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 7, 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** (Address of principal executive offices)		**77478** (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 7, 2026, Tvardi Therapeutics, Inc. (the "***Company***") issued a press release entitled "Tvardi Therapeutics' TTI-109 Phase 1 Study Confirms Prodrug Design, Improved Tolerability and Pharmacodynamic Evidence of STAT3 Target Engagement." The press release provides certain clinical updates on 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 7, 2026, the Company also made available an updated corporate presentation to be used to discuss the clinical updates on TTI-109. 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 7, 2026.
99.2	Corporate presentation, dated July 7, 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 7, 2026

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

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

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, TX – July 7, 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 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."

[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.

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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LifeSci Advisors
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pkelleher@lifesciadvisors.com

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.

Exhibit 99.2

Overview

July 2026

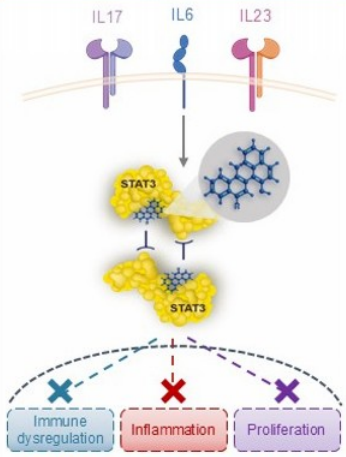
Disclaimer and Forward-Looking Statements

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 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 inflammation and proliferative disease

Translational Proof-of-Concept

Preclinical

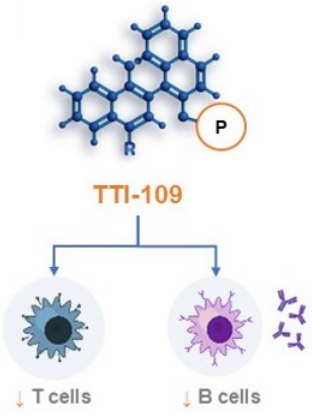
- ↓ pY-STAT3
- ↓ immune dysregulation
- ↓ inflammation
- ↓ proliferation

Confirmed in patients

Clinical

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

TTI-109 Validation in P1 Healthy Volunteers

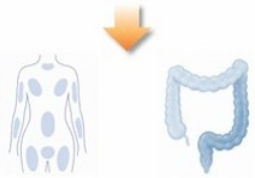


TTI-109 reduced key disease-associated immune populations

Therapeutic Areas

Diseases with shared biology:

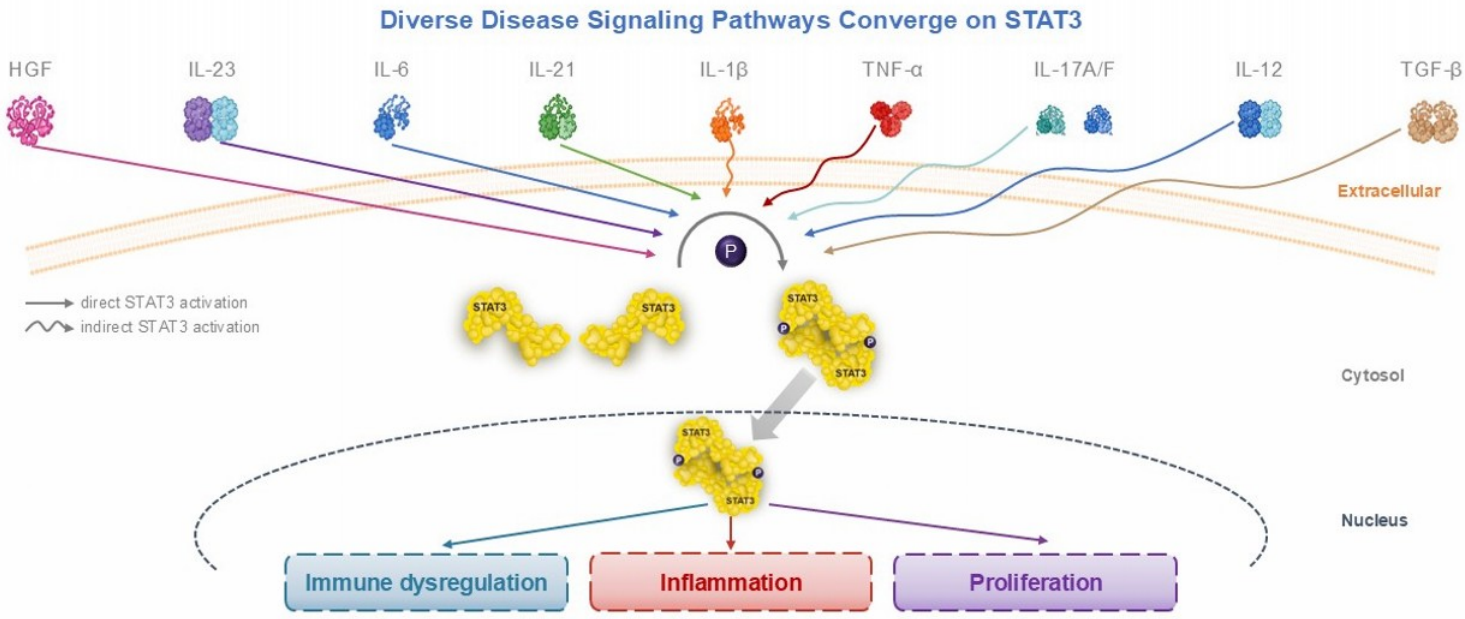
- pY-STAT3-driven
- cellular & humoral immune dysregulation
- inflammation
- proliferative tissue remodeling



