Ventyx Biosciences Highlights 2025 Pipeline Strategy and Provides Clinical Updates on its NLRP3 Inhibitor Portfolio

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First subjects dosed in a Phase 2 trial of VTX3232 in participants with obesity and cardiometabolic risk factors, with topline data expected in H2 2025

Phase 2 trial of VTX2735 in participants with recurrent pericarditis expected to initiate in January, with topline data expected in H2 2025

Topline data from ongoing Phase 2 biomarker trial of VTX3232 in participants with early Parkinson's disease expected in H1 2025

Cash, cash equivalents and marketable securities balance of $252.9M as of December 31, 2024 (unaudited) expected to fund operations into at least H2 2026

SAN DIEGO, Jan. 14, 2025 (GLOBE NEWSWIRE) -- Ventyx Biosciences, Inc. (Nasdaq: VTYX) ("Ventyx", "Company"), a clinical-stage biopharmaceutical company focused on developing innovative oral therapies for patients with autoimmune, inflammatory, and neurodegenerative diseases, today highlighted its 2025 pipeline strategy and provided clinical updates on its NLRP3 inhibitor portfolio, including VTX2735 and VTX3232.

"We believe that 2025 will be a transformative year for Ventyx with important clinical data readouts from our NLRP3 portfolio, including VTX2735, our peripherally restricted NLRP3 inhibitor and VTX3232, our CNS-penetrant NLRP3 inhibitor," said Raju Mohan, PhD, President and Chief Executive Officer. "With three trials expected to be underway by the end of January, we plan to report topline results from the Phase 2 biomarker trial of VTX3232 in patients with early Parkinson's disease in the first half of 2025, followed by results from the Phase 2 trial of VTX2735 in patients with recurrent pericarditis and the Phase 2 trial of VTX3232 in participants with obesity and cardiometabolic risk factors during the second half of 2025. With these readouts, we aim to establish Ventyx as a leader in the field of the NLRP3 inflammasome, with the potential to explore opportunities in multiple systemic and neurological diseases, including those in which IL-1 antagonism has already been validated as a therapeutic approach."

Pipeline Updates and Anticipated Milestones

NLRP3 Inhibitor Portfolio: Ventyx is advancing a portfolio of potential best-in-class oral NLRP3 inhibitors for systemic inflammatory conditions and neurodegenerative diseases, including VTX2735, a peripherally restricted NLRP3 inhibitor, and VTX3232, a CNS-penetrant NLRP3 inhibitor.

- **VTX2735 in Recurrent Pericarditis:** A single dose, open-label Phase 2 trial of VTX2735 in participants with recurrent pericarditis is expected to initiate in January. The trial will enroll approximately 30 participants for a 6-week primary treatment period, followed by a 7-week extension period. Key endpoints include safety, change in the NRS pain score, and change in high sensitivity C-reactive protein (hsCRP). Topline results are expected in the second half of 2025.

  Recurrent pericarditis is considered to be an autoinflammatory condition caused by over-activity of the innate-immune system. In particular, the disease pathophysiology is associated with aberrant activation of the NLRP3 inflammasome and IL-1, the initial cytokine of the innate immune system. Recently, concentrations of NLRP3 have been shown to be elevated in pericardial samples from patients with recurrent pericarditis compared to healthy controls. Patients refractory to non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine are commonly treated with injectable IL-1 therapies, though substantial unmet medical need remains. We believe that, by treating and preventing disease recurrence, VTX2735 has the potential to offer a safe, effective, and convenient oral therapy for patients suffering from recurrent pericarditis.

- **VTX3232 in Cardiometabolic Diseases:** Dosing has initiated in a randomized, placebo-controlled Phase 2 trial of VTX3232 in participants with obesity and cardiometabolic risk factors. The trial is expected to enroll approximately 160 subjects randomized to one of four groups for a 12-week primary treatment period: monotherapy placebo, monotherapy VTX3232, combination semaglutide + placebo, or combination semaglutide + VTX3232. Key endpoints include safety and change in hsCRP. The trial also includes a panel of exploratory endpoints, including biomarkers of inflammation and cardiometabolic disease, as well as imaging to assess body composition and liver fat. Topline results are expected in the second half of 2025.

  Activation of the NLRP3 inflammasome, and resulting chronic inflammation, has been linked to a range of cardiometabolic diseases including atherosclerosis, insulin resistance, and obesity. The Phase 2 trial of VTX3232 in participants with obesity and cardiometabolic risk factors is designed as a signal-finding trial to identify the effects of NLRP3 inhibition on a broad panel of inflammatory and metabolic biomarkers, including IL-6 and hsCRP. Data from the Phase 2 trial are

expected to inform future development of the Company's NLRP3 inhibitors in cardiometabolic diseases.

- **VTX3232 in Parkinson's Disease:** Enrollment is progressing in the ongoing Phase 2 biomarker and imaging trial of VTX3232 in participants with early Parkinson's disease. This trial is expected to enroll approximately 10 participants for a 28-day open-label treatment period. Key endpoints include safety, pharmacokinetics, and biomarkers in cerebrospinal fluid (CSF) and plasma. The trial also includes exploratory TSPO PET imaging as a marker of microglial activation. Topline results are expected in the first half of 2025.

  In a disease as complex as human Parkinson's disease, the regulatory networks in microglia and other neural cell types linking the pathological consequence of NLRP3-mediated neuroinflammation to the progression of Parkinson's disease are still unclear. However, overexpression of IL-1b and IL-18 has been observed in CSF samples from Parkinson's disease patients, suggesting NLRP3 inhibition in the CNS may offer a disease-modifying therapeutic approach.

