Tvardi Therapeutics Advances Next-Generation Oral STAT3 Inhibitor TTI-109 Toward IND in Inflammatory Bowel Disease Following FDA Pre-IND Feedback

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New analysis of Phase 1 exposure data supports the potential for sustained STAT3 inhibition at proposed clinical doses, with minimal predicted effect on STAT1 and STAT5

HOUSTON, Nov. 19, 2026 (GLOBE NEWSWIRE) -- Tvardi Therapeutics, Inc. ("Tvardi" or the "Company") (NASDAQ: TVRD), a clinical-stage biopharmaceutical company focused on the development of novel, oral small molecule therapies targeting STAT3 to treat inflammatory and proliferative diseases, today announced that it has received written responses from the U.S. Food and Drug Administration (FDA) to its pre-Investigational New Drug (pre-IND) meeting request for TTI-109, the Company's next-generation oral STAT3 inhibitor. The meeting package outlined the Company's plans for Phase 2 development of TTI-109 in inflammatory bowel disease (IBD).

Ulcerative colitis (UC) remains the Company's initial indication for TTI-109. In addition, Tvardi is evaluating Crohn's disease (CD), the other major form of IBD, as a potential additional indication. STAT3 is a key signaling protein in multiple pathways involved in both UC and CD, and the Company's STAT3 inhibitors have demonstrated activity in preclinical models of both diseases. Given this biological overlap, Tvardi sought and received FDA feedback on both UC and CD, which gives the Company the flexibility to advance the two indications either in parallel or sequentially.

The FDA's feedback was constructive and supports the Company's development approach. The FDA agreed that the types of nonclinical studies summarized in the meeting package are appropriate to support a Phase 2 clinical trial, and provided guidance on dosing, study design and patient selection to inform the Company's IND submission.

Tvardi plans to incorporate the FDA's feedback and submit an IND in 2027. Initiation of the Phase 2 study remains subject to FDA review and clearance of the IND submission, as well as the availability of additional funding.

In addition to the regulatory update, Tvardi is reporting new data on TTI-109. The Company compared levels of TTI-101, the active form of TTI-109, measured in healthy volunteers in the Phase 1 study with the levels needed to block STAT1, STAT3 and STAT5 in human immune cells in cell culture. This analysis supports the potential for TTI-109 to provide sustained inhibition of STAT3 at the proposed clinical doses, with minimal predicted effect on STAT1 and STAT5.

This selectivity profile observed differs from that of Janus kinase (JAK) inhibitors, which inhibit signaling through multiple STAT pathways. The JAK inhibitors approved in IBD carry boxed warnings for serious infections, mortality, malignancy, major adverse cardiovascular events and thrombosis. Inhibition of STAT1 and STAT5 signaling, which helps the immune system fight viruses and supports natural killer (NK) cell and T-cell function, is believed to contribute to some of the safety risks reflected in these warnings. The Company believes that preferential inhibition of STAT3, with minimal predicted inhibition of STAT1 and STAT5, has the potential to support a differentiated safety profile, although the safety of TTI-109 in patients with IBD has not yet been established.

"We are pleased with the FDA's constructive feedback, which is in line with our expectations, supports our overall approach to developing TTI-109 and gives us clear direction as we prepare our IND submission," said John Kauh, M.D., Chief Medical Officer of Tvardi. "STAT3 is a central driver of immune dysregulation, inflammation and fibrosis that underlie inflammatory bowel disease. Building on our positive Phase 1 results, including a new analysis supporting the potential for sustained STAT3 inhibition with minimal STAT1 and STAT5 inhibition at the proposed clinical doses, we believe TTI-109 may offer a differentiated oral treatment option for patients with inflammatory bowel disease. We look forward to advancing TTI-109 into Phase 2 development, subject to IND clearance and the availability of additional funding."

About TTI-109

TTI-109 is an orally administered prodrug of TTI-101, a small molecule inhibitor of signal transducer and activator of transcription 3 (STAT3). In a Phase 1 healthy volunteer study, TTI-109 delivered TTI-101-equivalent exposure with improved tolerability and demonstrated reductions in cellular and humoral immune populations known to correlate with UC disease severity, providing pharmacodynamic evidence of STAT3 target engagement.