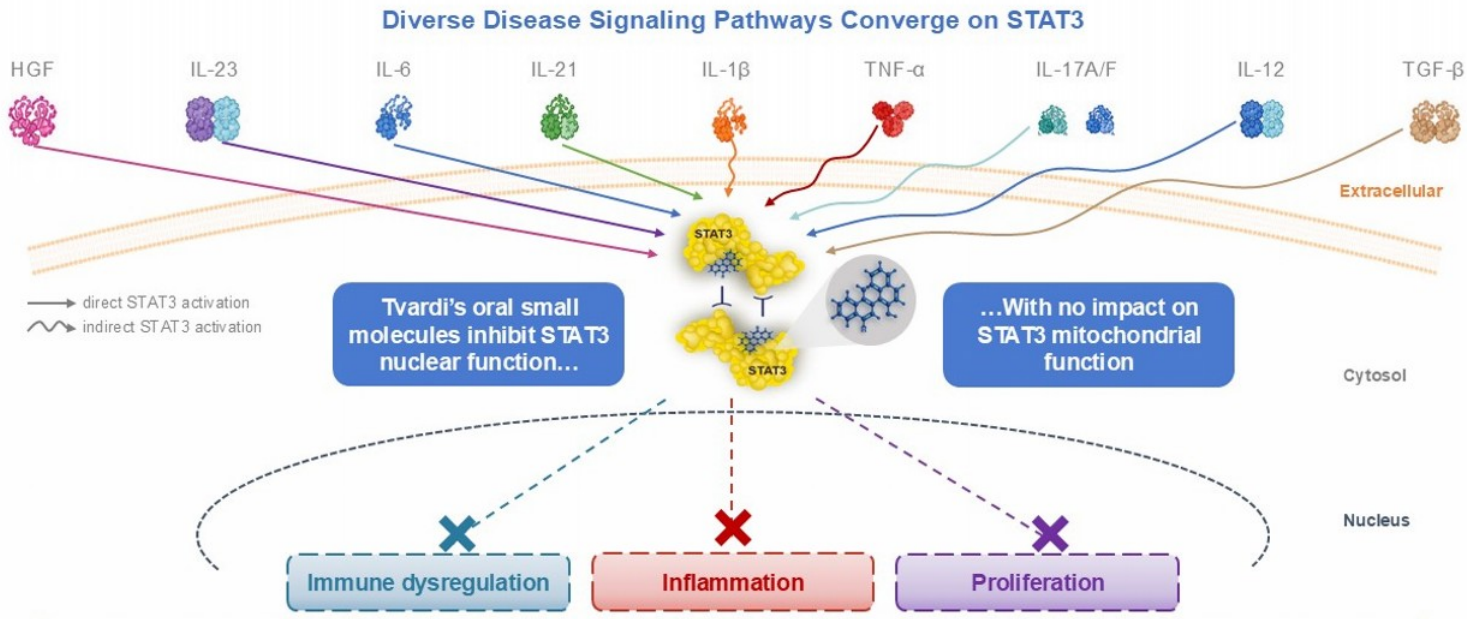
Dermatologic and GI Inflammatory and Proliferative Diseases

GI: Gastrointestinal; pY-STAT3: activated STAT3 induced by phosphorylation of tyrosine residue 705

Targeting STAT3: a Convergence Point of Inflammatory and Proliferative Disease



Targeting STAT3: a Convergence Point of Inflammatory and Proliferative Disease



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

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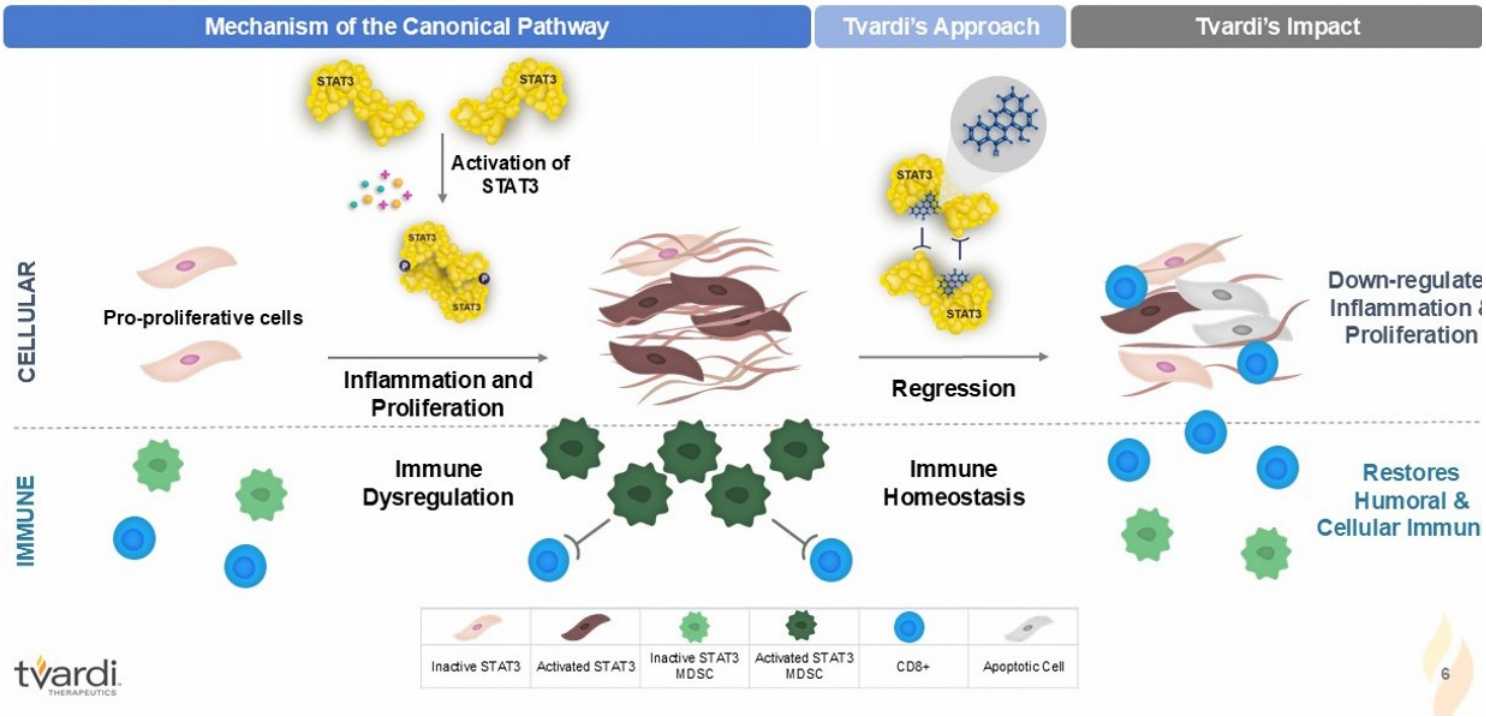
STAT3's Multi-modal Mechanism of Action in Inflammatory and Proliferative Diseases



