UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d) of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported) **July 30, 2026**

TVARDI THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-36279**	**75-3175693**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)
3 Sugar Creek Ctr. Blvd. **Suite 525** **Sugar Land, Texas**		**77478**
(Address of principal executive offices)		(Zip Code)

Registrant's telephone number, including area code: **(713) 489-8654**

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2.):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	TVRD	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On July 30, 2026, Tvardi Therapeutics, Inc. (the "***Company***") issued a press release entitled "Tvardi Therapeutics Selects Ulcerative Colitis as Initial Indication for TTI-109." The full text of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference.

On July 30, 2026, the Company also made available an updated corporate presentation. A copy of the presentation is attached as Exhibit 99.2 to this Current Report on Form 8-K.

The information in this Item 7.01 of this Current Report on Form 8-K (including Exhibits 99.1 and 99.2) is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "***Exchange Act***"), or otherwise subject to the liabilities of that Section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release issued on July 30, 2026.
99.2	Corporate presentation, dated July 30, 2026.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

TVARDI THERAPEUTICS, INC.

Date: July 30, 2026

By: /s/ Imran Alibhai
Name: Imran Alibhai
Title: Chief Executive Officer

Exhibit 99.1

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

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, TX – July 30, 2026 -- 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.

Exhibit 99.2

Overview

July 2026

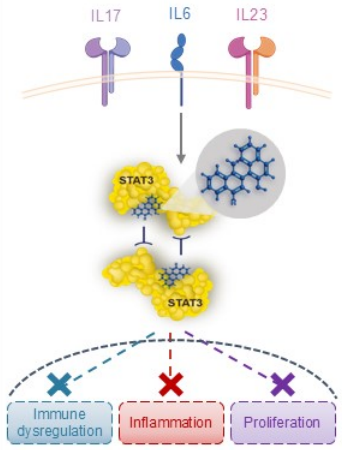
Disclaimer and Forward-Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements about our expectations regarding the potential benefits, activity, effectiveness, and safety of our product candidates, our expectations with regard to the design and results of our research and development programs, preclinical studies, and clinical trials, including the timing and availability of data from such studies and trials, our preclinical, clinical, and regulatory development plans for our product candidates, including the timing or likelihood of regulatory filings and approvals for our product candidates, our cash position and anticipated cash runway, and our ability access additional capital to advance our clinical programs, our expectations with regard to our ability to license, acquire, discover, and develop additional products candidates and advance such product candidates into, and successfully complete, preclinical studies and clinical trials, the potential market size and size of the potential patient populations for our product candidates and any future product candidates, our ability to maintain existing, and establish new, strategic collaborations, licensing, or other arrangements, the scope of protection we are able to establish and maintain for intellectual property rights covering our initial product candidates and any future product candidates, our business strategy, and our future results of operations and financial position, and our anticipated cash runway are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are subject to a number of risks, uncertainties and assumptions. Risks regarding our business are described in detail in our Securities and Exchange Commission filings, including in our Annual Report on Form 10-K for the year ended December 31, 2025, and our other filings with the SEC, which are available on the SEC's website at www.sec.gov. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements contained in this presentation reflect our current views with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Our STAT3 Inhibitors are Designed to Address the Unmet Need in Inflammatory and Proliferative Diseases

STAT3: Highly Validated Convergent Node



STAT3: central mediator in inflammatory and proliferative disease

Translational Proof-of-Concept

Preclinical

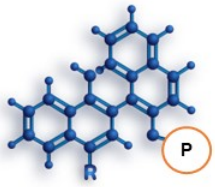
- ↓ pY-STAT3
- ↓ immune dysregulation
- ↓ inflammation
- ↓ proliferation

Confirmed in patients

Clinical

- ↓ pY-STAT3
- ↓ immune dysregulation
- ↓ inflammation
- ↓ proliferation

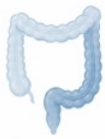
TTI-109 Validation in P1 Healthy Volunteers



TTI-109

- ✓ **PK**
- ✓ **GI tolerability**
- ✓ **Immune modulation**

TTI-109 Lead Indication



Ulcerative Colitis (UC)

- Targeting a single convergent node
- Oral therapy with targeted tissue exposure
- Assessment of STAT3-mediated inflammatory response signature

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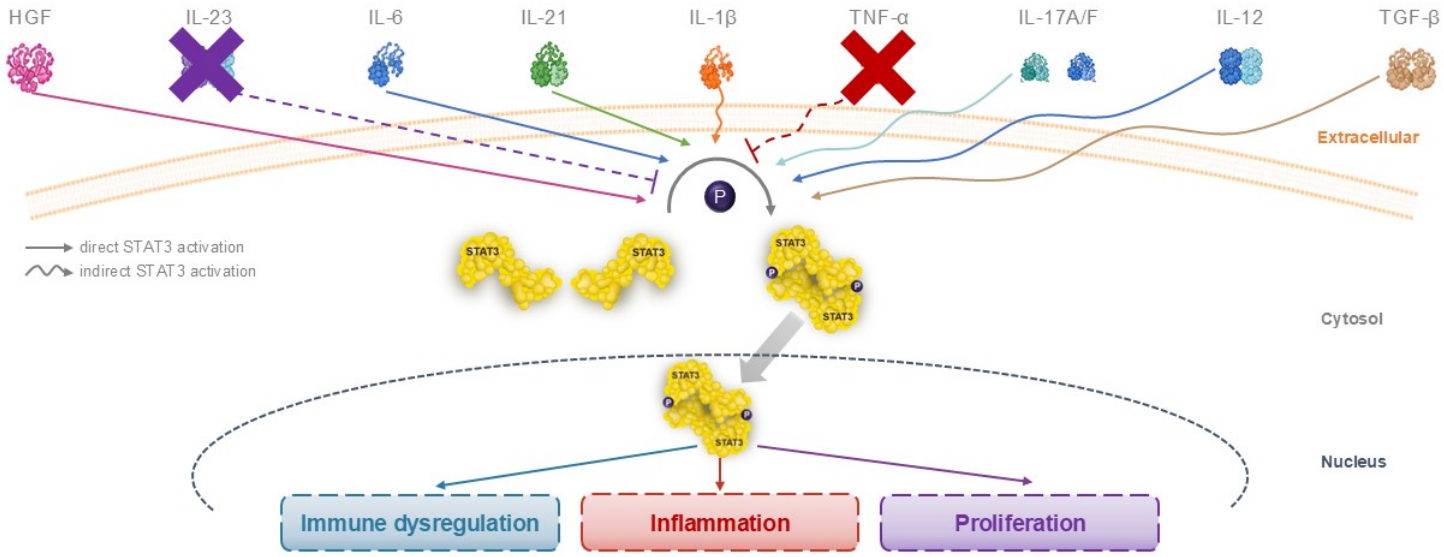
pY-STAT3: activated STAT3 induced by phosphorylation of tyrosine residue 705; PK: pharmacokinetics

Targeting STAT3: a Convergence Point of Inflammatory and Proliferative Disease

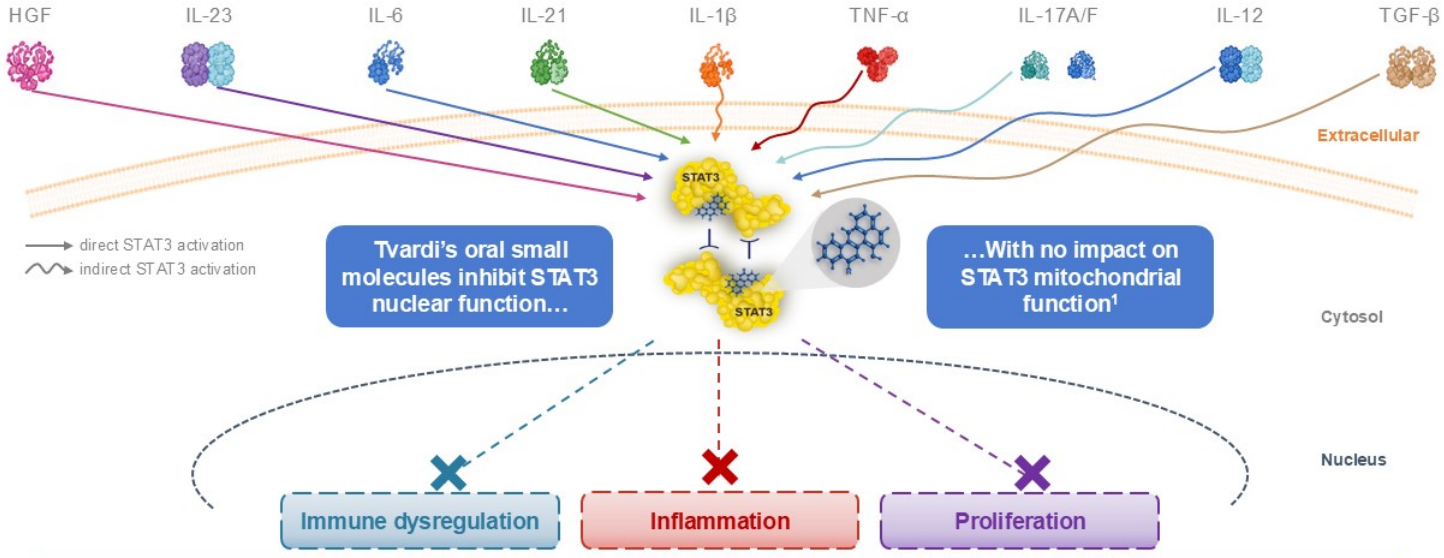
Current Therapies Target Individual Pathways



Single-pathway inhibition fails to suppress STAT3 due to redundant signaling cascades

Targeting STAT3: a Convergence Point of Inflammatory and Proliferative Disease

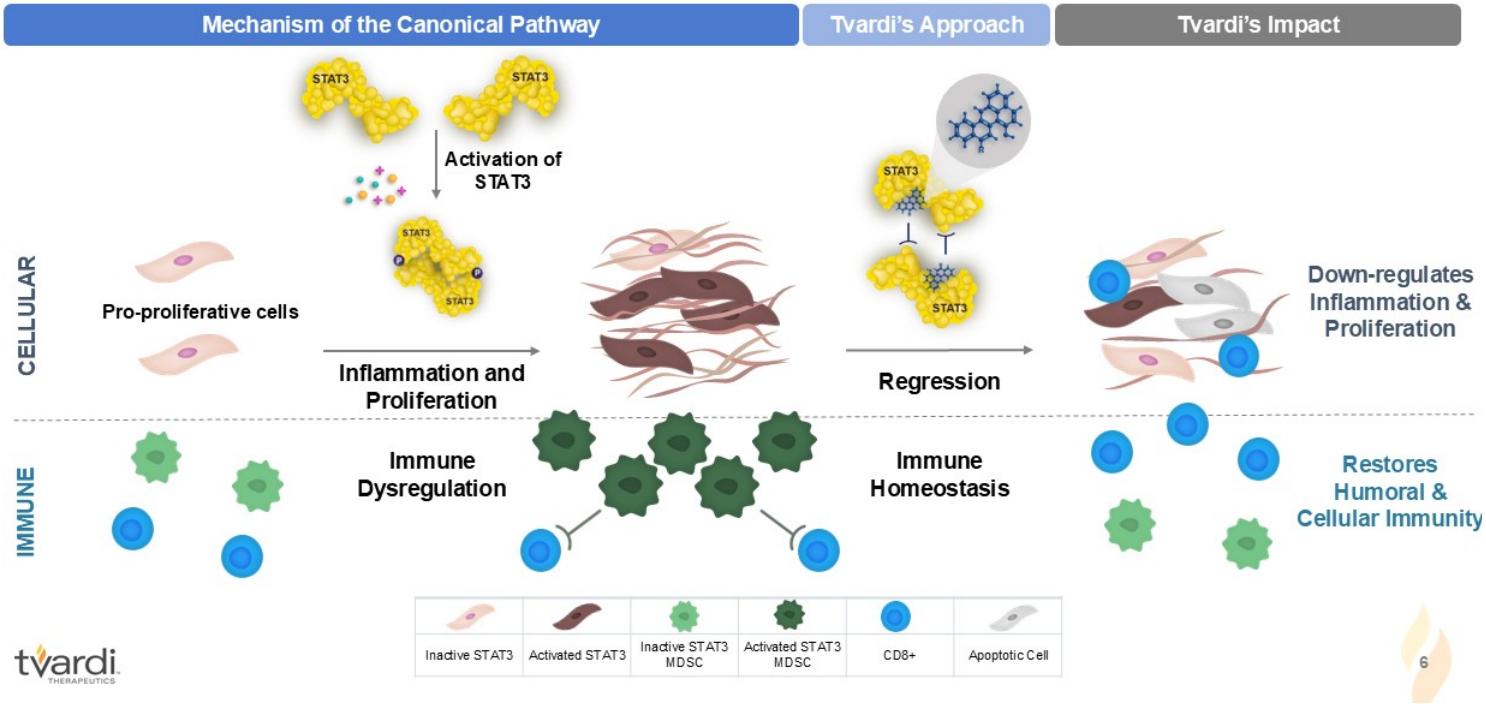
Diverse Disease Signaling Pathways Converge on STAT3



Selective inhibition of STAT3 nuclear function blocks three drivers of disease from a single target

1. Kasembeli et al. *Biochem Pharmacol.* 2021

STAT3's Multi-modal Mechanism of Action in Inflammatory and Proliferative Diseases



Seasoned Leadership: Deep R&D and Operational Expertise

Management Team

Imran Alibhai, PhD CEO & Director

DNAtrix THERAPEUTICS · SOLOMON · ALEXANDRIA Venture Investments · MPM

Dan Conn, JD, MBA CFO

DE Shaw & Co · SOLOMON · Morgan Stanley · Brookfield

John Kauh, MD CMO

HUTCHMED · Lilly · EMORY UNIVERSITY SCHOOL OF MEDICINE

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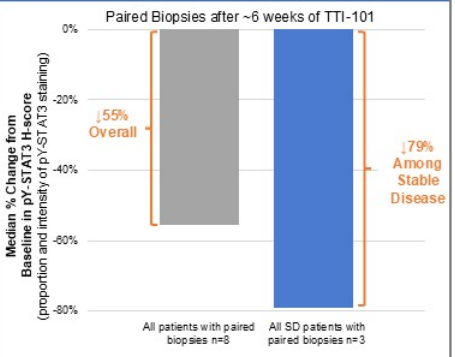
TTI-109

TTI-101 Clinical Foundation for Development of TTI-109

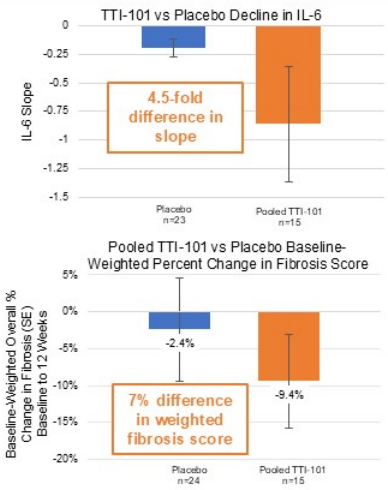
pY-STAT3 Target Engagement Oncology Phase 1[1]



