is now the change from baseline in the mean Crohn's disease activity index (CDAI) score at Week 12. We anticipate completing randomization of the trial during the first quarter of 2024 and expect to report topline results from the Phase 2 Crohn's disease trial during the middle of 2024.
- **Cash Runway:** We reported cash, cash equivalents and marketable securities of $252.2 million as of December 31, 2023. Combined with gross proceeds of approximately $100 million from our recent PIPE financing, and based on our revised pipeline priorities, we now expect our current cash, cash equivalents and marketable securities to fund planned operations into at least the second half of 2026.

Webcast and Conference Call Information

Ventyx will host a virtual investor event today, Monday, March 11, 2024 from 11:00AM to 12:30PM ET. To participate in the event, please dial (800) 343-4849 (U.S.) or (203) 518-9848 (international) and reference passcode VTYX0311. A live 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 for thirty days 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 inflammation and immunology markets from injectable to oral drugs. Our current pipeline includes internally discovered clinical programs targeting NLRP3, S1P1R and TYK2, positioning us to become a leader in the development of oral immunology therapies for peripheral and neuroinflammatory diseases. Ventyx is headquartered in San Diego, 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 potential of Ventyx's product candidates, including the potential of VTX3232 to emerge as a best-in-class CNS-penetrant NLRP3 inhibitor for the treatment of neuroinflammatory diseases, and the potential of VTX002 as a best-in-disease oral agent in UC ; the potentially differentiated profile of VTX002 in UC; the anticipated continued progression of the development pipeline for Ventyx's product candidates, including the anticipated timing for the initiation of Phase 2a trials of VTX3232 in Parkinson's disease and obesity in H2 2024, and the plan to evaluate VTX2735 in cardiovascular diseases; management's plans with respect to a potential pivotal Phase 3 trial for VTX002 in UC, supported by a partner or other source of non-dilutive financing; ; the anticipated timing of updates regarding the VTX958 Phase 2 trial in Crohn's disease; and the expected timeframe for funding Ventyx's operating plan with current cash, cash equivalents and marketable securities. 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; Ventyx's dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; disruptions in the supply chain, including raw materials needed for manufacturing and animals used in research, delays in site activations and enrollment of clinical trials; the results of preclinical studies and clinical trials; early clinical trials not necessarily being predictive of future results; interim results not necessarily being predictive of final results; the potential of one or more outcomes to materially change as a 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 Ventyx's 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 I, Item 1A (Risk Factors) of Ventyx's Annual Report on Form 10-K for the year ended December 31, 2023, filed on February 27, 2024, 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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