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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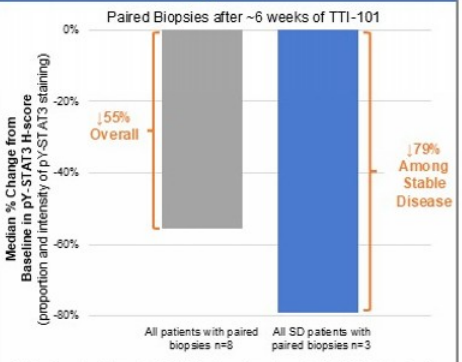
TTI-109

TTI-101 Clinical Foundation for Development of TTI-109

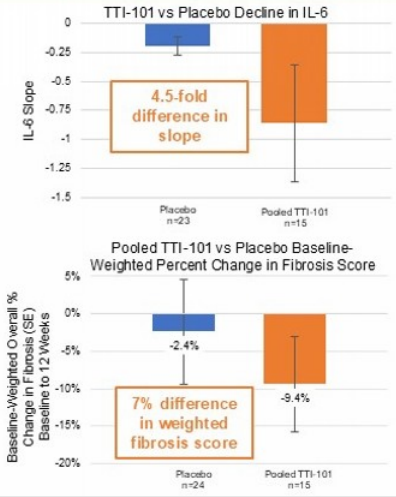
pY-STAT3 Target Engagement Oncology Phase 1[1]



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:

- Serious infection
- 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

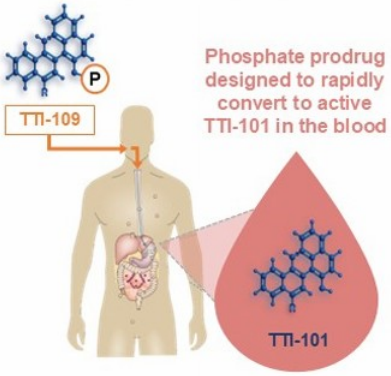
TTI-109 Designed as a Prodrug to Enhance Delivery of STAT3 Inhibitor and Establish Favorable Target Product Profile

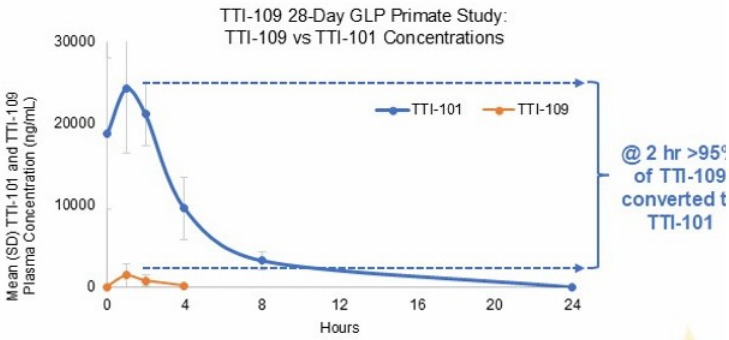
TTI-109 Design Objectives

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

TTI-109 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





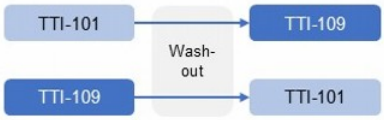
*The pharmacokinetics of TTI-109 and TTI-101 were evaluated in GLP toxicology studies in rats and monkeys. Systemic exposures to TTI-101 from TTI-109 administration were predictable in terms of molar equivalent amounts of anticipated TTI-101

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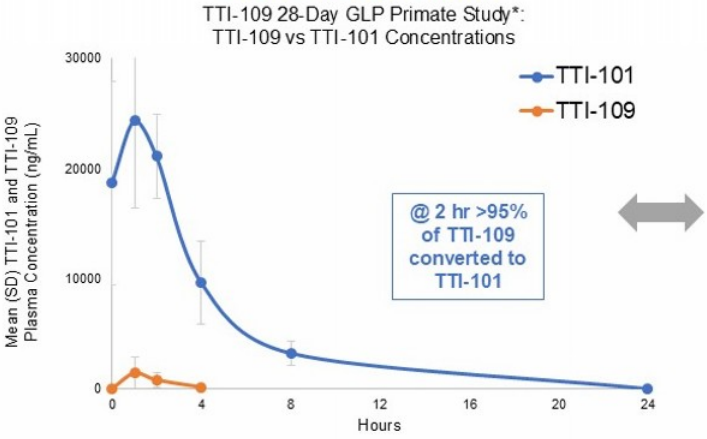
TTI-101 recommended phase 2 dose of TTI-101 (400mg BID) determined in oncology studies; PK: pharmacokinetics; BID: twice daily