8/10 patients had elevated pY-STAT3 at baseline; elevated pY-STAT3 defined as H-score >30 on a 0-300 scale

- 100% of patients with elevated baseline pY-STAT3 demonstrated a decrease within ~6 weeks; greater decrease in pY-STAT3 among patients with stable disease

IL-6 & Fibrosis Reduction REVERT IPF Phase 2[2]



Overall TTI-101 Safety

In over 300 subjects treated with TTI-101:

Mitochondrial toxicities observed with other STAT3 inhibitors[3] not observed with TTI-101:

- Peripheral neuropathy
- Lactic acidosis

Safety signals observed with JAK inhibitors[4] not observed with TTI-101:

- Major cardiovascular events
- Malignancy
- Cytopenias

Most commonly reported adverse event with TTI-101: diarrhea[1]

TTI-109 is designed to enhance delivery & improve tolerability while preserving mechanism of action

1. Tsimberidou et al. *Clin Cancer Res*. 2025;: 2. Tvardi Press Release: January 8, 2026; 3. Kasembeli et al. *Biochem Pharmacol*. 2021; 4. FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions; pY-STAT3: activated STAT3 induced by phosphorylation of tyrosine residue 705; SD: stable disease

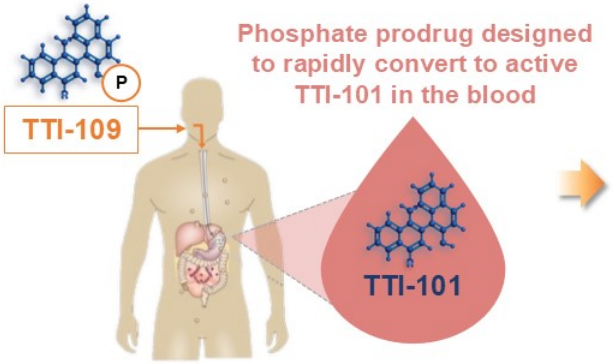
TTI-109 Designed as a Prodrug to Enhance Delivery of STAT3 Inhibitor and Establish Favorable Target Product Profile

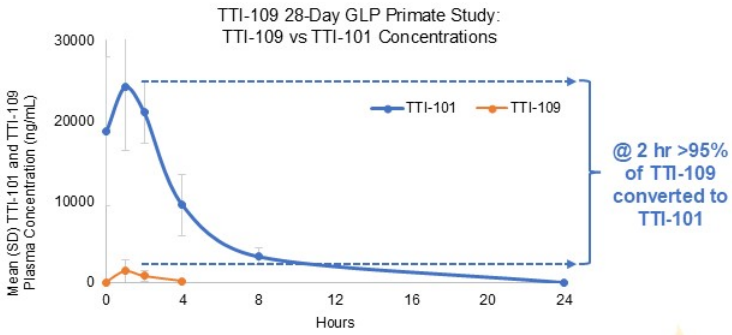
TTI-109 Design Objectives

- Preserve mechanism of action and observed clinical activity of TTI-101
- Improve drug delivery
- Diminish GI exposure

IND-Enabling GLP Results

- No toxicology findings with TTI-109, mirroring TTI-101
- At equal molar doses, TTI-109 and TTI-101 had equivalent exposures
- TTI-109 rapidly converted to active moiety TTI-101





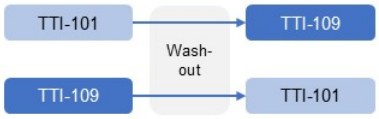
*The pharmacokinetics of TTI-109 and TTI-101 were evaluated in GLP toxicology studies in rats and monkeys. Systemic exposures to TTI-101 from TTI-109 administration were predictable in terms of molar equivalent amounts of anticipated TTI-101.

Phase 1 Clinical Program Validated TTI-109 as the Oral Prodrug of TTI-101

Part A: Single Ascending Dose (SAD)

Randomized, double blind, placebo-controlled
Single dosing of TTI-109 vs placebo

Part B: Bioequivalence Crossover Study



Randomized sequence of treatment of n=6 into each group

Part C: Multiple Ascending Dose (MAD)

Randomized, double blind, placebo-controlled
21-day BID dosing of TTI-109 vs placebo
with additional TTI-101 arm

Primary & Secondary Objectives:

- Confirm rapid PK conversion of TTI-109 to TTI-101 in humans
- Confirm equivalent exposures of active moiety with TTI-101 and TTI-109 dosing
- Demonstrate dose-dependent increases in TTI-101 exposures from TTI-109 administration
- Characterize safety/tolerability of TTI-109 relative to TTI-101 after repeated doses

Exploratory Objectives:

- Evaluate pharmacodynamics of TTI-109 in healthy participants

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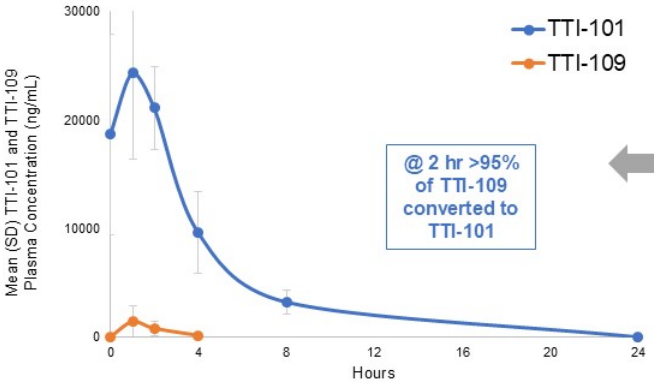
TTI-101 recommended phase 2 dose of TTI-101 (400mg BID) determined in oncology studies; PK: pharmacokinetics; BID: twice daily

TTI-109 Rapidly Converted to Active TTI-101: Consistent from Primate to Human

SAD

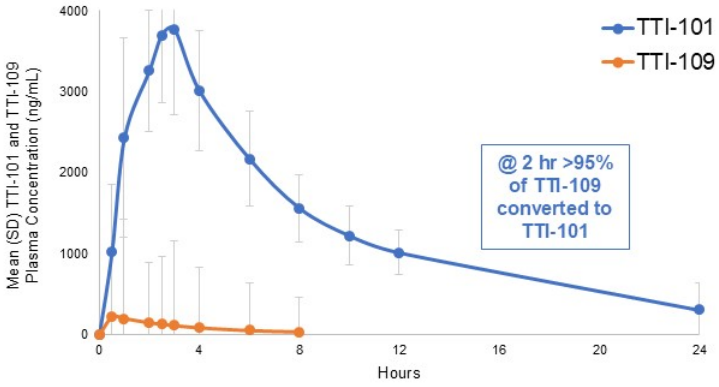
Primate Study: Rapid conversion of TTI-109 to active moiety TTI-101

TTI-109 28-Day GLP Primate Study*:
TTI-109 vs TTI-101 Concentrations



Human Study: Rapid conversion of TTI-109 to active moiety TTI-101

Plasma Concentrations of TTI-101 vs TTI-109 (500mg)

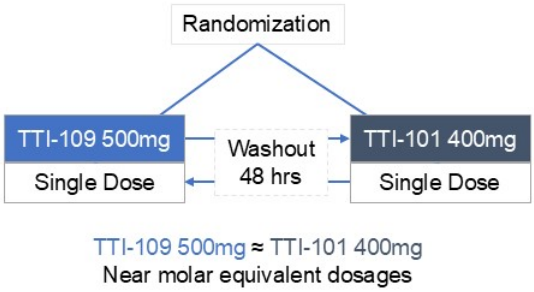


TTI-109 dosing yielded rapid conversion to the active moiety, TTI-101, consistent with animal studies

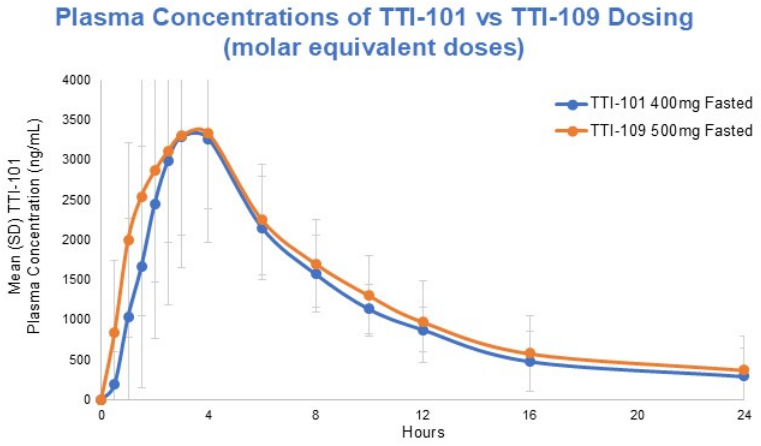
*The pharmacokinetics of TTI-109 and TTI-101 were evaluated in GLP toxicology studies in rats and monkeys. Systemic exposures of TTI-101 from TTI-109 administration were predictable in terms of molar equivalent amounts of anticipated TTI-101. SAD: Single Ascending Dose

TTI-109 Achieved Equivalent Active Moiety Exposure to TTI-101

Bioequivalence Cross-over Study



TTI-109 500mg ≈ TTI-101 400mg
Near molar equivalent dosages

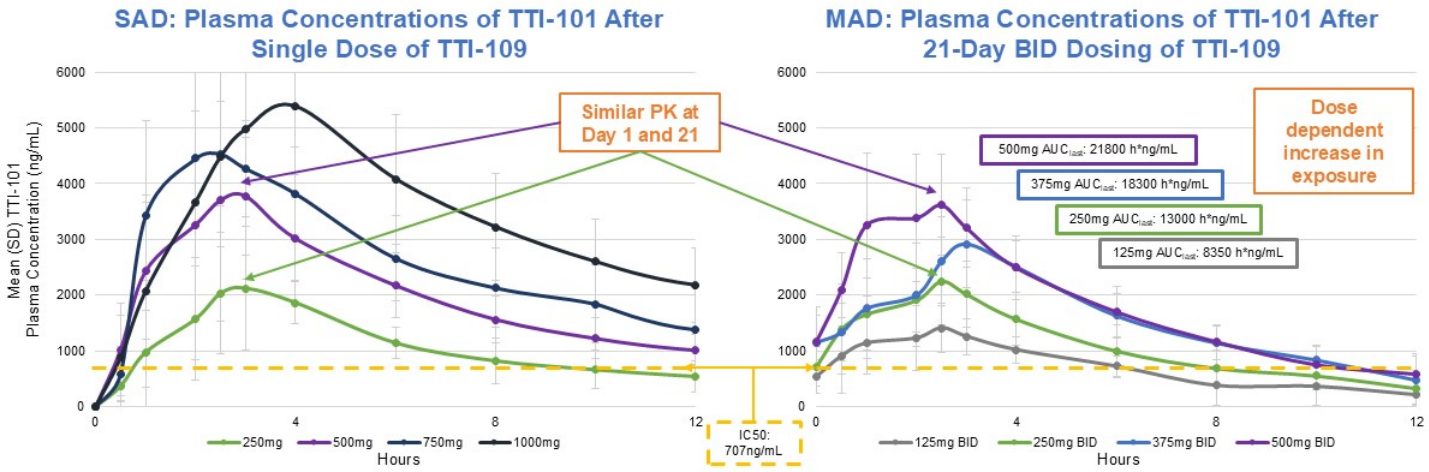


Equal molar dosing confirmed equivalent exposures of active moiety with TTI-101 and TTI-109

TTI-101 plasma concentrations following dosing with TTI-101 400 mg vs TTI-109 500 mg (427 mg TTI-101 molar eq.) in fasted state; Fed and fasted resulted in similar concentrations

TTI-109 Repeat Dosing Delivered Predictable Steady State Parameters

SAD MAD



Predictable, dose-proportional PK with exposures above STAT3 IC_{50}

SAD: Single Ascending Dose; MAD: Multiple Ascending Dose; PK = Pharmacokinetics; STAT3 IC_{50}: in a controlled system where proliferation is driven by pY-STAT3, TTI-101 inhibits cell growth with an IC_{50} of approximately 1.5µM (707ng/mL)

TTI-109 Phase 1 TEAE Profile

MAD

TTI-109 500mg ≈ TTI-101 400mg
Near molar equivalent dosages

Adverse Event Preferred Term	Placebo (N=8)		TTI-109 Doses 1-4 (N=32)		TTI-109 500mg (N=8)		TTI-101 400mg (N=8)	
No. of participants reporting at least one TEAE	5 (63%)		19 (59%)		6 (75%)		6 (75%)	
AEs leading to drug withdrawal	-		1 (3%)*		-		1 (3%)**	
TEAEs observed in ≥ 2 subjects per cohort	Grade 1	Grade 2	Grade 1	Grade 2	Grade 1	Grade 2	Grade 1	Grade 2
Diarrhea	2 (25%)	-	10 (31%)	1 (3%)	2 (25%)	-	3 (38%)	-
Abdominal pain	-	-	3 (9%)	1 (3%)	2 (25%)	-	3 (38%)	-
Headache	1 (13%)	-	4 (13%)	1 (3%)	-	-	1 (13%)	-
Constipation	1 (13%)	-	1 (3%)	-	1 (13%)	-	1 (13%)	1 (13%)

*TTI-109 250mg BID subject discontinued due to grade 3 transaminitis; however, transaminases began to improve while on TTI-109, suggesting AE was unlikely related: bilirubin remained normal throughout treatment; **TTI-101 400mg BID subject discontinued due to diarrhea

- No serious adverse events
- No dose dependent pattern in the TEAEs
- No clinically relevant changes in vital signs or ECGs

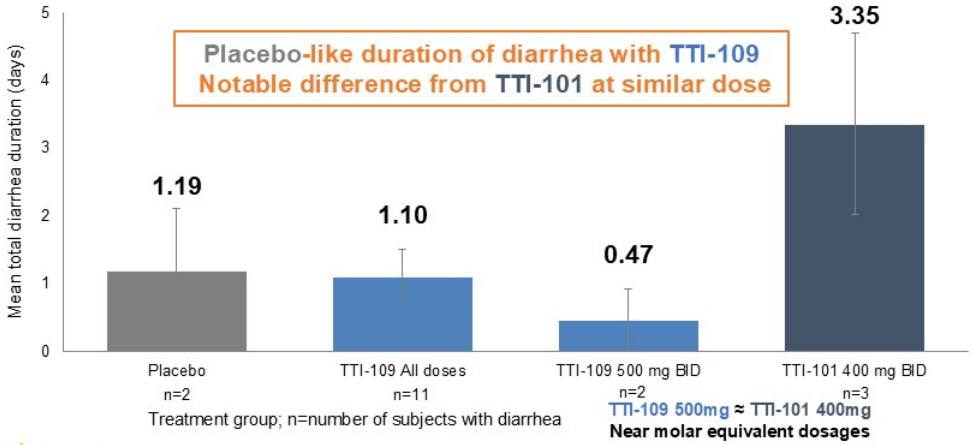
Similar incidence of TEAEs across all groups