  The Phase 2 trial of VTX3232 in early Parkinson's disease is designed to generate data in support of this therapeutic hypothesis by demonstrating the ability to modulate key inflammatory and disease-related biomarkers in the CSF, downstream of NLRP3 activation. Beyond Parkinson's disease, NLRP3 inhibition in the CNS may have therapeutic utility in a range of neurodegenerative diseases with high unmet medical need, including Alzheimer's disease, multiple sclerosis, and amyotrophic lateral sclerosis, among others.

Inflammatory Bowel Disease (IBD) Portfolio:

- **Tamuzimod (VTX002, S1P1R Modulator, ulcerative colitis):** Phase 2 long-term extension (LTE) data presented in October 2024 at the United European Gastroenterology Week meeting continue to reinforce the potential best-in-class profile of tamuzimod in ulcerative colitis (UC). While tamuzimod achieved high rates of clinical and endoscopic remission, a therapeutic ceiling may have been reached with monotherapies. Combination treatment is an emerging therapeutic concept in IBD, and its efficacy and safety profile could position tamuzimod as the backbone of future combination regimens with another oral or biologic agent. The Company continues to explore partnership opportunities for tamuzimod in ulcerative colitis.

- **VTX958 (TYK2 Inhibitor, Crohn's disease):** As previously announced, in a Phase 2 trial, VTX958 did not meet the primary endpoint of change from baseline in the Crohn's Disease Activity Index (symptomatic outcome) due to an abnormally high placebo response. VTX958 did demonstrate robust, dose-dependent, nominally statistically significant endoscopic response at Week 12 as measured by Simple Endoscopic Score-Crohn's Disease (SES-CD; an objective endpoint) and showed a greater magnitude of decrease compared to placebo in two key biomarkers of inflammation, CRP and fecal calprotectin. Recognizing the opportunity for a safe and effective oral TYK2 inhibitor as early-line therapy in Crohn's disease, we are continuing the analysis of the Phase 2 data including data from the 52-week treat-through LTE phase. Full analysis of the Phase 2 data is expected to inform a future development strategy for VTX958 in Crohn's disease, including potential partnership opportunities.

About Ventyx Biosciences

Ventyx Biosciences is a clinical-stage biopharmaceutical company developing innovative oral therapies for patients with autoimmune, inflammatory, and neurodegenerative diseases. Our expertise in medicinal chemistry, structural biology, and immunology enables the discovery of differentiated small molecule therapeutics for conditions with high unmet medical need, and our extensive experience in clinical development allows the rapid progression of these drugs through clinical trials. Our lead portfolio of NLRP3 inhibitors includes VTX2735, a peripherally restricted NLRP3 inhibitor in Phase 2 development for recurrent pericarditis, and VTX3232, a CNS-penetrant NLRP3 inhibitor in Phase 2 development for neurodegenerative and cardiometabolic diseases. Our inflammatory bowel disease portfolio includes tamuzimod (VTX002), an S1P1R modulator, and VTX958, a TYK2 inhibitor, both of which have completed Phase 2 clinical trials.

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 expected year-end 2024 cash balance based on preliminary, unaudited information for the year ended December 31, 2024; the potential of each of Ventyx's product candidates, including the potential of VTX2735 and VTX3232, to emerge as best-in-class NLRP3 inhibitors for the treatment of systemic inflammatory conditions or neurodegenerative diseases, the potential of VTX2735 to be a safe, effective or convenient oral therapy for recurrent pericarditis and to have therapeutic potential in additional chronic peripheral inflammatory diseases, and the potential of tamuzimod as a best-in-class profile for Ulcerative Colitis (UC) or a part of a combination therapy for inflammatory bowel disease; the hypothesis that NLRP3 inhibition in the CNS may offer a disease-modifying therapeutic approach, and that the Phase 2 study of VTX3232 will support such hypothesis; the anticipated timing for commencing the Phase 2 trial of VTX2735 in recurrent pericarditis; the anticipated timing of enrollment of subjects, and the estimated total subjects enrolled, in each of the Phase 2 trials; the anticipated timing for the topline results of the ongoing Phase 2 trials of VTX3232 subjects in Parkinson's disease in H1 2025, and in the setting of obesity with cardiometabolic risk factors in H2 2025, and the Phase 2 trial of VTX2735 in recurrent pericarditis in H2 2025; management's plans with respect to the commitment of internal resources toward further analysis, or development, including future studies, partnerships or other source of non-dilutive financing, for tamuzimod in UC, VTX958 in Crohn's disease, and

VTX3232 and VTX2735 in multiple cardiometabolic, systemic or neurological diseases; and the expected timeframe for funding Ventyx's operating plan with current cash, cash equivalents and marketable securities.

We are in the process of finalizing our financial statements for the year ended December 31, 2024, and the preliminary, unaudited information presented in this press release for the year ended December 31, 2024 is based on management's initial review of the information presented and its current expectations and is subject to adjustment as a result of, among other things, the completion of Ventyx's end-of-period reporting processes and related activities, including the audit by Ventyx's independent registered public accounting firm of Ventyx's financial statements. As such, any financial information contained in this press release may differ materially from the information reflected in Ventyx's financial statements as of and for the year ended December 31, 2024. You should carefully review our audited, consolidated financial statements for the year ended December 31, 2024 when they become available.

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 II, Item 1A (Risk Factors) of Ventyx's Quarterly Report on Form 10-Q for the quarter ended September 30, 2024, filed on or about November 7, 2024, and Ventyx's 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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