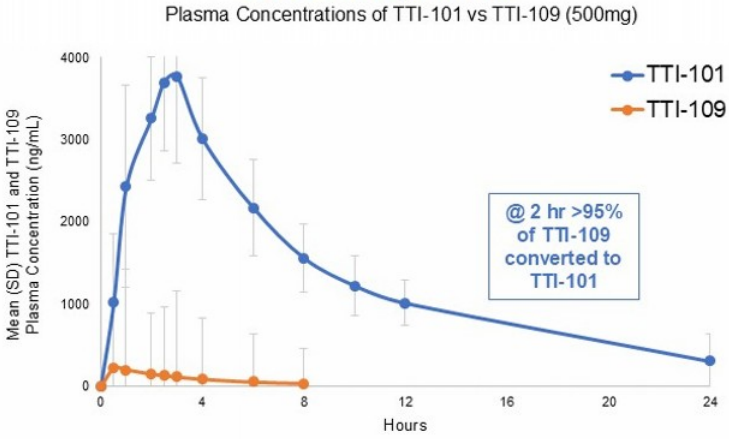
TTI-109 Rapidly Converted to Active TTI-101: Consistent from Primate to Human

SAD

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



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

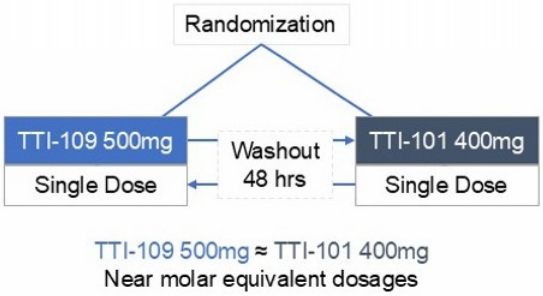


TTI-109 dosing yielded rapid conversion to the active moiety, TTI-101, consistent with animal studies

*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

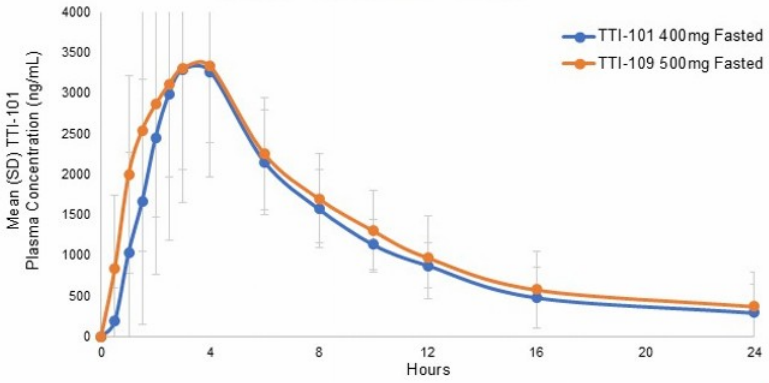
TTI-109 Achieved Equivalent Active Moiety Exposure to TTI-101

Bioequivalence Cross-over Study



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

Plasma Concentrations of TTI-101 vs TTI-109 Dosing (molar equivalent doses)



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

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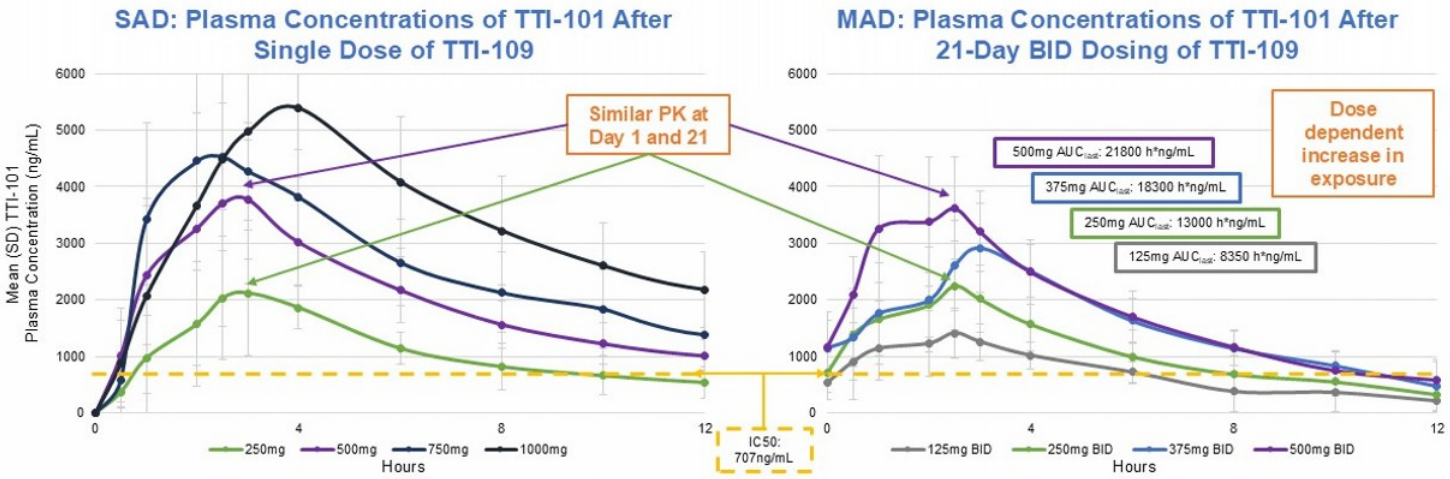
TTI-101 plasma concentrations following dosing with TTI-101 400 mg vs TTI-109 500 mg (427 mg TTI-101 molar eq.) in fasted state; Fed and fasted resulted in similar concentrations