Differential Diarrhea Pattern: TTI-109 vs. TTI-101

TTI-109 500mg ≈ TTI-101 400mg
Near molar equivalent dosages

MAD

Adverse Event Preferred Term	Placebo (N=8)		TTI-109 Doses 1-4 (N=32)		TTI-109 500mg (N=8)		TTI-101 400mg (N=8)	
	Grade 1	Grade 2	Grade 1	Grade 2	Grade 1	Grade 2	Grade 1	Grade 2
Diarrhea	2 (25%)	-	10 (31%)	1 (3%)	2 (25%)	-	3 (38%)	-
Discontinuation	0 (0%)		0 (0%)		0 (0%)		1 (13%)	



TTI-109:

- Comparable to placebo
- Shorter duration than TTI-101
- Transient and resolved without interruption

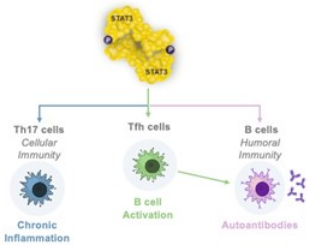
TTI-101:

- Trend for longer duration versus TTI-109 or placebo
- 1 subject discontinued due to diarrhea

MAD: Multiple Ascending Dose; TTI-101 400 mg vs TTI-109 500 mg (427 mg TTI-101 molar eq.); Duration calculated as total per subject

Preclinical Framework for Exploratory Pharmacodynamic Objectives

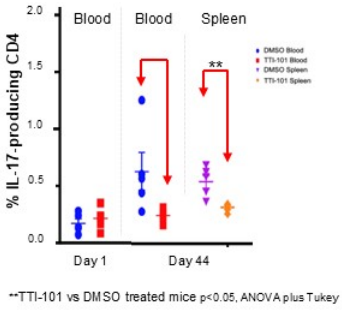
pY-STAT3 drives cellular and humoral immunity



STAT3 is an essential regulator of Th17 and B cells: T cell and B cell-specific STAT3 knockout mice are Th17-deficient and unable to produce autoantibodies, respecitvely[1]

Observed reduction of Th17 in healthy mice with TTI-101[2]

Th17 in healthy mice

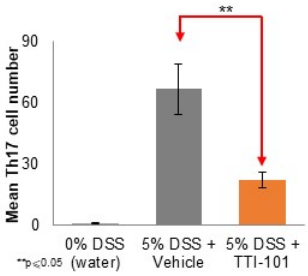


**TTI-101 vs DMSO treated mice $p<0.05$, ANOVA plus Tukey

In healthy mice, observed a 50% decrease in number of IL-17-producing CD4+ cells

Observed reduction of Th17 in diseased mice with TTI-101[3]

Colonic Th17 cells in IBD Model (5% DSS)[3]



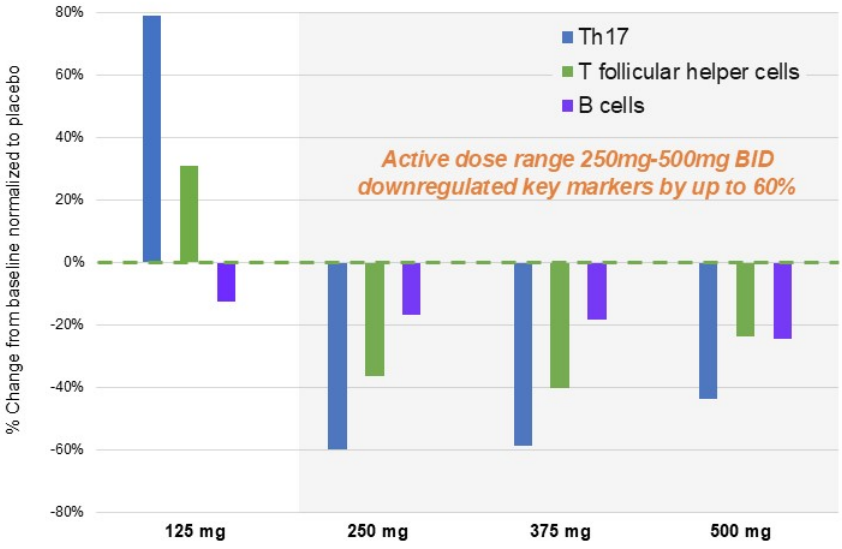
Recapitulated modulation of the immune system in diseased mouse models

Evaluating pharmacodynamics from HV

- ↓ Th17 immune cell populations in healthy volunteers?
- Additional STAT3 driven-immune cell populations modulated in the expected direction?

TTI-109 Selectively Reduced Immune Cell Populations Driven by STAT3 in Phase 1 MAD Cohort

MAD



At active doses, downregulation of STAT3-driven immune populations observed:

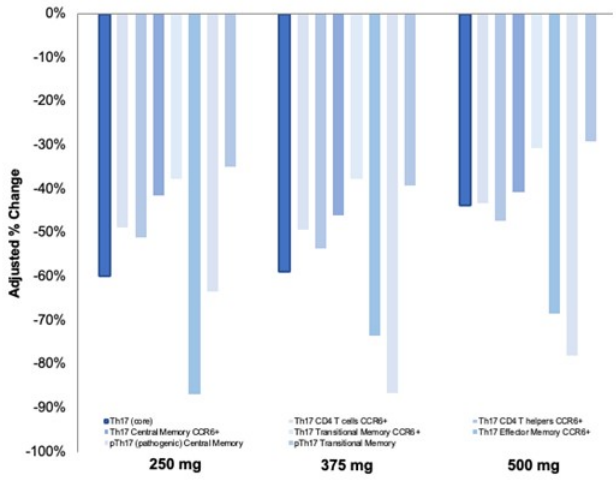
- ✓ Effects **sustained** across active dose range
- ✓ **Reduced** Th17, Tfh and B cell populations
- ✓ **Reductions** across 16 cellular and humoral immune subsets recognized as pathologic markers of inflammatory and proliferative diseases

TTI-109 modulated STAT3-driven cellular (T cell) and humoral (B cell) immune populations

TTI-109 by dose paired %Δ = (Post−Pre)/Pre; placebo-adjusted (n=8 per dose). Cell population changes assessed by flow cytometry (FACS) on peripheral blood mononuclear cells (PBMC) collected from subjects in the Phase 1 multiple ascending dose (MAD) cohort; values shown represent percentage change from baseline, normalized to placebo, for each active dose cohort. Th17, T follicular helper (Tfh), and B cell populations identified by surface marker immunophenotyping

TTI-109 Reduced Th17 Cells Implicated in UC Pathology

MAD



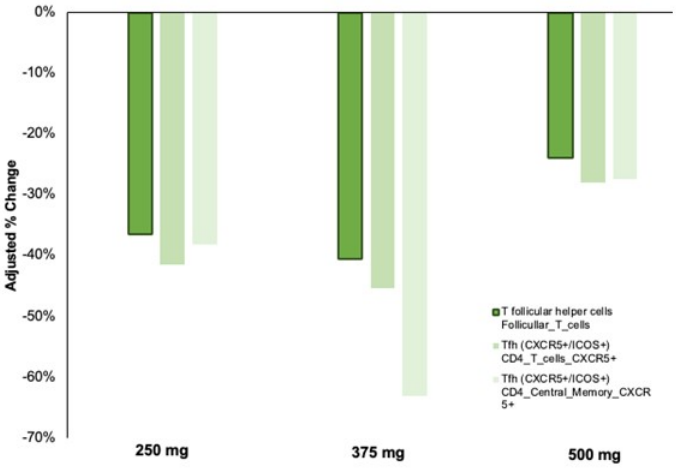
Broad suppression of pathogenic Th17-associated immune populations

Cell Type	%Δ	UC Rationale
Th17 cells (core)	**-54%**	**Central pathogenic effectors in UC and drive mucosal inflammation.**[1]
CD4 T cells CCR6+	-47%	Enriched in active UC biopsies.[2]
CD4 T helpers CCR6+	-51%	Drive IL-21-mediated B cell activation and pathogenic antibody production in UC.[2]
CD4 Central Memory CCR6+	-43%	Expanded in UC patients and drive pathogenic Th17 differentiation[2]
CD4 Transitional Memory CCR6+	-35%	Enriched in UC mucosa and contribute to the sustained Th17 cytokine milieu driving colonic inflammation.[1]
CD4 Effector Memory CCR6+	-76%	Accumulate in inflamed UC mucosa and are a major source of pathogenic IL-17 and IFN-γ.[1]
CD4 Central Memory CXCR3+CCR4−CCR6+ (pTh17)	-76%	Strongly associated with mucosal destruction and treatment-refractory UC.[1,4]
CD4 Transitional Memory CXCR3+CCR4−CCR6+ (pTh17)	-34%	Co-produce IL-17 and IFN-γ, accumulating in IBD mucosa and sustaining tissue-destructive inflammation.[1]

*Placebo-adjusted % change (%Δ)= TTI-109 dose-group mean − pooled placebo mean (per-subject % change). Paired n: D2=8, D3=8, D4=8; pooled placebo n=8. 1. Wen Y, et al. *Therap Adv Gastroenterol*. 2024; 2. Meitei HT, et al. *iScience*. 2025; 3. Sun L, et al. *Gastroenterol Res Pract*. 2021; 4. Paroni M, et al. *J Crohns Colitis*. 2026

TTI-109 Reduced T Follicular Cells Implicated in UC Pathology

MAD



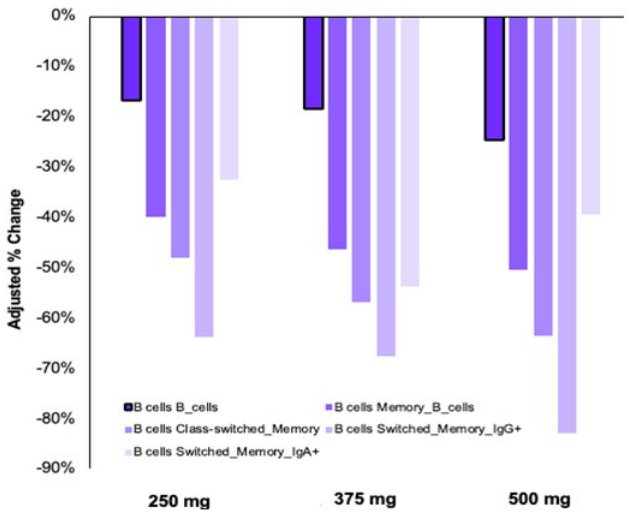
Cell Type	%Δ	UC Rationale
T follicular helper cells (Tfh)	-34%	**Drive UC through humoral autoantibody production and direct cellular Bcl6-dependent mucosal inflammation.[1,2]**
CD4 T cells CXCR5+	-38%	Track with UC disease activity and provide IL-21-driven B-cell help.[3]
CD4 Central Memory CXCR5+	-43%	Elevated in active UC, correlating with disease activity, memory B cell expansion, and plasmablast generation.[2]

Suppression extended beyond cellular immunity to the Tfh immune populations that drive mucosal B cell responses

*Placebo-adjusted % change (%Δ)= TTI-109 dose-group mean − pooled placebo mean (per-subject % change). Paired n: D2=8, D3=8, D4=8; pooled placebo n=8. 1. Sun L, et al. *Gastroenterol Res Pract.* 2021; 2. Long Y, et al. *Front Immunol.* 2020; 3. Xue G, et al. *Medicine.* 2019

TTI-109 Reduced B Cells Implicated in UC Pathology

MAD

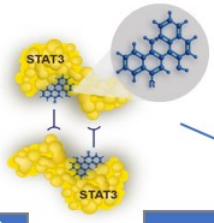


Cell Type	%Δ	UC Rationale
B cells	**-20%**	**Mucosal B-cell and plasma cell expansion is a hallmark of active UC, contributing directly to colonic inflammation and tissue injury.**[1]
Memory B cells	-46%	Track serum Ig levels and humoral activity in active UC.[2]
Class-switched Memory	-56%	Plasmablast-skewed, class-switched humoral response correlates with UC disease activity.[1]
Switched Memory IgG+	-71%	Accumulate in the inflamed colon and generate autoantibodies against the gut lining, directly linking class-switched IgG B cells to mucosal damage.[1]
Switched Memory IgA+	-42%	Aberrantly express cytotoxic granzyme B, contributing to epithelial damage.[3]

Suppression extended to B cell (humoral) immunity associated with colonic inflammation and tissue damage

*Placebo-adjusted % change (%Δ)= TTI-109 dose-group mean − pooled placebo mean (per-subject % change). Paired n: D2=8, D3=8, D4=8; pooled placebo n=8. 1. Uzzan M, et al. *Nat Med.* 2022; 2. Masaki Y, et al. *Clin Exp Immunol.* 2016; 3. Cupi ML, et al. *J Immunol.* 2014

We Believe TTI-109 Advances TTI-101's Clinical Profile Across PK, GI Tolerability and Immune Modulation



TTI-101 Clinical Observations[1,2]

- ✓ **Target Engagement**
  - ↓ pY-STAT3
- ✓ **Inflammation**
  - ↓ IL-6
- ✓ **Proliferation**
  - ↓ Fibrosis

+

TTI-109 Clinical Observations

- ✓ **PK**
  - Rapid conversion with dose-proportional exposure >STAT3 IC_{50}
- ✓ **GI Tolerability**
  - Similar to placebo and improved over TTI-101
- ✓ **Immune Modulation**
  - ↓ Cellular and ↓ humoral disease related immune populations

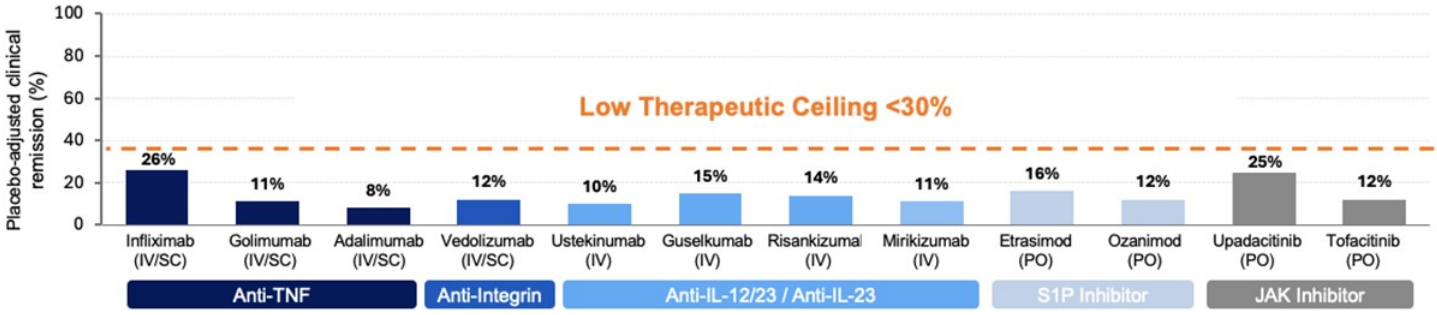
TTI-109 enhanced characteristics support clinical development in UC

