Tvardi Therapeutics' TTI-109 Phase 1 Study Confirms Prodrug Design, Improved Tolerability and Pharmacodynamic Evidence of STAT3 Target Engagement

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TTI-109 delivered TTI-101-equivalent exposure with improved tolerability and meaningful reductions in disease-relevant STAT3-driven immune cell populations including Th17, T follicular helper (Tfh) and B cells

Company plans to advance TTI-109 into STAT3-driven dermatologic and gastrointestinal (GI) diseases - subject to additional funding

Company to host investor webcast today, July 7th, at 8:30am ET

HOUSTON, July 07, 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 Phase 1 results for TTI-109, its next-generation STAT3 inhibitor. TTI-109 is a phosphate prodrug of TTI-101 designed to improve delivery and tolerability while preserving the parent compound's mechanism of action. The study confirmed rapid prodrug conversion, dose-proportional pharmacokinetics with exposures above the STAT3 IC_{50}[1] and, in an exploratory pharmacodynamic analysis, reductions of up to 60% in STAT3-driven immune cell populations across Th17, Tfh and B cell subsets.

Key findings include:

- **Confirmed prodrug conversion and exposure equivalence:** Validating its prodrug design, TTI-109 rapidly converted to TTI-101 within two hours and produced nearly identical plasma levels at molar-equivalent doses.
- **Sustained target-level exposure:** 21-day repeat dosing showed stable, dose-proportional pharmacokinetics, with TTI-101 concentrations above the STAT3 IC_{50}.
- **Evidence of target engagement:** Pharmacodynamic data showed reductions of up to 60% across disease-relevant STAT3-driven immune cell populations including Th17 cells, Tfh and B cell subsets.
- **Improved tolerability vs. TTI-101:** Compared with placebo, diarrhea events with TTI-109 were similar in duration, transient, and resolved without treatment interruption. Compared with TTI-101 at near-equivalent doses, diarrhea events with TTI-109 were substantially shorter in duration (0.46 vs. 3.35 days).

Imran Alibhai, Ph.D., Chief Executive Officer of Tvardi, stated, "These Phase 1 results validate our prodrug strategy on every objective we set out to test. TTI-109 matched TTI-101's exposure at molar-equivalent doses with substantially better tolerability and delivered a pharmacodynamic signal across disease-relevant immune cell populations that we would not typically expect to see in healthy volunteers. That combination of findings supports our development pathway into Phase 2."

The study was conducted in three parts. Part A was a randomized, double-blind, placebo-controlled single ascending dose study of TTI-109 at four doses (n=8/cohort). Part B was a bioequivalence crossover comparing TTI-101 and TTI-109 in both sequences with a 48-hour washout (n=6/sequence). Part C was a randomized, double-blind, placebo-controlled multiple ascending dose study with 21 days of twice-daily dosing at four doses, plus a TTI-101 reference arm (n=8/cohort).

Primary objectives were to confirm rapid conversion of TTI-109 to TTI-101, demonstrate equivalent exposures at molar-equivalent doses, demonstrate dose-dependent increases in TTI-101 exposure and characterize safety and tolerability versus TTI-101 and placebo. Pharmacodynamic effects were an exploratory objective.

Tvardi Plans to Advance TTI-109 Across Dermatologic and GI Therapeutic Areas

The Company has identified dermatologic and gastrointestinal therapeutic areas with shared STAT3-driven disease biology, specifically the convergence of cytokines, growth factors and Th17 and B cell immune pathways at the STAT3 node. TTI-109 is designed to address both the cellular and humoral components of inflammation and proliferation with a single oral agent. Recent programs in related STAT3-driven indications have validated the underlying biology, but each acts on a single upstream target, while TTI-109 targets STAT3, the downstream node where these pathways converge.

STAT3 sits at the center of the core disease processes in dermatologic and gastrointestinal diseases, including inflammation,

proliferation and cellular and humoral dysregulation. Tvardi's STAT3 inhibitors have demonstrated biologic activity in these pathways in both preclinical models and in the clinic. In preclinical disease models, the Company's STAT3 inhibitors reduced inflammatory cascades, fibrosis and modulated immune activity. Similarly, in humans, TTI-101 reduced activated STAT3 levels, inflammatory cascades and fibrosis. The TTI-109 healthy volunteer study extended this translational profile, with reductions in STAT3-driven immune cell populations.

"The diseases we are targeting are still largely managed with parenteral therapies that each block a single pathway," said Dr. Alibhai. "Because STAT3 sits downstream of multiple convergent signals, a single oral STAT3 inhibitor has the potential to do what no single-pathway biologic can and we believe our preclinical, clinical and now pharmacodynamic data are building a consistent case that TTI-109 is a promising molecule to test this hypothesis."

Tvardi's ability to initiate these programs is subject to clearance of an Investigational New Drug application (IND) and the availability of additional funding.

Webcast

Tvardi management will host a webcast today, Tuesday, July 7th, 2026, at 8:30 am ET to discuss these results in more detail.

The webcast can be accessed here: https://lifescievents.com/event/t349t28y/.

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 clinical trials of TTI-109 in dermatologic and GI diseases, 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 Phase 2 trials of TTI-109; the results from the Phase 1 trial of TTI-109 validating the Company's prodrug strategy and supporting its development pathway into Phase 2; the Company's plans to develop TTI-109 in dermatologic and GI therapeutic areas, 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 dermatologic and GI therapeutic areas 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.

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[1] In a controlled system where proliferation is driven by WT STAT3, TTI-101 inhibits cell growth with an IC_{50} of approximately 1.5μM. Kasembeli MM, Kaparos E, Bharadwaj U, et al. Aberrant function of pathogenic STAT3 mutant proteins is linked to altered stability of monomers and homodimers. *Blood*. 2023;141(12):1411-1424. doi:10.1182/blood.2021015330.