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

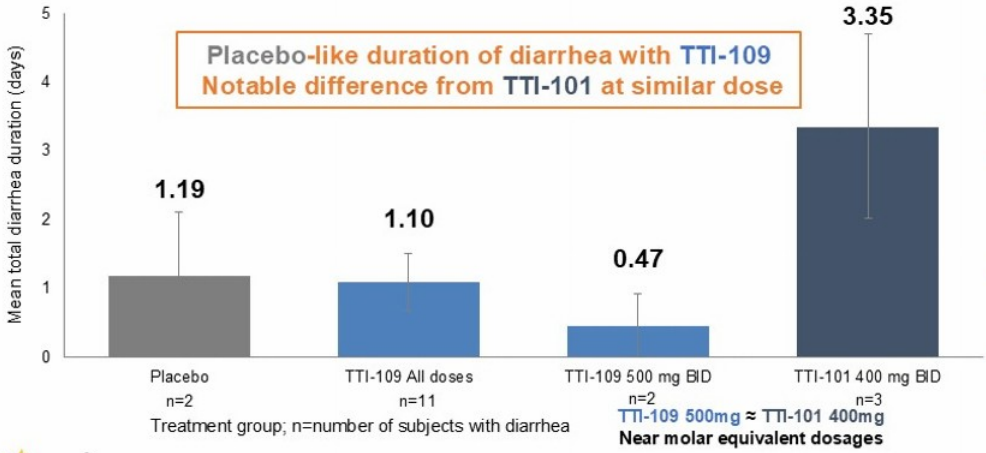
Similar incidence of TEAEs across all groups

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

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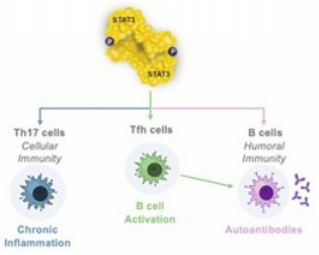
MAD: Multiple Ascending Dose; TTI-101 400 mg vs TTI-109 500 mg (427 mg TTI-101 molar eq.); Duration calculated as total per subject

Preclinical Framework for Exploratory Pharmacodynamic Objectives

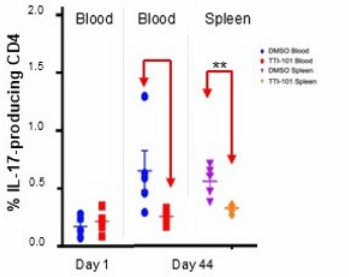
pY-STAT3 drives cellular and humoral immunity



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

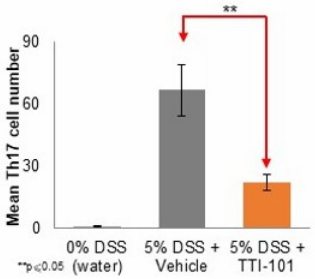


**TTI-101 vs DMSO treated mice p<0.05, ANOVA plus Tukey

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?

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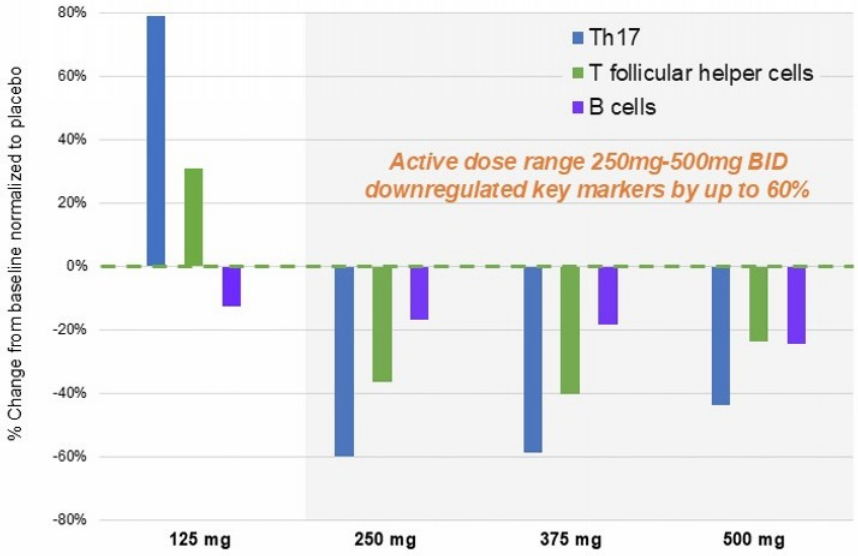
1. Steward-Tharp et al. *Immunobiology* 2014; 2. Tweardy et al. *Trans Am Clin Climatol Assoc.* 2022; 3. Figures digitized from Robinson et al. *Cancers* 2023: Dextran sodium sulfate (DSS) model

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

MAD



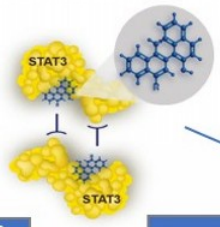
At active doses, downregulation of STAT3-driven immune populations observed:

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

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

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 position it for STAT3-driven dermatologic and gastrointestinal indications

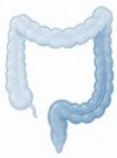
1. Tsimberidou et al. *Clin Cancer Res.* 2025; SD: Stable Disease; 2. Tvardi Press Release: January 8, 2026; pY-STAT3: activated STAT3 induced by phosphorylation of tyrosine residue 705; STAT3 IC_{50}: in a controlled system where proliferation is driven by pY-STAT3, TTI-101 inhibits cell growth with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

One Target, Three Mechanisms: pY-STAT3 Drives the Shared Biology of Inflammatory & Proliferative Dermatologic and GI Diseases

Dermatologic

Activated STAT3

- Drives the shared biology of inflammatory and proliferative disease



Gastrointestinal

Immune dysregulation:

- STAT3 orchestrates T-cell (cellular) and B-cell (humoral) immunity – driving immune dysregulation

Inflammation:

- STAT3 integrates multiple inflammatory pathways – driving chronic inflammation

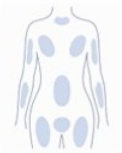
Proliferation:

- STAT3 sustains cell survival – driving epithelial hyperproliferation and fibrosis

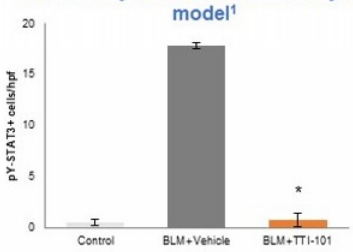
pY-STAT3 Reduction Demonstrated in Preclinical Models and Clinical Biopsies

Activated STAT3

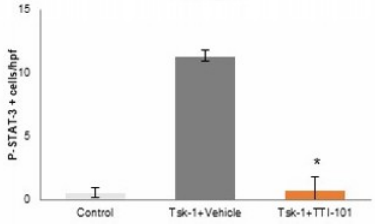
pY-STAT3 levels restored to baseline after TVRD STAT3 inhibitor treatment

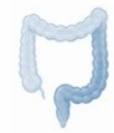


Chemically-induced inflammatory skin model[1]

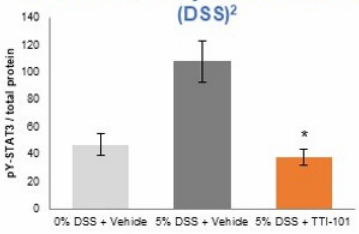


Genetically-induced proliferative skin model[1]

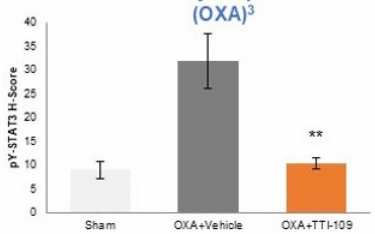




GI model driven by innate immune axis (DSS)[2]

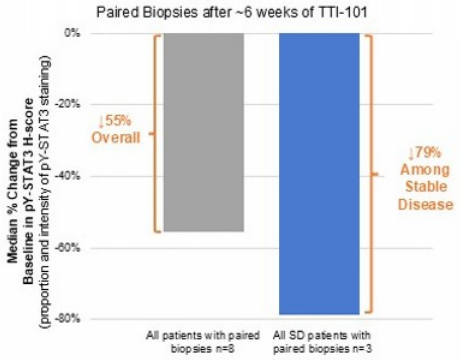


GI model driven by adaptive immune axis (OXA)[3]



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

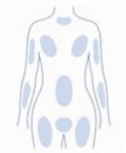
100% of patients with elevated baseline pY-STAT3 demonstrated a decrease within ~6 weeks; greater decrease in pY-STAT3 among patients with SD

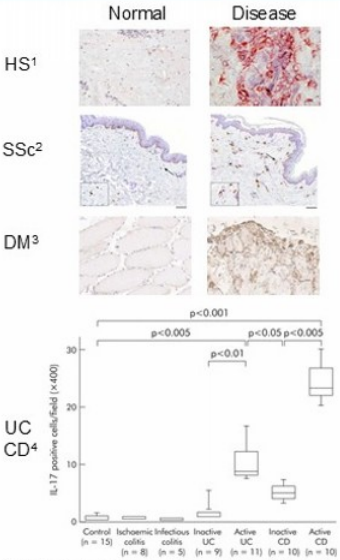
1. Pedroza et al. *Rheumatology*. 2018; 2. Figures digitized from Robinson et al. *Cancers* 2023: dextran sodium sulfate (DSS) model; 3. Tvardi data generated with CRO: WuXi oxazolone (OXA) model; n=8 per group statistical comparison using exact Mann-Whitney + Kruskal-Wallis; 4. Tsimberidou et al. *Clin Cancer Res* 2025; SD: Stable Disease; pY-STAT3: activated STAT3 induced by phosphorylation of tyrosine residue 705 *p≤0.05; **p<0.001

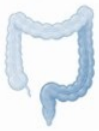
STAT3 Inhibition Normalized Preclinical and Clinical Pathogenic Immune Cell Populations

Immune dysregulation

Th17/IL-17 are elevated in clinical samples

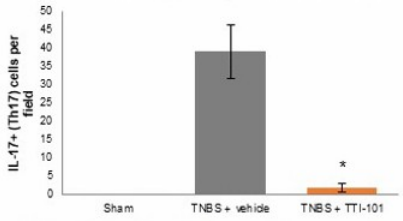




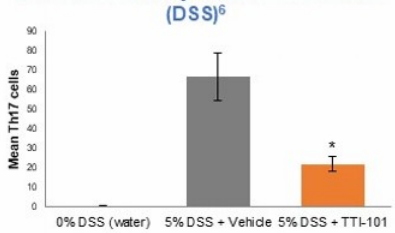


Th17 restored to homeostatic levels after TVRD STAT3 inhibitor treatment

GI model driven by adaptive immune axis (TNBS)[5]