1. Tsimberidou et al. *Clin Cancer Res.* 2025; SD: Stable Disease; 2. Tvardi Press Release: January 8, 2026; pY-STAT3: activated STAT3 induced by phosphorylation of tyrosine residue 705; STAT3 IC_{50}: in a controlled system where proliferation is driven by pY-STAT3, TTI-101 inhibits cell growth with an IC_{50} of approximately 1.5μM (707ng/mL)

UC: Large Market Opportunity with High Unmet Medical Need

UC Therapy Landscape

>1.25M[1]	$9B[2]	~$3B[2]
Diagnosed US Patients	Global Market (2024)	US Market (2024)

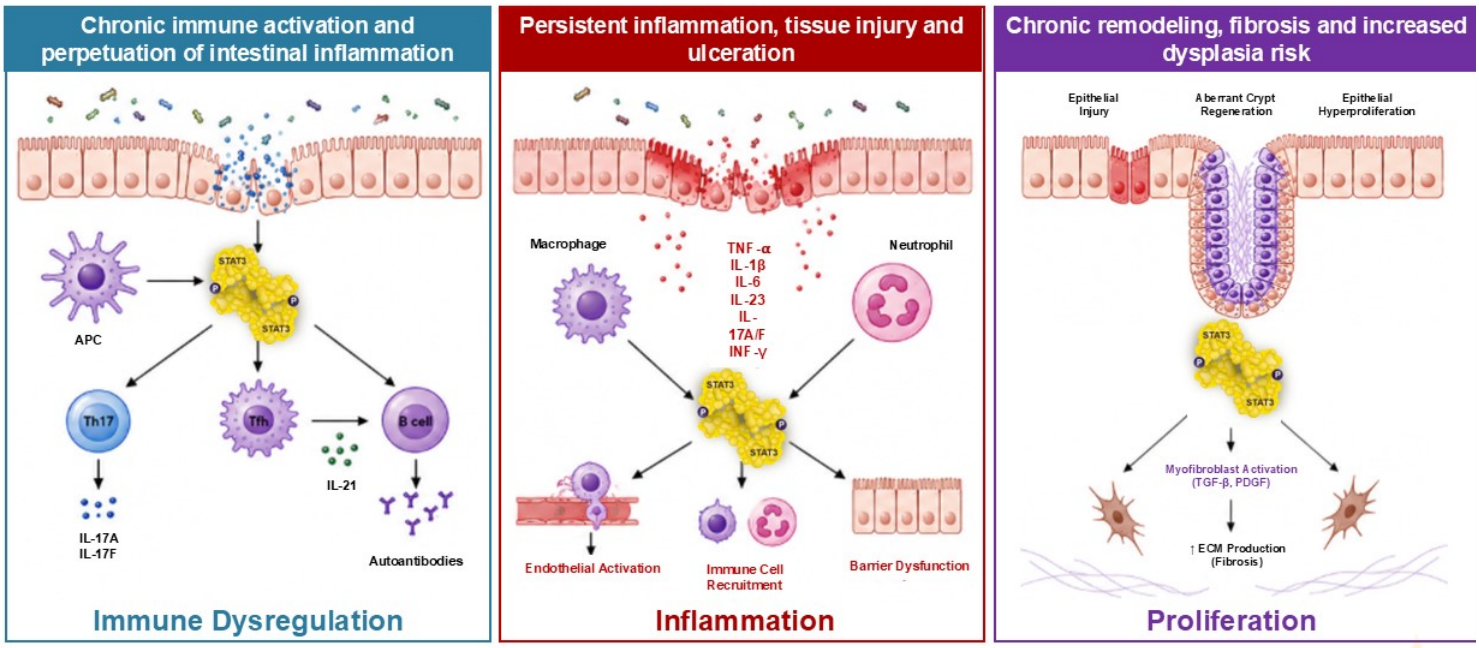


Placebo-adjusted clinical remission (induction) rates by MoA in UC[3]

>70% of patients do not achieve clinical remission with existing therapies

1. Lewis *Gastroenterology*. 2023; 2. S&S Insider. Estimate includes patients identified with indeterminate IBD. 3. Clinical remission rates from product labels; UC: ulcerative colitis; MoA: mechanism of action; IV: intravenous; SC: subcutaneous; PO: oral; MACE: major adverse cardiovascular events; Values represent placebo-adjusted clinical remission rates from pivotal induction studies and are intended for cross-mechanism comparison only. Direct comparisons across trials should be interpreted cautiously due to differences in study design, patient populations, and assessments

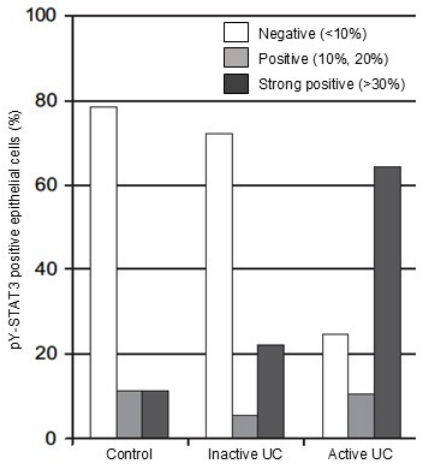
One Target, Three Mechanisms: pY-STAT3 Drives the Shared Biology of UC



pY-STAT3 Reduction Demonstrated in Preclinical Models and Clinical Biopsies

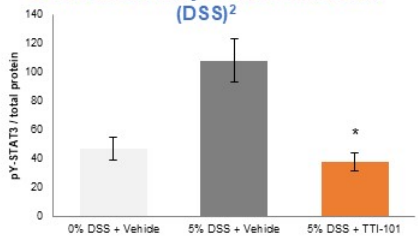
Activated STAT3

pY-STAT3 is associated with UC clinical activity[1]

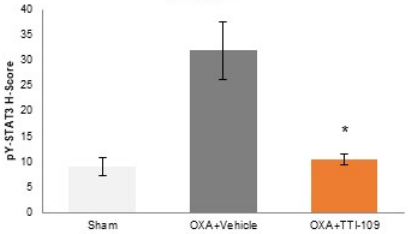


pY-STAT3 levels restored to baseline after TVRD STAT3 inhibitor treatment

GI model driven by innate immune axis (DSS)[2]

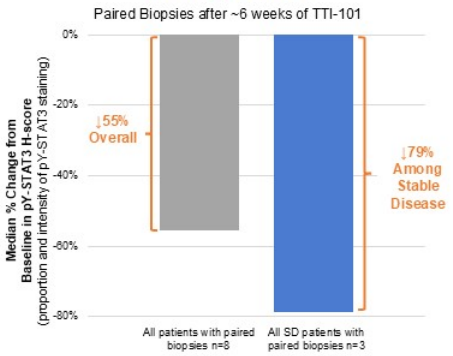


GI model driven by adaptive immune axis (OXA)[3]



Clinical PoC: Reduced pY-STAT3

Oncology Phase 1[4]



8/10 patients had elevated pY-STAT3 at baseline; elevated pY-STAT3 defined as H-score >30 on a 0-300 scale

100% of patients with elevated baseline pY-STAT3 demonstrated a decrease within ~6 weeks

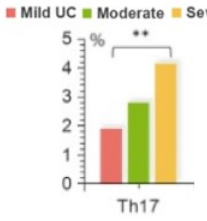
1. Li et al. *Gut* 2010 2. Figures digitized from Robinson et al. *Cancers* 2023: dextran sodium sulfate (DSS) model; 3. Tvardi data generated with CRO: WuXi oxazolone (OXA) model; n=8 per group statistical comparison using exact Mann-Whitney + Kruskal-Wallis; 4. Tsimberidou et al. *Clin Cancer Res.* 2025; SD: Stable Disease; pY-STAT3: activated STAT3 induced by phosphorylation of tyrosine residue 705; *$p \leq 0.05$

STAT3 Inhibition Normalized Preclinical and Clinical Pathogenic Immune Cell Populations

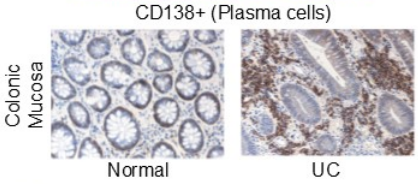
Immune dysregulation

Cellular (Th17) and Humoral (B cell) dysregulation in UC patients

Th17 cell frequency increases with UC disease severity ($p<0.01$). Th17 positively correlated with Mayo score ($p < 0.001$)[1]

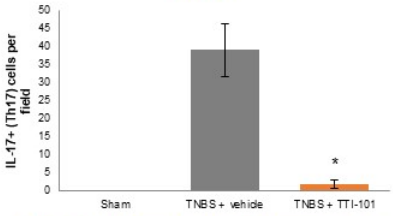


B cells/plasma cells heavily infiltrate the inflamed mucosa of UC patients[2]

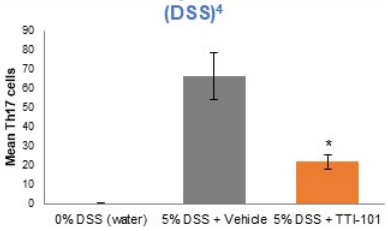


Th17 restored to homeostatic levels after TVRD STAT3 inhibitor

GI model driven by adaptive immune axis (TNBS)[3]

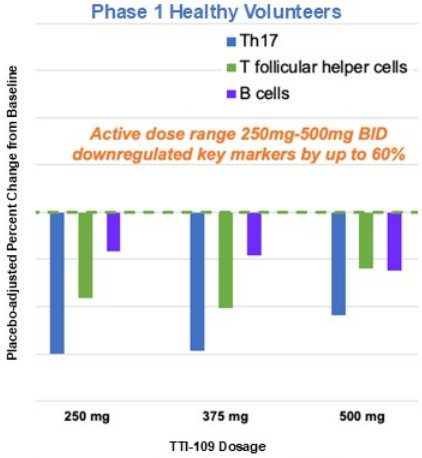


GI model driven by innate immune axis (DSS)[4]



Clinical PoC: Reduced key immune cell populations

Phase 1 Healthy Volunteers



Downregulation of STAT3-driven immune populations observed with TTI-109

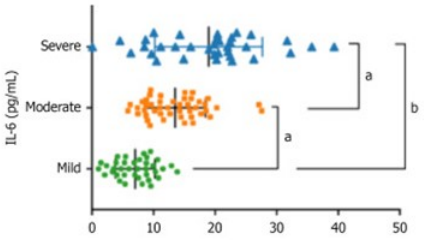
1. Zhang et al. *European Journal of Inflammation*. 2023; 2. Uo et al. *Gut* 2013; 3. Figures digitized from Robinson et al. *J Clin Med* 2022: 2,4,6-trinitrobenzene sulfonic acid (TNBS) model; 4. Figures digitized from Robinson et al. *Cancers* 2023: dextran sodium sulfate (DSS) model; *$p \leq 0.05$ TTI-101 vs vehicle

STAT3 Inhibition Reduced IL-6 and Inflammation Preclinically and in Patients

Inflammation

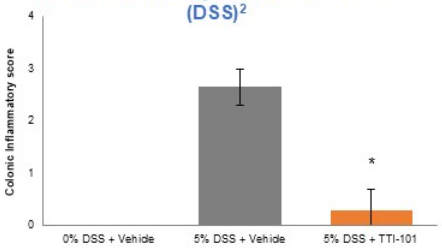
Inflammatory cytokine IL-6 correlates with UC severity

Increases in serum levels of inflammatory marker IL-6 significantly associated with worsening disease activity[1]

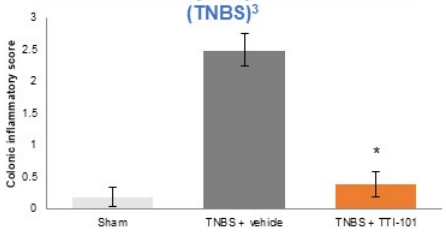


Colonic inflammation significantly attenuated with TVRD STAT3 inhibitor

GI model driven by innate immune axis (DSS)[2]



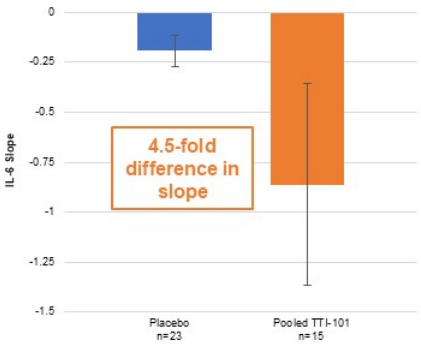
GI model driven by adaptive immune axis (TNBS)[3]



Clinical PoC: Reduced IL-6

IPF Phase 2[4]

TTI-101 vs Placebo Decline in IL-6



IL-6: a key pro-inflammatory cytokine that signals via STAT3

Greater decrease in IL-6 slope among pooled patients treated with TTI-101 vs placebo

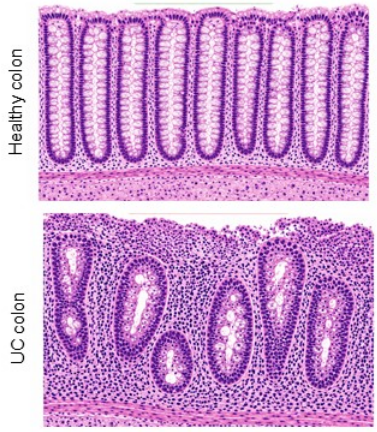
1. Fu et al. *World J Gastrointest Surg.* 2025; [a]$P < 0.01$; [b]$P < 0.001$; 2. Figures digitized from Robinson et al. *Cancers* 2023: dextran sodium sulfate (DSS) model; 3. Figures digitized from Robinson et al. *J Clin Med* 2022: 2,4,6-trinitrobenzene sulfonic acid (TNBS) model; 4. Tvardi Press Release: January 8, 2026; *$p \leq 0.05$ TTI-101 vs vehicle

STAT3 Inhibition Reduced Proliferative Signaling and Fibrosis Preclinically and in Patients

Proliferation

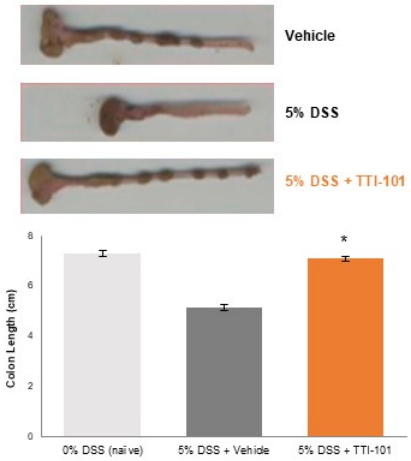
Proliferation and fibrosis correlate with UC severity

Disease severity indices integrate histologic architecture[1]



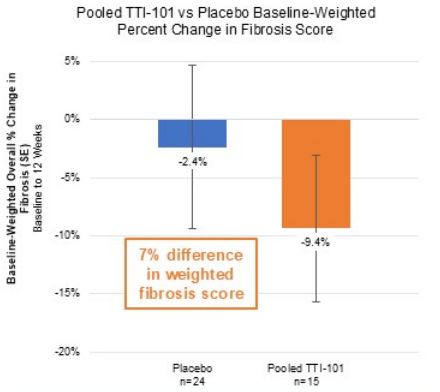
Preserved tissue integrity and colon length with TVRD STAT3 inhibitor