About Inflammatory Bowel Disease

Ulcerative colitis and Crohn's disease are the two main forms of inflammatory bowel disease (IBD), chronic immune-mediated conditions that cause inflammation of the gastrointestinal tract. Despite the availability of biologic and small molecule advanced therapies, many patients do not respond adequately or lose response over time, leaving a significant need for new treatment

options with novel mechanisms of action.

About Tvardi Therapeutics

Tvardi is a clinical-stage biopharmaceutical company focused on the development of novel, oral small molecule therapies targeting STAT3 to treat inflammatory and proliferative diseases with significant unmet need. STAT3 is a central mediator across critical signaling pathways that drive immune dysregulation, inflammation and proliferation. STAT3 is also positioned at the intersection of many signaling pathways integral to the survival and immune evasion of cancer cells. The Company has completed a Phase 1 healthy volunteer study of TTI-109 and plans to initiate clinical trials of TTI-109 in ulcerative colitis pending IND clearance and the availability of additional funding. The Company is also conducting a Phase 1b/2 clinical trial of TTI-101 in hepatocellular carcinoma (NCT05440708). To learn more, please visit tvarditherapeutics.com or follow us on LinkedIn and X (Twitter).

Cautionary Statement Regarding Forward-looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Examples of these forward-looking statements include statements concerning the FDA's pre-IND feedback; the anticipated timing and content of the Company's submission of the IND for TTI-109 and the FDA's review thereof; the planned design and conduct of clinical trials of TTI-109 and its potential development in UC and CD; the predicted STAT pathway selectivity of TTI-109 and its potential to offer a differentiated safety profile relative to JAK inhibitors; the anticipated benefits of Tvardi's product candidates; its ongoing clinical trials and anticipated timing of reporting data from such trials; potential indications for its product candidates; its anticipated cash runway and the availability of additional funding to advance Tvardi's clinical development of TTI-109 in UC and/or CD; and other statements regarding management's intentions, plans, beliefs, expectations or forecasts for the future, and, therefore, you are cautioned not to place undue reliance on them.

Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These forward-looking statements are subject to a number of risks, including, among other things: the uncertainties associated with Tvardi's product candidates, as well as risks associated with the clinical development and regulatory approval of product candidates, including potential delays in the completion of clinical trials or safety or other complications related to its product candidates; the ability to obtain IND clearance for TTI-109 in UC and/or CD on the timelines expected or at all; the fact that pre-IND feedback from the FDA is non-binding and may change upon the FDA's review of the full IND submission; the possibility that the FDA may raise additional comments, request additional data or not agree with the proposed doses or study design upon review of the IND submission; the ability to replicate results for preclinical studies and early clinical trials in later trials; the risk that the predicted STAT3 selectivity of TTI-109, which is based on modeling of exposures in healthy volunteers relative to in vitro data, may not be observed in patients or may not result in a differentiated safety profile or other clinical benefit; the requirement for additional capital to continue to advance these product candidates, which may not be available on favorable terms or at all; the significant net losses Tvardi has incurred since inception; Tvardi's ability to initiate and complete ongoing and planned preclinical studies and clinical trials and advance its product candidates through clinical development; the timing of the availability of data from Tvardi's clinical trials; the outcome of preclinical testing and clinical trials of Tvardi's product candidates, including the ability of those trials to satisfy relevant governmental or regulatory requirements; Tvardi's plans to research, develop and commercialize its current and future product candidates; the clinical utility, potential benefits and market acceptance of Tvardi's product candidates; Tvardi's anticipated cash runway; Tvardi's ability to attract, hire, and retain skilled executive officers and employees; Tvardi's ability to protect its intellectual property and proprietary technologies; Tvardi's reliance on third parties, contract manufacturers, and contract research organizations; the possibility that Tvardi may be adversely affected by other economic, business, or competitive factors; risks associated with changes in applicable laws or regulations; those factors discussed in Tvardi's filings with the Securities and Exchange Commission, including the "Risk Factors" section of the Annual Report on Form 10-K for the year ended December 31, 2025, and Tvardi's other documents subsequently filed with or furnished to the SEC, all of which are available on the SEC's website at www.sec.gov. All forward-looking statements contained in this press release speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

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