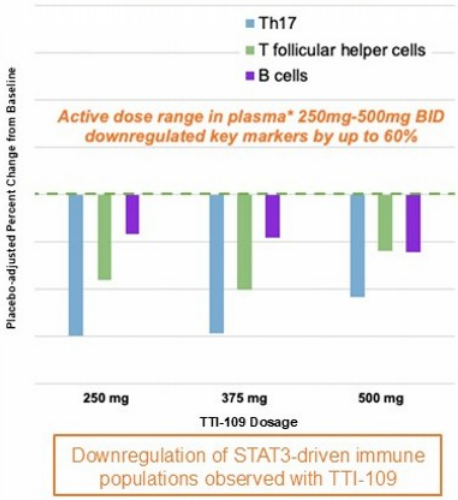


GI model driven by innate immune axis (DSS)[6]



Clinical PoC: Reduced key immune cell populations

Phase 1 Healthy Volunteers



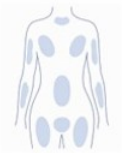
Downregulation of STAT3-driven immune populations observed with TTI-109

1. Schlapbach et al. *J Am Acad Dermatol.* 2011 Hidradenitis suppurativa (HS); 2. Lonati et al. *PLoS ONE.* 2014 Systemic sclerosis (SSc); 3. Li et al. *Mod Rheumtol.* 2023 Dermatomyositis (DM); 4. Fujino et al. *Gut.* 2003 Ulcerative colitis and Chron's disease (UC and CD); 5. Figures digitized from Robinson et al. *J Clin Med* 2022: 2,4,6-trinitrobenzene sulfonic acid (TNBS) model; 6. Figures digitized from Robinson et al. *Cancers* 2023: dextran sodium sulfate (DSS) model; *$p \leq 0.05$ TTI-101 vs vehicle

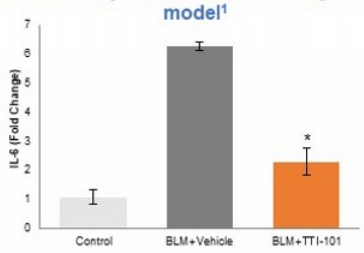
STAT3 Inhibition Reduced IL-6 and Inflammation Preclinically and in Patients

Inflammation

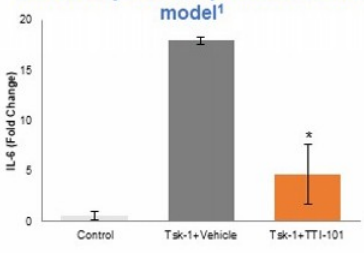
Inflammatory cytokine IL-6 and colonic inflammation significantly attenuated with TVRD STAT3 inhibitor treatment

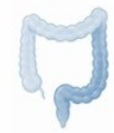


Chemically-induced inflammatory skin model[1]

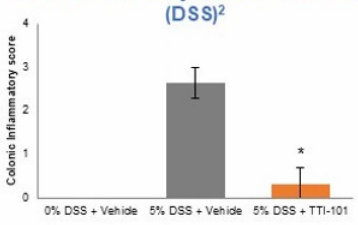


Genetically-induced proliferative skin model[1]

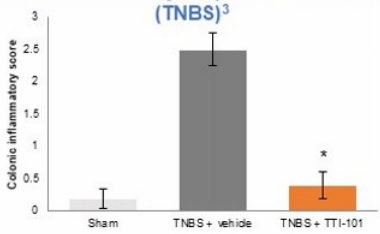




GI model driven by innate immune axis (DSS)[2]

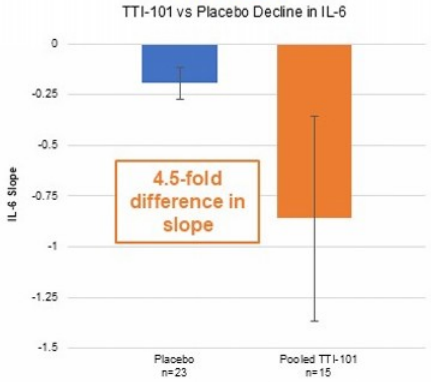


GI model driven by adaptive immune axis (TNBS)[3]



Clinical PoC: Reduced IL-6

IPF Phase 2[4]



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

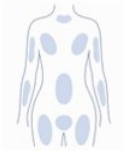
1. Pedroza et al. *Rheumatology*. 2018; 2. Figures digitized from Robinson et al. *Cancers* 2023: dextran sodium sulfate (DSS) model; 3. Figures digitized from Robinson et al. *J Clin Med* 2022: 2,4,6-trinitrobenzene sulfonic acid (TNBS) model; 4. Tvardi Press Release: January 8, 2026; *$p \leq 0.05$ TTI-101 vs vehicle

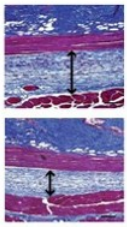
STAT3 Inhibition Reduced Proliferative Signaling and Fibrosis Preclinically and in Patients