GI model driven by innate immune axis (DSS)[2]



Clinical PoC: Reduced fibrosis

IPF Phase 2[3]



Greater decrease in fibrosis score (improvement in fibrosis) among pooled patients treated with TTI-101 vs placebo

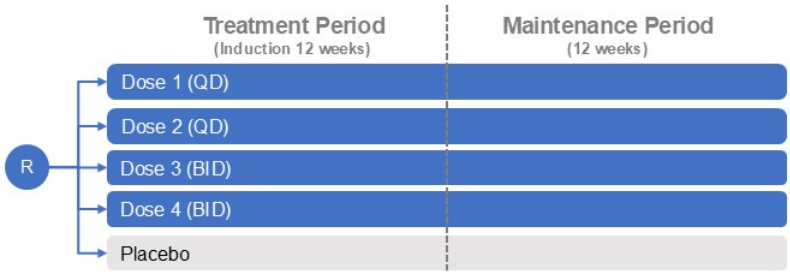
1. Vespa et al. *J. Clin Med.* 2022; 2. Figures digitized from Robinson et al. *Cancers* 2023: dextran sodium sulfate (DSS) model; 3. Tvardi Press Release: January 8, 2026; *$p \leq 0.05$ TTI-101 vs vehicle

Proposed Clinical Trial Designed to Address Key Challenges in UC

Study Design

Key inclusion criteria:

- Moderate to severe UC
- Inadequate response to prior advanced therapies



Endpoints

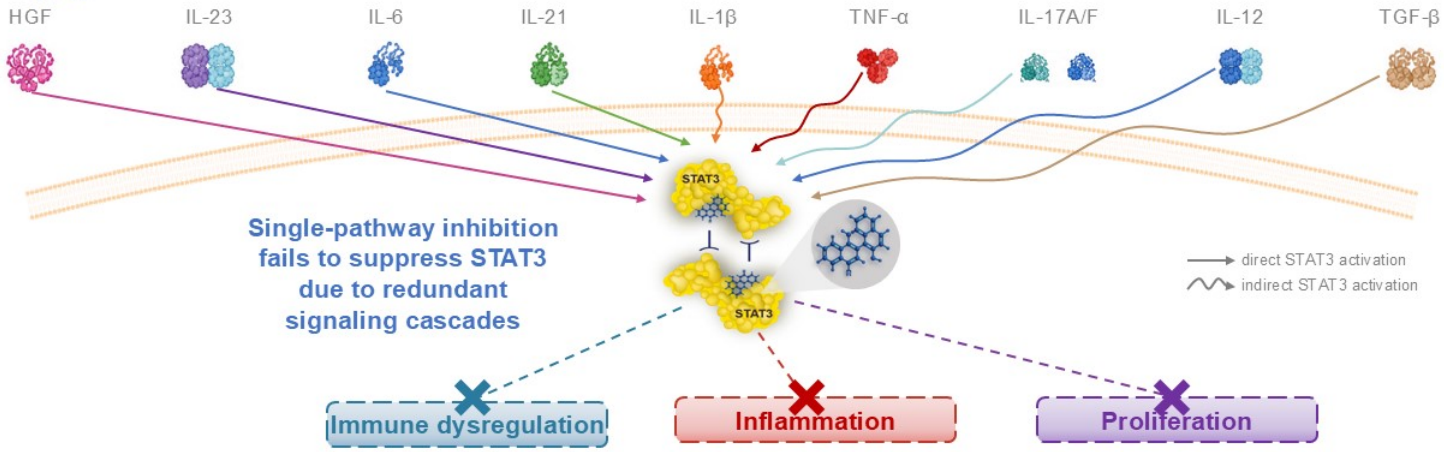
- Primary: Safety
- Secondary: Efficacy
  - Clinical remission at 12 weeks
- Exploratory: Pharmacodynamics
  - Serum biomarkers
  - Tissue analysis
  - Genetic SNPs

Key Challenges in UC	Why Target STAT3 with TTI-109?
Overcoming persistent disease biology	STAT3 integrates multiple mechanisms of disease modification
A differentiated oral therapy with targeted exposure	Favorable safety profile, target-specific design with rapid biologic effect
Enabling precision medicine	Targeting STAT3 offers a distinct opportunity to develop a STAT3-mediated response signature

tvardi THERAPEUTICS

QD: once daily dosing; BID: twice daily dosing; SNP: single nucleotide polymorphisms; Subject to IND submission and the availability of additional funding

Overcoming Persistent Disease Biology



	Immune dysregulation	Inflammation	Proliferation
UC Murine Models with TTI-101/109	↓ Pathogenic Th17[1,2]	↓ Colonic inflammatory score[1,2,3]	Preserved colon integrity[2]
Human Data with TTI-101/109	↓ Key immune cell populations	↓ Inflammatory cytokine IL-6[4]	↓ Fibrosis score[4]

Targeting STAT3 integrates multiple mechanisms of UC

1. Robinson et al. *J Clin Med* 2022; 2. Robinson et al. *Cancers* 2023; 3. Tvardi data generated with CRO; 4. Tvardi Press Release: January 8, 2026

A Differentiated Oral Therapy with Targeted Exposure

Current oral therapies	TVRD STAT3 inhibitors (STAT3i)

Safety
• Class-related safety risks with JAK inhibitors[1] and S1P[2,3] modulators:
  • MACE
  • Venous thromboembolism
  • Malignancy
  • Immunosuppression
Targeted exposure
• UC therapies often require loading or extended induction periods
	Differentiated safety profile
	• Safety profile with TVRD STAT3i ~400 subjects: differentiated from JAK inhibitors and S1P modulators
	Designed for diseased tissue
	• **>8x:** Target-dependent accumulation in colon tissue (vs plasma) in UC models[4]
	Rapid biologic effect
	• 83% of objective responses observed by week 8 (Ph1 oncology)[5]
	• Decline in key immune subsets observed by day 21 (Phase 1 HV)
	• Observed reduction in fibrosis score by week 12 (Phase 2 IPF)[6]

Favorable safety profile, target-specific design with rapid biologic effect

1. FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions; 2. Ozanimod Prescribing Information; 3. Etrasimod Prescribing Information; 4. Robinson et al. *Int. J. Mol. Sci* 2025; 5. Tsimberidou et al. *Clin Cancer Res* 2025; 6. Tvardi Press Release: January 8, 2026

Enabling Precision Medicine

Limited Molecular Insight

- Current available therapies have broad unselected patient populations
- Response remains unpredictable
- Molecular characterization of responders and non-responders remains an important unmet need

Exploratory Candidate Biomarkers

pY-STAT3 associated with clinical activity[1,2]

- Reduction of pY-STAT3 is correlated with response to treatment
- Non-responders demonstrated little or no reduction of pY-STAT3

Genetic SNPs and inflammatory signatures may inform future patient enrichment strategy

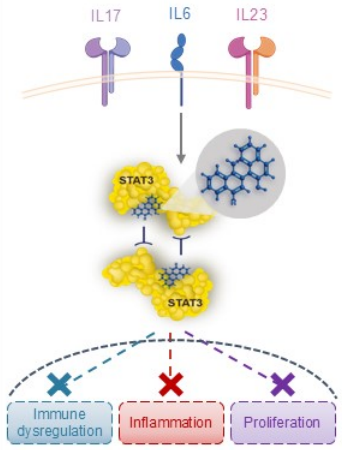
- Polymorphisms of STAT3 that increase risk of developing UC[3,4]
  - rs744166; rs2293152
- STAT3-mediated immune signatures
  - Pathogenic Th17, Th17/Th1
  - Inflammatory macrophages
  - CD4+ Tfh

We believe targeting STAT3 offers a distinct opportunity to develop a STAT3-mediated response signature

1. Schreiber et al *Gastroenterology* 2021; 2. Verstockt et al *J. Crohn's and Colitis* 2025; 3. Zhang et al *Plos One* 2014; 4. Wang et al *Genet Mol Res.* 2014

Our STAT3 Inhibitors are Designed to Address the Unmet Need in Inflammatory and Proliferative Diseases

STAT3: Highly Validated Convergent Node



STAT3: central mediator in inflammatory and proliferative disease

Translational Proof-of-Concept

Preclinical

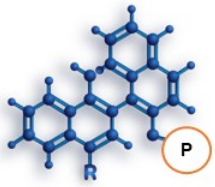
- ↓ pY-STAT3
- ↓ immune dysregulation
- ↓ inflammation
- ↓ proliferation

Confirmed in patients

Clinical

- ↓ pY-STAT3
- ↓ immune dysregulation
- ↓ inflammation
- ↓ proliferation

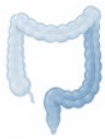
TTI-109 Validation in P1 Healthy Volunteers



TTI-109

- ✓ **PK**
- ✓ **GI tolerability**
- ✓ **Immune modulation**

TTI-109 Lead Indication



Ulcerative Colitis (UC)

- Targeting a single convergent node
- Oral therapy with targeted tissue exposure
- Assessment of STAT3-mediated inflammatory response signature

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pY-STAT3: activated STAT3 induced by phosphorylation of tyrosine residue 705; PK: pharmacokinetics

Our Pipeline

Program	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
TTI-109	Ulcerative Colitis (UC)	IND submission expected 2027*				• Study initiation expected 2027*
TTI-101	Hepatocellular Carcinoma (HCC)	Phase 1b/2				• Phase 1b/2 topline data 2H:2026

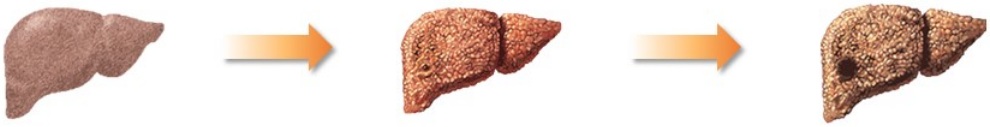
*Tvardi's ability to initiate these programs is subject to clearance of Investigational New Drug (IND) application and the availability of additional funding

TTI-101 in HCC

TTI-101 Reversed Multiple Pathogenic Steps of Liver Cancer in a NASH-induced HCC Model

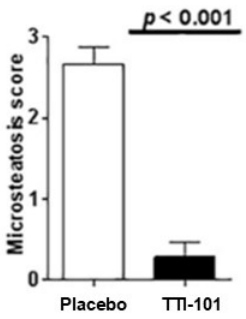
STAT3-mediated pathogenesis

Inflammation → Fibrosis/Cirrhosis → HCC

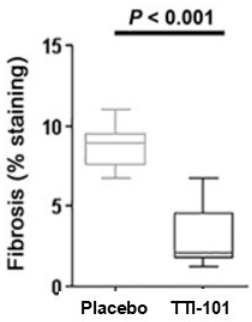


TTI-101 STAT3-inhibition in NASH-induced HCC

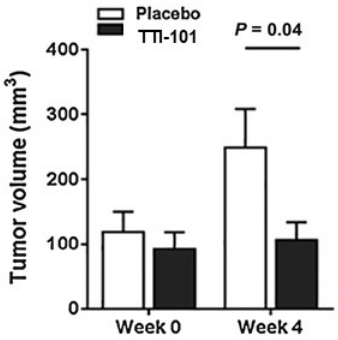
Microsteatosis



Fibrosis



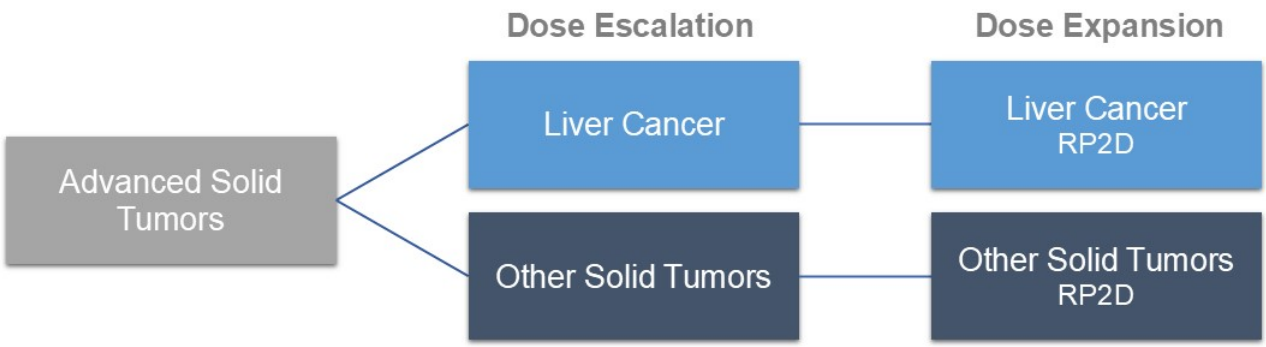
Tumor volume



After formation of tumors at 11 months, we observed treatment with TTI-101 therapeutically reduced inflammation, fibrosis, and tumor growth

Jung KH et al. *Clin Cancer Res* 2017. Genetically engineered HepPTEN- murine model that replicates nonalcoholic steatohepatitis (NASH) induced hepatocellular carcinoma (HCC)

Phase 1 Clinical Trial: First in Human TTI-101 Monotherapy Study Design



Objectives:

- **Primary:** Maximum tolerated dose, safety, and pharmacokinetics
- **Secondary:** Clinical efficacy and pharmacodynamics

tvardi THERAPEUTICS Tsimberidou et al. *Clin Cancer Res.* 2025

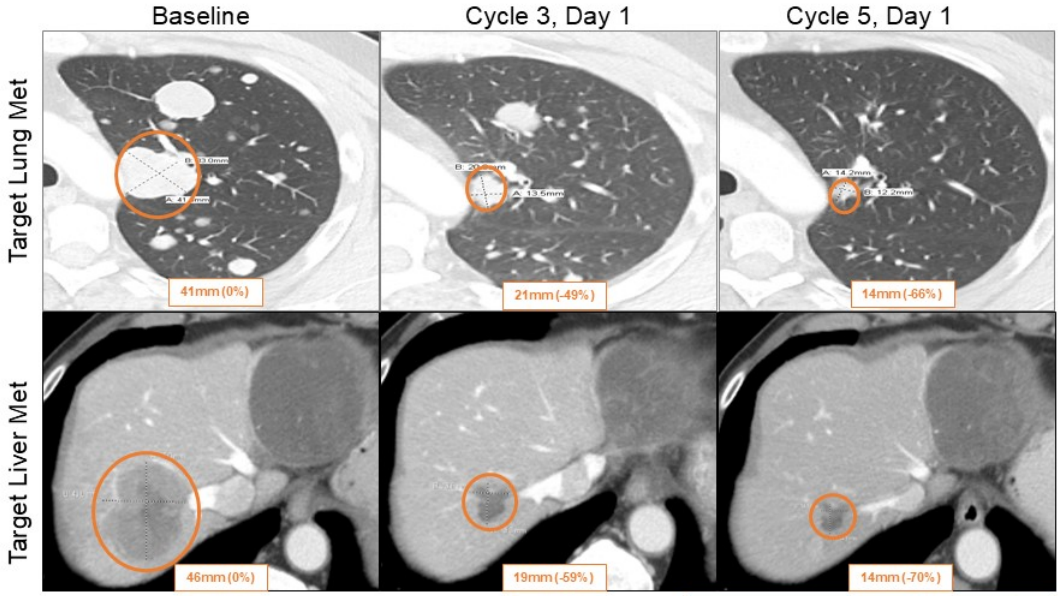
Phase 1 Clinical Trial: TTI-101 Monotherapy Led to Durable Partial Responses in Fibrotic Tumors

