Tvardi Therapeutics Selects Ulcerative Colitis as Initial Indication for TTI-109

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STAT3 acts as a convergent node downstream of multiple signaling pathways implicated in ulcerative colitis (UC), integrating immune dysregulation, inflammation and tissue remodeling

More than 70% of patients do not achieve clinical remission with currently approved UC therapies, which target individual upstream pathways; TTI-109 is designed to directly inhibit STAT3 where these pathways intersect

Selection follows completion of the TTI-109 Phase 1 healthy volunteer study, which demonstrated placebo-adjusted reductions across cellular and humoral immune cell subsets implicated in UC pathology

Company to host KOL webinar with Dr. Randy Longman, M.D., Ph.D. on Wednesday, August 19 at 11:00 AM ET to discuss current treatment landscape and share new data supporting the potential of TTI-109 in UC

HOUSTON, July 30, 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 selected ulcerative colitis (UC) as the initial disease indication for its next generation STAT3 inhibitor, TTI-109.

Tvardi’s decision follows its successful Phase 1 healthy volunteer study, in which TTI-109 successfully modulated multiple STAT3-driven immune cell populations, including Th17, T follicular helper (Tfh) and B cells. These same cell types are known to expand with UC disease severity and infiltrate the inflamed colon.

Further analysis of immune cell populations across the active dose range elucidated:

- Broad suppression of pathogenic Th17-associated immune populations, including up to 76% reduction in subsets associated with mucosal destruction and treatment-refractory UC
- The Tfh immune populations that drive mucosal B cell responses were reduced up to 43% in Tfh subsets associated with disease UC activity
- Suppression extended to B cell (humoral) immunity, including up to 71% decline in subsets associated with colonic inflammation

STAT3 sits at the center of the three interconnected processes that drive UC: immune dysregulation, chronic inflammation and the tissue remodeling that leads to fibrosis, positioning it as a single, convergent therapeutic target for a disease with multiple underlying drivers. These findings are further supported by published clinical studies linking reductions in activated STAT3 with higher rates of clinical remission across multiple UC therapeutic classes.

UC is a large and underserved market. More than 1.25 million patients are diagnosed with UC in the United States, representing an addressable market of approximately $3 billion in the U.S. and $9 billion globally. Currently approved therapies, including anti-TNF, anti-integrin, anti-IL-12/23, S1P and JAK inhibitors, achieve placebo-adjusted clinical remission rates below 30%, and most are administered parenterally. Additionally, JAK inhibitors carry a black box warning for major adverse cardiovascular events, mortality, thrombosis, serious infections and malignancy.

By contrast, TTI-109, an oral small molecule, is designed to inhibit STAT3 directly, addressing the inflammation, immune dysregulation and proliferation that single-pathway therapies leave unresolved. Across more than 400 subjects dosed to date with Tvardi’s STAT3 inhibitors demonstrated a differentiated safety profile from JAK inhibitors. TTI-109 is administered orally without a loading dose, and in preclinical models of UC, achieved more than eight-fold greater drug concentration in target tissue relative to plasma.

Imran Alibhai, Ph.D., Chief Executive Officer of Tvardi, stated, “In our healthy volunteer study we observed reductions across immune cell populations that the published literature implicates in UC pathogenesis, and we saw them consistently across the active dose range. STAT3 sits downstream of the cytokines that drive UC, including IL-23, IL-6 and IL-17. We believe a single oral agent acting at that convergence point has the potential to help patients who have not responded adequately to a biologic or JAK inhibitor. This is what led us to prioritize UC as our initial indication for TTI-109.”

Planned UC Clinical Trial

Tvardi plans to initiate a study of TTI-109 in patients with moderate-to-severe UC in 2027, subject to clearance of Investigational New Drug (IND) application and additional funding. The primary endpoint will be safety, and the secondary endpoint will be clinical remission at 12 weeks. Exploratory pharmacodynamic endpoints will include serum/tissue biomarkers and analysis of single nucleotide polymorphisms (SNPs).

Key Opinion Leader Webinar

Tvardi will host a Key Opinion Leader (KOL) webinar featuring Randy Longman, MD, PhD, of Weill Cornell Medicine on Wednesday, August 19, at 11:00 a.m. ET. During the event, Tvardi management will present new data supporting the therapeutic potential of TTI-109 in ulcerative colitis, while Dr. Longman will provide an overview of the evolving UC treatment landscape, remaining unmet needs and the potential role of novel therapies.

To register for the webinar, please click here or visit the Investor Relations section of Tvardi's website.

KOL Biography – Randy Longman, MD, PhD

Randy Longman is the Director of the Jill Roberts Center for IBD and an Associate Professor of Medicine in the Jill Roberts Institute for Research in IBD at Weill Cornell Medicine. He received his undergraduate degree from Yale University, his M.D. from Weill Cornell Medical College, and his Ph.D. in immunology from The Rockefeller University. He completed clinical training in Internal Medicine and Gastroenterology at Columbia University Medical Center and a post-doctoral research fellowship with Dr. Dan Littman at the Skirball Institute, NYU School of Medicine. His research focuses on defining the cellular and molecular mechanisms underlying host-microbiota interactions that drive the pathogenesis of mucosal and systemic inflammation in IBD. He has received research funding from many foundations including the NIH, Rainin Foundation, and the Crohn's and Colitis Foundation. In recognition of his research, he has received the Irma T. Hirschl Career Scientist Award and was recently elected to the American Society for Clinical Investigation. He is currently an associate editor at Journal for Crohn's and Colitis and a member of the National Scientific Advisory Committee for the Crohn's and Colitis Foundation.

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 uncontrolled proliferation, survival and immune dysregulation. 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 a clinical trial of TTI-109 in its initial indication, 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).

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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 anticipated benefits of Tvardi's product candidates, including TTI-109 in dermatologic and GI therapeutic areas and of the Company's STAT3 inhibitors, including as compared to single-pathway biologics; the potential benefits of TTI-109 as compared to TTI-101, including improved delivery and tolerability; its ongoing and planned clinical trials, including its ongoing Phase 1b/2 clinical trial of TTI-101 in hepatocellular carcinoma and its planned future trials of TTI-109; the results from the Phase 1 trial of TTI-109 validating the Company's prodrug strategy and supporting its continued development pathway; the Company's plans to develop TTI-109 in UC, subject to clearance of an IND application and receipt of additional funding; 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 on the timelines expected or at all; 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 the 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; the estimated patient populations and total addressable markets for the indications in which Tvardi seeks to develop its 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.