Partial Responder A: HCC

- Failed sorafenib, pembro, nivo, nivo+bev
- Best Response: **42% Reduction in Sum of Targets Overall**
- Sustained PR for 10 months

Partial Responder B: HCC

- Failed lenvatinib, nivo
- Best Response: **66% Reduction in Sum of Targets Overall**
- Sustained PR for 14 months



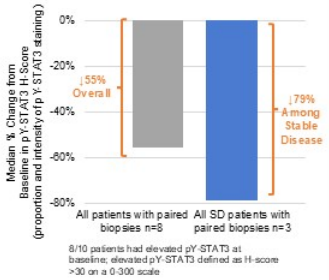
tvardi THERAPEUTICS Tsimberidou et al. *Clin Cancer Res.* 2025

Phase 1: TTI-101 Monotherapy Clinical Trial Summary

PK / PD

- Exposures in humans above the level required for efficacy in preclinical inflammatory and proliferative models
- Linear PK from DL1-3
- Exposures above IC_{50} for STAT3 induced growth*
- Exposure plateaued at DL3, resulting in a RP2D of 12.8mg/kg/day
- 100% of patients with elevated pY-STAT3 levels at baseline demonstrated decrease within ~6 weeks of TTI-101 therapy
- 55% decrease in pY-STAT3 overall; 79% in SD

Paired Biopsies after ~6 weeks of TTI-101



8/10 patients had elevated pY-STAT3 at baseline; elevated pY-STAT3 defined as H-score >30 on a 0-300 scale

Tolerability

- Well-tolerated BID oral dosing
- No DLTs

TRAEs Occurring in >10% of Patients

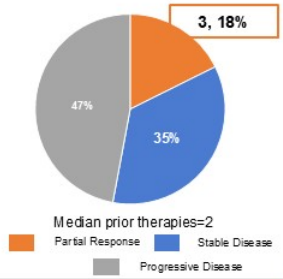
Formulation	F1 N=15		F2 N=47		F3 N=7**	
Grade, n (%)	G1/2	G3	G1/2	G3	G1/2	G3
Diarrhoea	3 (20)	3 (20)	16 (34)	6 (13)	2 (29)	0 (0)
Nausea	4 (26)	0 (0)	6 (13)	1 (2)	0 (0)	1 (14)
Fatigue	6 (40)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)
Elevated ALT/AST***	1 (7)	1 (7)	1 (2)	4 (8)	1 (14)	1 (14)
Dose reduction	3 (20)		2 (4)		0 (0)	
Dose discont.	0 (0)		2 (4)		0 (0)	

*Most severe AE counted per subject by grade (G1/2=grade 1 or 2, G3=grade 3) **5 subjects started on F2 and transitioned to F3 ***Elevated alanine aminotransferase/aspartate aminotransferase (ALT/AST) is the sum of elevated ALT and AST events

Biological Activity

- Enhanced biological activity in fibrotic cancers with ORR that exceeds current standard of care in HCC
- Current expected ORR in 2L HCC is <5%

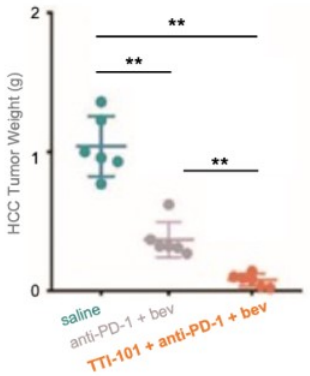
Best Overall Response Among HCC Patients, N=17



Strong Rationale for TTI-101 and ICI Combination Therapy

Preclinical Model

TTI-101 additive to 1L SoC (ICI + Bev)[1]



POC Established for STAT3 Inhibition + ICI

Ph 2: Danvatirsen (STAT3 ASO) + Durvalumab (ICI) in 2L HNSCC[2]

	Durva[3]	Dan+Durva[2]
ORR	9% →	**23%**
CR	0% →	**7%**

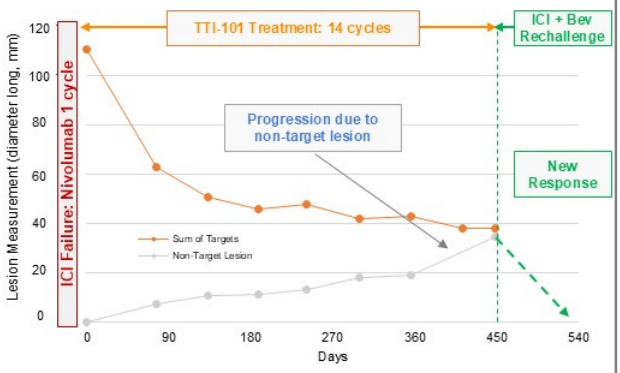
Danvatirsen key limitations:

- Observed AEs: Thrombocytopenia and transaminitis
- Onerous dosing: IV 3x week 1 then Q weekly
- Poor PD: Inhibition of STAT3 not observed in tumor, only in stroma

Danvatirsen development suspended by AZN/Ionis

Phase 1 Trial Responder Overcame ICI Resistance After TTI-101 Monotherapy

Sum of Tumor Responses After ICI Failure, On TTI-101 Therapy and After ICI+Bev Rechallenge[4]



1. Adapted from Zhao, Y et al. *Hepatology*. 2021 2. Cohen et al. *Ann Oncol* 2018 3. Siu et al. *JAMA Oncol*. 2019. ICI: Immune Checkpoint Inhibition; Bev: Bevacizumab. Certain data on this slide are based on cross-study comparisons and are not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences. The values shown in the cross-study comparisons are directional and may not be directly comparable. 4. Tsimberidou et al. *Clin Cancer Res*. 2025

TTI-101 is Designed to Provide a Distinct and Synergistic Mechanism for Unmet Need in HCC

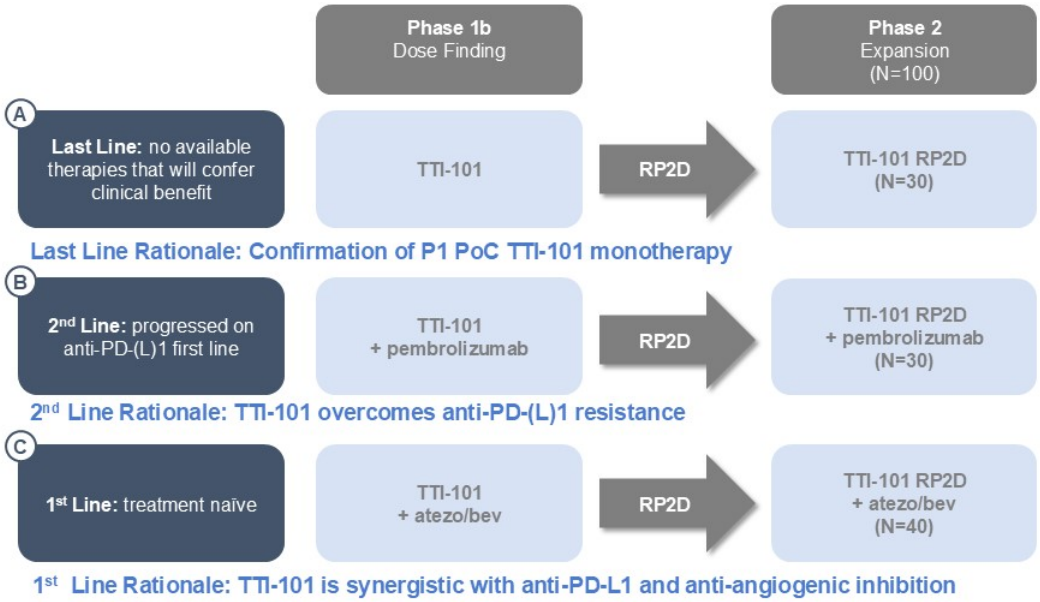
HCC Disease Overview

- HCC is 3rd leading cause of cancer deaths in the world[1]
- Annually in the US, >42,000 new cases of HCC and ~32,000 deaths recorded[2]
- Incidence has more than tripled since 1980[3]

Overview of Current Treatment Landscape + Role of TTI-101

1. World Health Organization (WHO) 2. WHO US Statistics 3. American Cancer Society 4. Represents range of ORRs from previous studies (MORPHEUS, Tempest, IMBrave150). 5. 2nd line ORR expected to be <5% as 2nd line therapies inhibit VEGF/angiogenesis as common mechanism with bevacizumab and pembrolizumab (anti-PD-1) has common mechanism with atezolizumab (anti-PDL-1).

REVERT$_{\text{Liver Cancer}}$: Phase 2 Study of TTI-101 in HCC



FDA Fast Track

revert™ LIVER CANCER

(21 US Sites)

- Overall Response Rate (ORR)
- Duration of Response (DoR)
- Progression-free survival
- Liver stiffness (elastogram)
- Biomarkers (IL-6/AFP)
- pY-STAT3 in tumor

Early clinical data suggests clinical benefit across treatment lines

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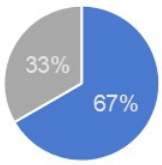
NCT05440708; Dayyani et al. JCO. 2024; Data as of April 2025

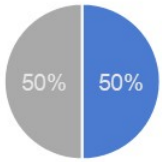
REVERT$_{\text{Liver Cancer}}$: Interim Phase 1b/2 Data

Cohort A:
TTI-101 Monotherapy at RP2D



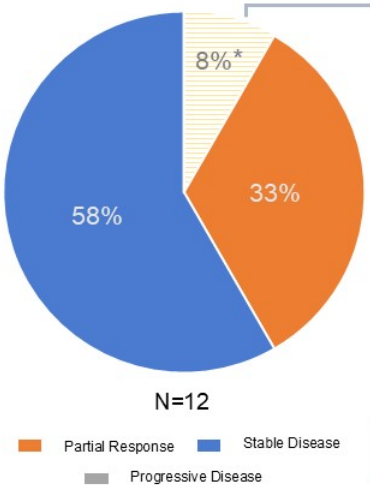
N=21

Cohort B:
TTI-101 (RP2D) + Pembro



N=8

Cohort C:
TTI-101 + Atezo/Bev



N=12

Partial Response | Stable Disease | Progressive Disease

*One patient on protocol for 6 weeks. Patient discontinued combination due to an unrelated AE. After recovery from AE, patient continued with atezo/bev and investigator reported complete response.

Patient considered non-evaluable for efficacy. As DCR (disease control rate: CR+PR+SD) and ORR (objective response rate: CR+PR) are based on intent to treat population of all patients this patient is only included in denominator.

Early results compare favorably to 3rd party trials†:

Study	Publication Date	DCR	ORR
REVERT$_{\text{HCC}}$ Prelim	**Ongoing**	**92%**	**33%**
Tempest[1]	2023	63%	10%
MORPHEUS[2]	2023	56%	11%
IMBrave150[3]	2020-22	74%	27%

49% of patients in IMBrave150 atezo/bev arm had HBV-associated HCC and demonstrated a higher likelihood of benefit relative to non-HBV patients[4]
REVERT$_{\text{HCC}}$ Cohort C has **no patients with** HBV-associated HCC

Preliminary radiographic change from baseline RECIST measurements (best response). Data as of Aug 2024. This interim data set was not subject to the standard quality control measures typically associated with final clinical trial results. 1. Tempest press release 23 Apr 2023 of Phase 2 Study. Tempesttx.com 2. Roche Phase 2: Finn et al. *J Clin Oncol*. 2023 3. Roche Phase 3: Finn et al. *NEJM*. 2020. 4. Cheng et al. J Hepatol. 2022
† Certain data on this slide are based on cross-study comparisons and are not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences. The values shown in the cross-study comparisons are directional and may not be directly comparable.

Key Takeaways: TTI-101 in HCC

STAT3: Well-Established Biology

STAT3 long recognized as prime target in oncology; >95% of patients with HCC have activated STAT3 in their tumors

Differentiated Approach

Inhibition of STAT3 activation to have dual therapeutic effect on cancer cells – overcoming tumorigenesis and immune suppression

Encouraging Clinical Activity

Clinically meaningful activity in both monotherapy and combination therapy in areas of unmet need

Near-Term Clinical Milestone

Topline results from ongoing Phase 2 REVERT$_{\text{LIVER CANCER}}$ trial expected in 2H:2026

Appendix A.
Preclinical Support

TVRD STAT3 Inhibition Demonstrated Activity Across Multiple Validated IBD Immune Axes

Model Systems and Select Therapies Approved or Developed for IBD		TVRD STAT3i	Anti-TNFα	Anti-IL12/23	Anti-TL1A	Anti-IL-6	JAK1i	JAK2/3i	TyK2i	S1P1m
Model	**Immune Axis / Key Cytokines**									
DSS (UC)	• Innate → Th1/Th17 • IL-6, IL-1ß, IL-17	✅		✓	✓	✓				✓
TNBS (CD)	• Adaptive (Th1) • IFN-ɣ, TNF-α, IL-12	✅	✓	✓	✓	✓	✓		✓	✓
OXA (UC)	• Adaptive (Th2/NKT) • IL-13, IL-4	✅					✓	✓		

Unlike single-axis competitor mechanisms, TVRD STAT3-inhibitors demonstrated biologic activity across multiple, validated immune axes underlying IBD disease

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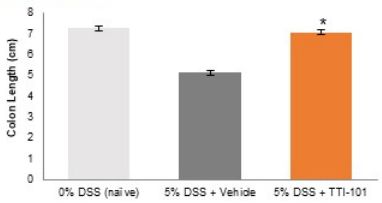
Tvardi data generated with CRO: WuXi; Comparative targets in the IBD space and select therapies approved or developed for IBD used for demonstrative purposes; DSS: dextran sodium sulfate ulcerative colitis (UC) model; TNBS: 2,4,6-trinitrobenzene sulfonic acid Crohn's disease (CD) model; OXA: oxazolone ulcerative colitis (UC) model

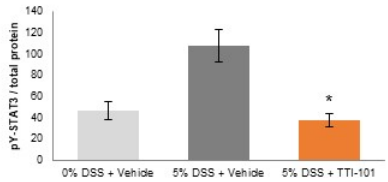
TVRD STAT3 Inhibitors in the DSS-UC Model

5% DSS UC Model with TTI-101[1]

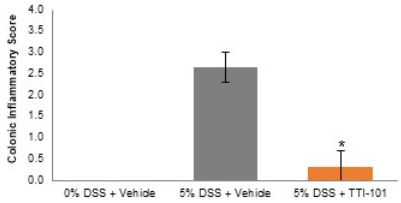
Colon Morphology and Length



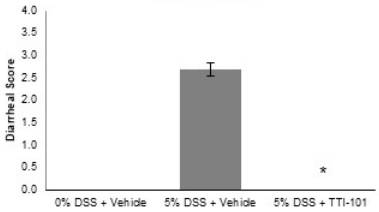
pY-STAT3



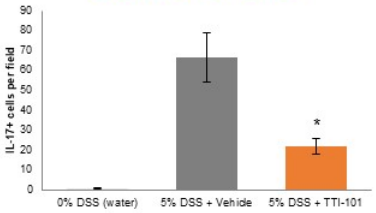
Colonic inflammation



Diarrhea



Colonic IL-17⁺ Cells



*p ≤0.05 for all TTI-101 arms relative to DSS + vehicle

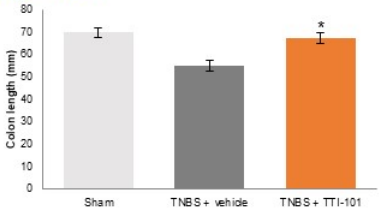
TTI-101 treatment in DSS model normalized all hallmarks of UC

1. Figures digitized from Robinson et al. *Cancers* 2023: dextran sodium sulfate (DSS) model

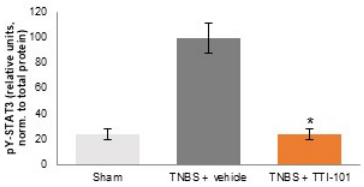
TVRD STAT3 Inhibitors in the TNBS-CD Model

TNBS UC Model with TTI-101[1]

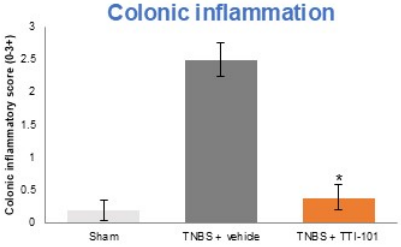
Colon Morphology and Length



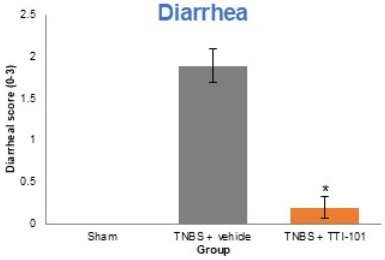
pY-STAT3



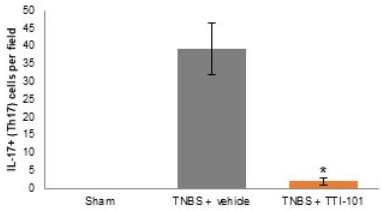
Colonic inflammation



Diarrhea



Colonic IL-17⁺ Cells



*p ≤0.05 for all TTI-101 arms relative to TNBS + vehicle

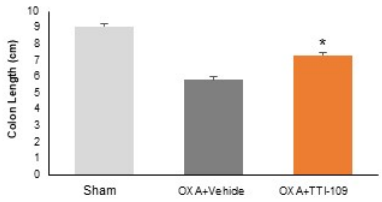
TTI-101 treatment in TNBS model normalized all hallmarks of CD

1. Figures digitized from Robinson et al. *J Clin Med* 2022: 2,4,6-trinitrobenzene sulfonic acid (TNBS) model

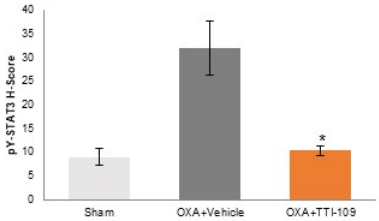
TVRD STAT3 Inhibitors in the OXA-UC Model

OXA UC Model with TTI-101[1]

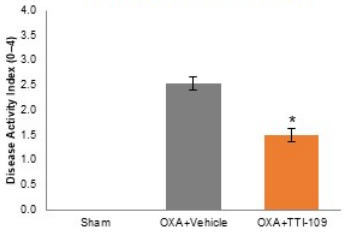
Colon Morphology and Length



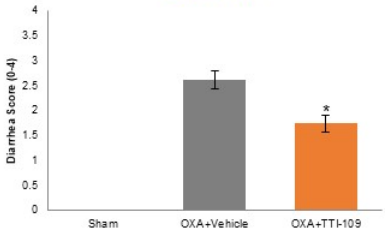
pY-STAT3



Colonic inflammation



Diarrhea



** p ≤0.05 for all TTI-101 arms relative to OXA + vehicle

TTI-101 treatment in OXA model normalized all hallmarks of UC

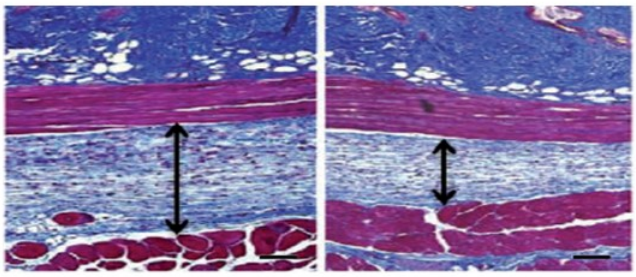
1. Tvardi data generated with CRO: WuXi; n=8 per group statistical comparison using exact Mann-Whitney + Kruskal-Wallis

TTI-101 Attenuated *Growth Factor* Driven Fibrosis and Dermal Thickening

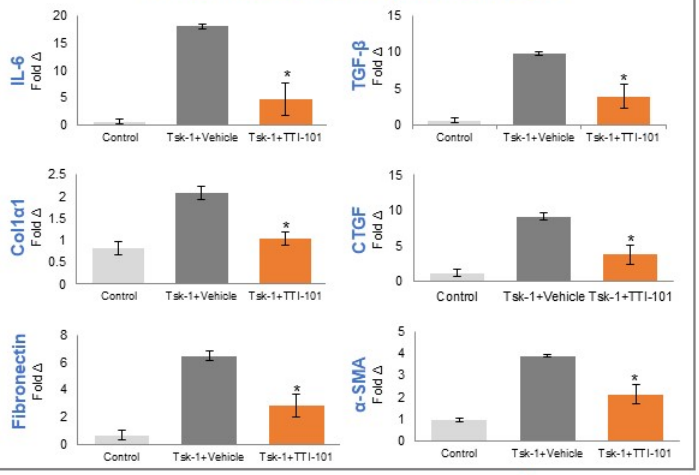
Genetically-induced proliferative skin model

Therapeutic treatment with TTI-101 significantly reduced dermal thickness…

Tsk-1 mice + Placebo | Tsk-1 mice + TTI-101



…and significantly reduced key drivers of inflammation and proliferation



* $p \leq 0.05$ for all TTI-101 arms relative to Tsk-1 + vehicle

TTI-101 reversed both dermal thickening and inflammatory/pro-fibrotic hallmarks of skin fibrosis

Figures digitized from Pedroza et al. *Rheum.* 2017: SSc: systemic sclerosis; Genetically engineered model (GEM) of Tight skin (Tsk-1) mice which spontaneously develop fibrosis as a result of a duplication in the fibrillin-1 gene and BLM (bleomycin-induced SSc) model; Fold Δ = Fold Change

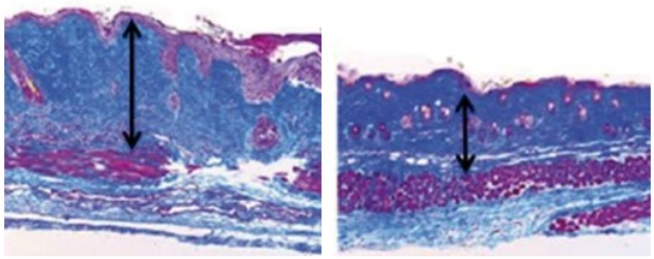
TTI-101 Attenuated *Inflammation* Driven Fibrosis and Dermal Thickening

Chemically-induced inflammatory skin model

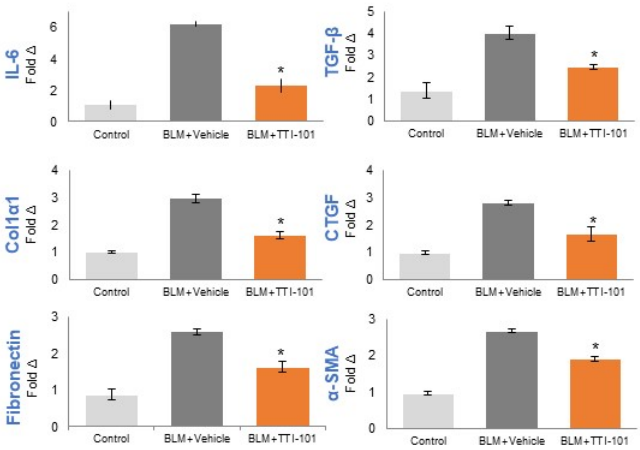
Therapeutic treatment with TTI-101 significantly reduced dermal thickness

BLM mice + Placebo

BLM mice + TTI-101



…and significantly reduced key drivers of inflammation and proliferation



* $p \leq 0.05$ for all TTI-101 arms relative to BLM + vehicle

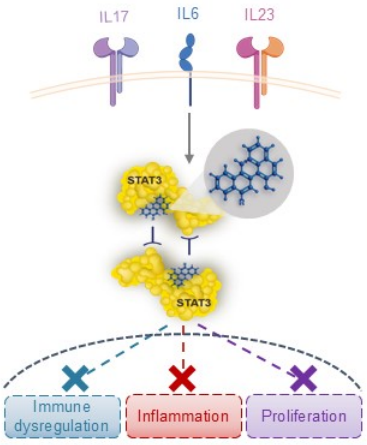
TTI-101 reversed both dermal thickening and inflammatory/pro-fibrotic hallmarks of skin fibrosis

Figures digitized from Pedroza et al. *Rheum.* 2017: SSc: systemic sclerosis; Bleomycin (BLM) treated mice develop fibrosis through an inflammatory mechanism; Fold Δ = Fold Change

Appendix B.
TTI-101 in IPF

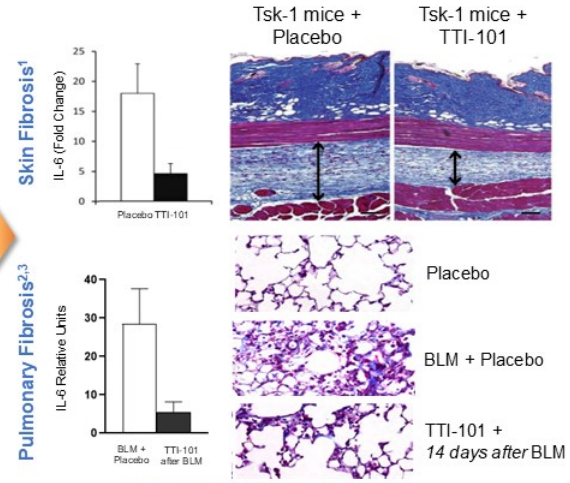
Our STAT3 Inhibitors are Designed to Address the Unmet Need in Inflammatory and Proliferative Diseases

Well-Established Target



STAT3: central mediator in inflammation and proliferative disease

Preclinical Biological Activity



↓ IL-6 levels and ↓ fibrosis in models of proliferative disease

Initial Clinical Proof of Mechanism: IPF

revert™ IPF

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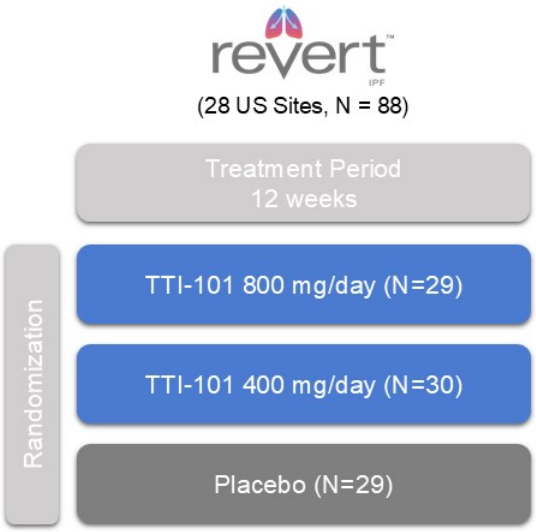
1. Pedroza et al. *Rheum.* 2017; Genetically engineered model of Tight skin (Tsk-1) mice which spontaneously develop fibrosis as a result of a duplication in the fibrillin-1 gene; 2. Pedroza et al. *FASEB J.* 2016; 3. Kauh et al. *CHEST.* 2024. Pulmonary fibrosis bleomycin (BLM) model

REVERT$_{IPF}$: Preliminary Conclusions Released October 2025



- Placebo arm overperformed compared to historical data
- FVC change from baseline overlapped between treatment arms, with large variability within each cohort
- Treatment emergent adverse events resulted in early discontinuations leading to a small number of patients available for efficacy analysis at the 12-week time point

tvardi THERAPEUTICS Tvardi Therapeutics October 13, 2025 Press Release

Patient Characteristics

Characteristic	Placebo (n=29)	TTI-101 400mg/day (n=30)	TTI-101 800mg/day (n=29)
Age	72.0 (9.3)	72.4 (6.9)	72.8 (7.7)
Sex, Male – no. (%)	23 (79.3)	25 (83.3)	21 (72.4)
Time since diagnosis of IPF – yrs., mean (SD)	2.4 (2.0)	2.6 (1.7)	2.5 (1.5)
Standard of care use, nintedanib – no. (%)	17 (58.6)	18 (60.0)	17 (58.6)
FVC – L, mean (SD)	2.59 (0.75)	2.84 (0.71)	3.03 (1.00)
Percent of predicted FVC (ppFVC), mean (SD)	70.08 (16.72)	74.05 (13.38)	81.12 (19.90)
GI comorbidity at baseline, mean (%)[1]	21 (72.4)	26 (86.7)	20 (69.0)

GI comorbidities were prevalent among the patient population

SD: standard deviation; [1]GI comorbidity: gastrointestinal medical history collected at baseline

Summary of Treatment-Emergent Adverse Events

Characteristic	Placebo (n=29)	TTI-101 400mg/day (n=30)	TTI-101 800mg/day (n=29)
Any TEAEs	21 (72.4)	30 (100)	26 (89.7)
TEAE leading to death	1 (3.4)	1 (3.3)[1]	1 (3.4)
TEAE leading to discontinuation	3 (10.3)	17 (56.7)	18 (62.1)
Gastrointestinal disorders		6 (20.0)	11 (37.9)
Investigations (Labs)[2]		4 (13.3)	6 (20.7)
Respiratory, thoracic and mediastinal disorders	1 (3.4)	5 (16.7)	3 (10.3)

Incidence of respiratory adverse events leading to discontinuation is consistent with adverse events expected in this patient population

Treatment-emergent adverse event: any adverse event that emerges after treatment with TTI-101 or placebo. Safety analysis performed on all patients treated with at least one dose of TTI-101. [1]Occurred during safety follow-up after 12-week treatment period ended; [2]No instances of drug-induced liver injury reported across visits or treatment groups. All increases in investigations (labs) were transient

Treatment-Emergent Adverse Events Resulting in Discontinuations by Concomitant Nintedanib Use

Dose	Placebo (n=29)		TTI-101 400mg/day (n=30)		TTI-101 800mg/day (n=29)	
Reason for discontinuation by concomitant nintedanib use	**Nintedanib (n=17)**	**Placebo (n=12)**	**TTI-101 + Nintedanib (n=18)**	**TTI-101 alone (n=12)**	**TTI-101 + Nintedanib (n=16)**	**TTI-101 alone (n=13)**
Gastrointestinal disorders			2	4	7	4
Investigations (Labs)[1]			4		4	2
Respiratory, thoracic and mediastinal disorders		1	3	2	1	2

Majority of discontinuations were observed with concomitant nintedanib

Treatment emergent adverse event: any adverse event that emerges after treatment with TTI-101 or placebo. Safety analysis performed on all patients treated with at least one dose of TTI-101. [1]No instances of drug-induced liver injury reported across visits or treatment groups. All increases in investigations (labs) were transient

Most Common Adverse Events Reported in INPULSIS vs REVERT$_{IPF}$ Trials

	INPULSIS-1 and 2[1]		Pooled TTI-101	
	Placebo (N=423)	**Nintedanib (N=638)**	**TTI-101 alone (n=25)**	**TTI-101 + Nintedanib (n=34)**
Any adverse event	379 (89.6)	609 (95.5)	23 (92.0)	33 (97.1)
Diarrhea	78 (18.4)	398 (62.4)	11 (44.0)	25 (73.5)
Nausea	28 (6.6)	156 (24.5)	4 (16.0)	10 (29.4)
Nasopharyngitis	68 (16.1)	87 (13.6)	1 (4.0)	0 (0.0)
Cough	57 (13.5)	85 (13.3)	3 (12.0)	4 (11.8)
Progression of IPF	61 (14.4)	64 (10.0)	2 (8.0)	2 (5.9)
Bronchitis	45 (10.6)	67 (10.5)	2 (8.0)	0 (0.0)
Upper respiratory tract infection	42 (9.9)	58 (9.1)	0 (0.0)	4 (11.8)
Dyspnea	48 (11.4)	49 (7.7)	1 (4.0)	4 (11.8)

- TTI-101 treated patients reported adverse events consistent with overall expectations for an IPF population
- However, addition of nintedanib meaningfully increased incidence of diarrhea

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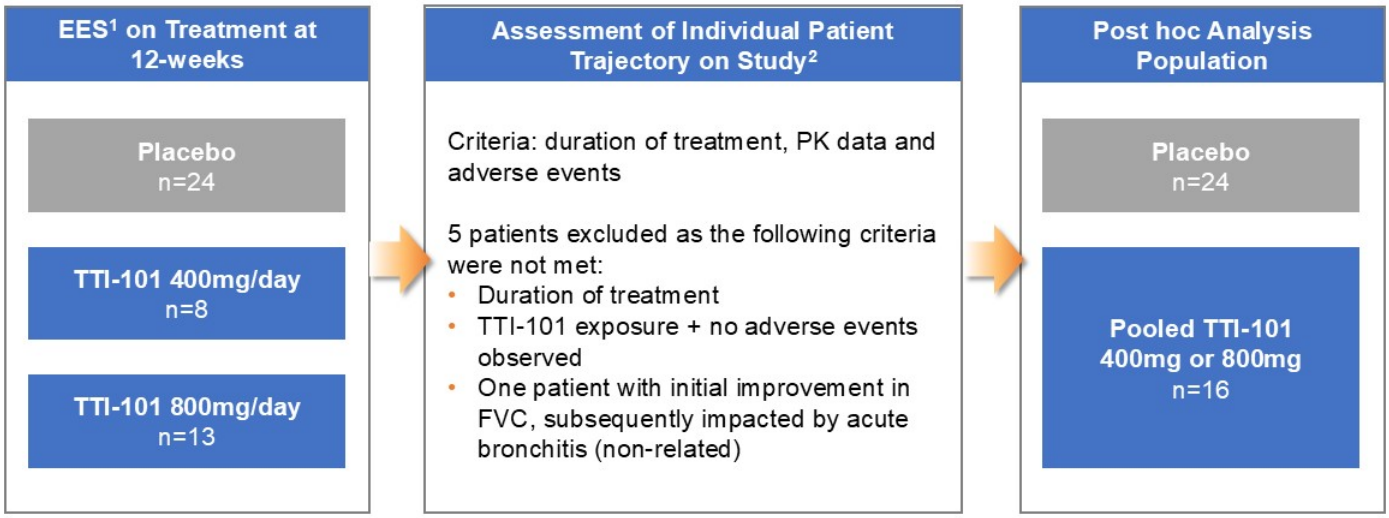
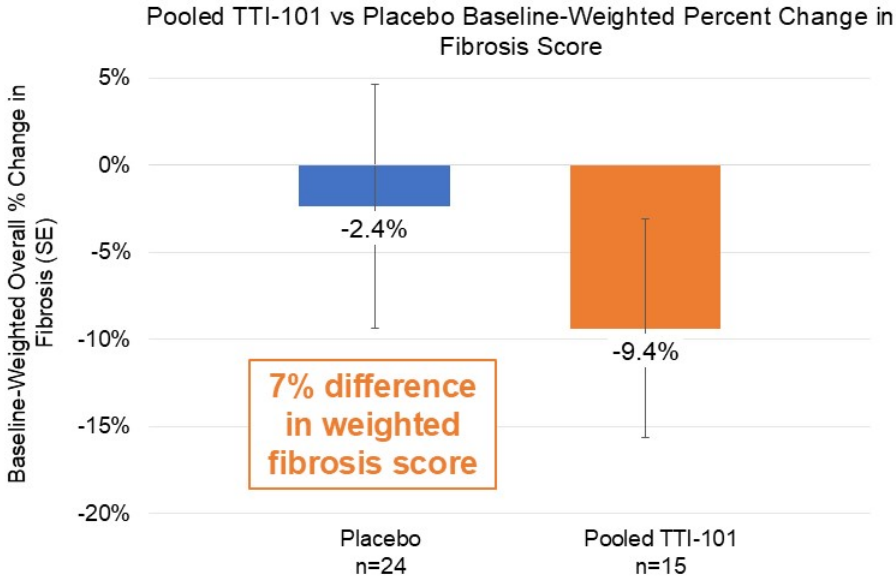
Adverse events selected to align with INPULSIS categories; safety analysis performed on all patients treated with at least one dose of TTI-101. Certain data on this slide are based on cross-study comparisons and are not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences. The values shown in the cross-study comparisons are directional and may not be directly comparable. [1]Richeldi et al. *NEJM*, 2014

Preliminary Conclusions and Additional Analyses



[1]The Efficacy Evaluable Set (EES) consists of all patients defined as all randomized patients who received at least one dose of IP and have at least one post-baseline acceptable or borderline acceptable forced vital capacity (FVC) result while on-treatment. On treatment is defined as spirometry values obtained when actively receiving IP at protocol-defined collection time points and spirometry values when on IP hold at protocol-defined collection time points; excludes spirometry values collected > 14 days of last IP dosing after they have been permanently discontinued from IP. [2] Post hoc analysis population: The additional analysis was limited to patients who were exposed to study drug for 12 weeks. One patient was not exposed to TTI-101 at 12 weeks; one patient was removed from the analysis due to receiving less than 60% of the expected dosing; two patients were removed due to no measurable TTI-101 observed in the blood as well as no reported adverse events; and one additional patient was removed as an outlier for the 12-week analysis as their pulmonary function initially improved on treatment, but was subsequently severely impacted by acute bronchitis deemed unrelated to study drug

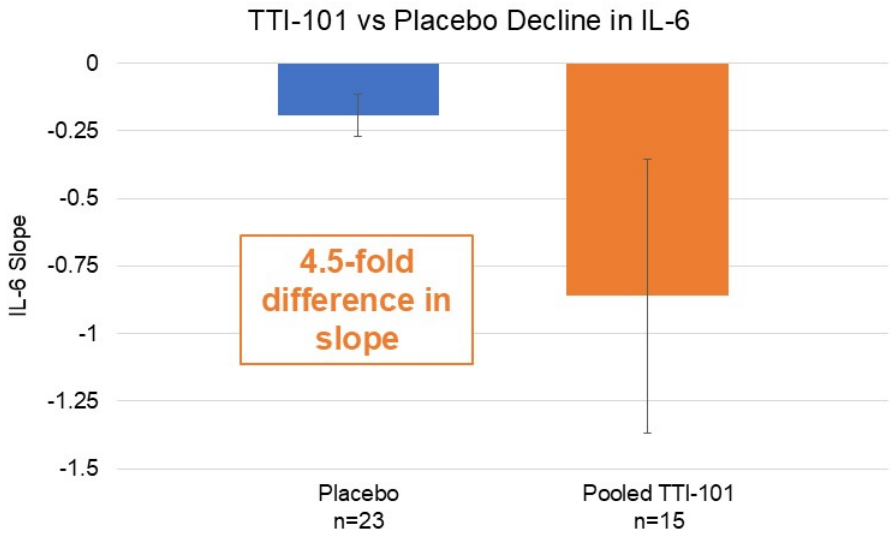
TTI-101-treated Patients Demonstrated Greater Decline in Fibrosis Score (Baseline to 12 Weeks) vs Placebo



Greater decrease in fibrosis score (improvement in fibrosis) among patients treated with TTI-101 (either arm) vs placebo

Analysis performed on post hoc analysis population comparing baseline to 12 weeks. One patient missing fibrosis score; overall percent change from baseline was calculated using baseline-weighted aggregation to account for differences in initial fibrosis severity with bootstrap-based standard error (SE)

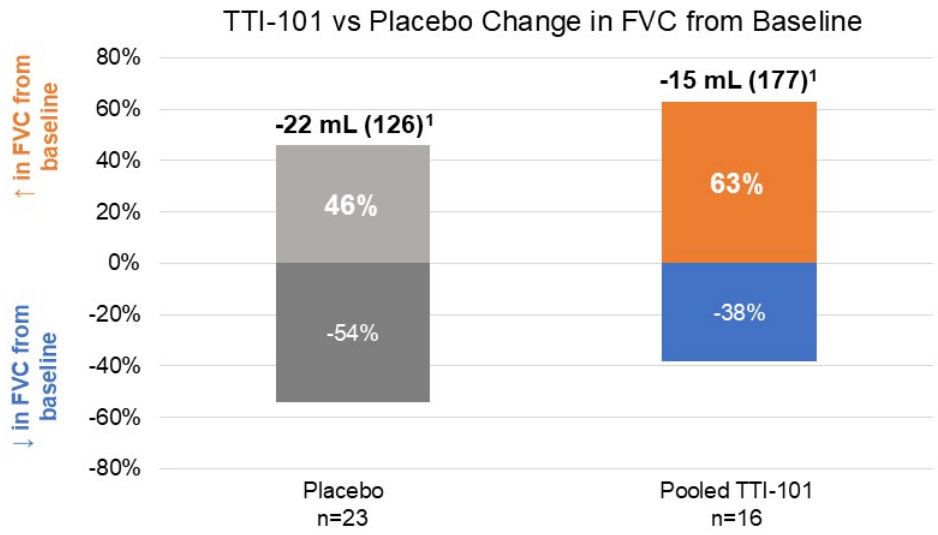
TTI-101-treated Patients Demonstrated Greater IL-6 Decline vs Placebo



IL-6 is a key pro-inflammatory cytokine that signals through STAT3; inhibition of STAT3 is expected to reduce downstream inflammatory signaling associated with disease

Analysis performed on post hoc analysis population comparing baseline to 12 weeks. Two patients missing IL-6 change scores (one placebo, one TTI-101); Decline assessed using OLS: ordinary least squares regression model and standard errors

A Greater Proportion of TTI-101-treated Patients Demonstrated Increase in FVC vs Placebo

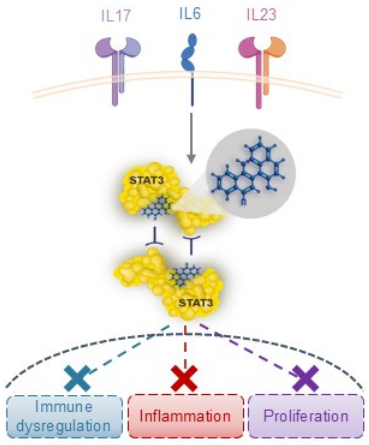


63% of patients treated with TTI-101 demonstrated an increase in FVC at 12 weeks, and less of a decline when compared to the REVERT and historical placebo groups

tvardi THERAPEUTICS Analysis performed on post hoc analysis population comparing baseline to 12 weeks; [1]Actual mean FVC change in mL (SD) at 12 weeks

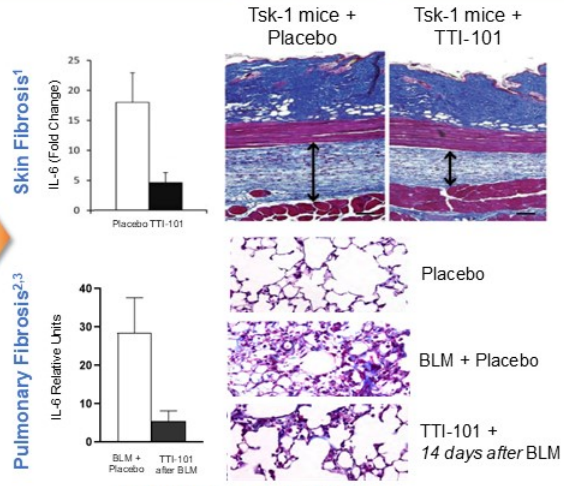
Our STAT3 Inhibitors are Designed to Address the Unmet Need in Inflammatory and Proliferative Diseases

Well-Established Target



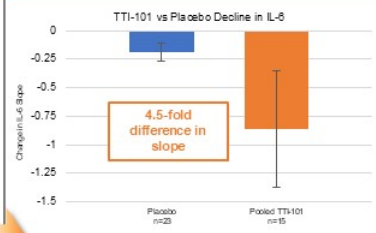
STAT3: central mediator in inflammation and proliferative disease

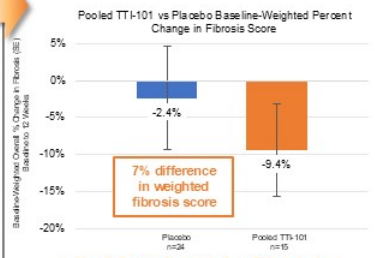
Preclinical Biological Activity



↓ IL-6 levels and ↓ fibrosis in models of proliferative disease

Clinical Proof of Mechanism





↓ IL-6 levels and ↓ fibrosis in humans

1. Pedroza et al. *Rheum.* 2017; Genetically engineered model of Tight skin (Tsk-1) mice which spontaneously develop fibrosis as a result of a duplication in the fibrillin-1 gene; 2. Pedroza et al. *FASEB J.* 2016; 3. Kauh et al. *CHEST.* 2024. Pulmonary fibrosis bleomycin (BLM) model