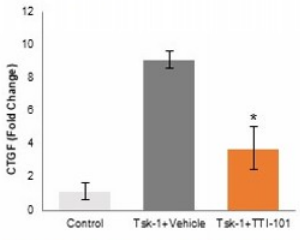
Proliferation

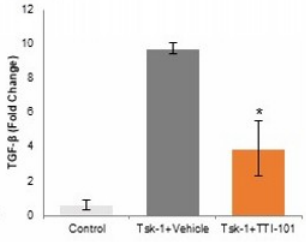
Preserved tissue integrity and reduced expression of pY-STAT3-induced proliferative genes with TVRD STAT3 inhibitor treatment

Genetically-induced proliferative skin model[1]

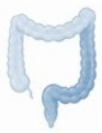


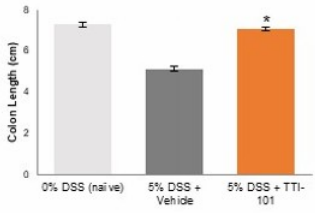






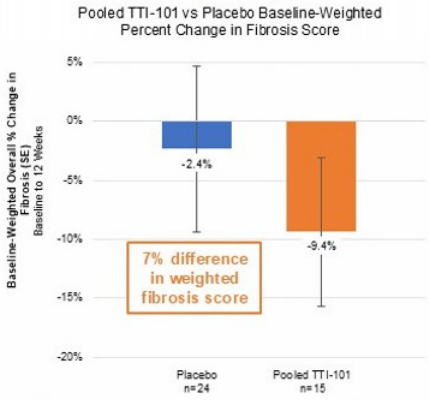
GI model driven by innate immune axis (DSS)[2]





Clinical PoC: Reduced fibrosis

IPF Phase 2[3]

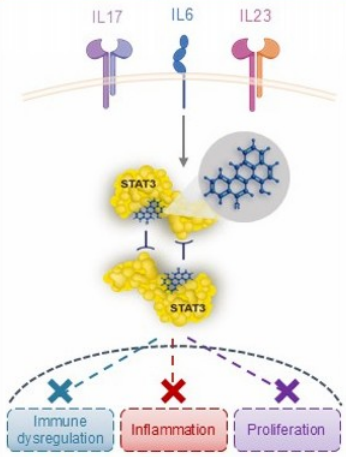


Greater decrease in fibrosis score (improvement in fibrosis) among pooled patients treated with TTI-101 vs placebo

1. Figures digitized from Pedroza et al. *Rheumatology*. 2018; 2. Figures digitized from Robinson et al. *Cancers* 2023; dextran sodium sulfate (DSS) model; 3. Tvardi Press Release: January 8, 2026; *p≤0.05 TTI-101 vs vehicle

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

STAT3: Highly Validated Convergent Node



STAT3: central mediator in inflammation and proliferative disease

Translational Proof-of-Concept

Preclinical

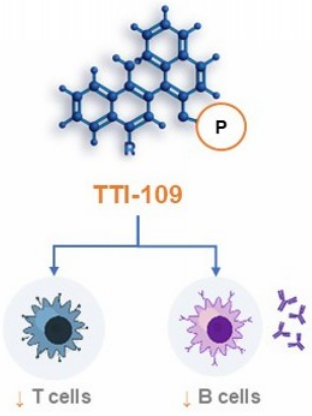
- ↓ pY-STAT3
- ↓ immune dysregulation
- ↓ inflammation
- ↓ proliferation

Confirmed in patients

Clinical

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

TTI-109 Validation in P1 Healthy Volunteers

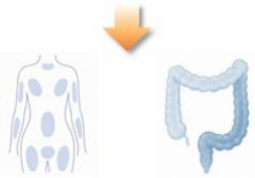


TTI-109 reduced key disease-associated immune populations

Therapeutic Areas

Diseases with shared biology:

- pY-STAT3-driven
- cellular & humoral immune dysregulation
- inflammation
- proliferative tissue remodeling



Dermatologic and GI Inflammatory and Proliferative Diseases

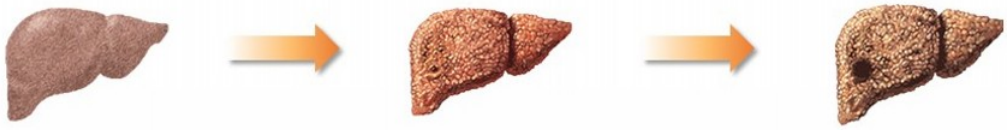
GI: Gastrointestinal; pY-STAT3: activated STAT3 induced by phosphorylation of tyrosine residue 705

TTI-101 in HCC

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

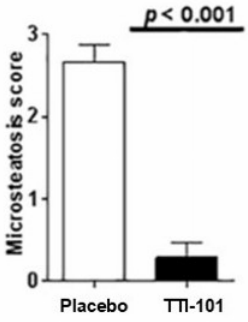
STAT3-mediated pathogenesis

Inflammation → Fibrosis/Cirrhosis → HCC

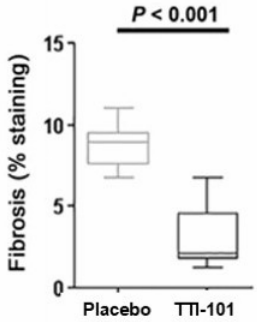


TTI-101 STAT3-inhibition in NASH-induced HCC

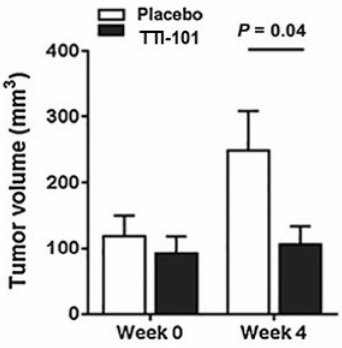
Microsteatosis



Fibrosis



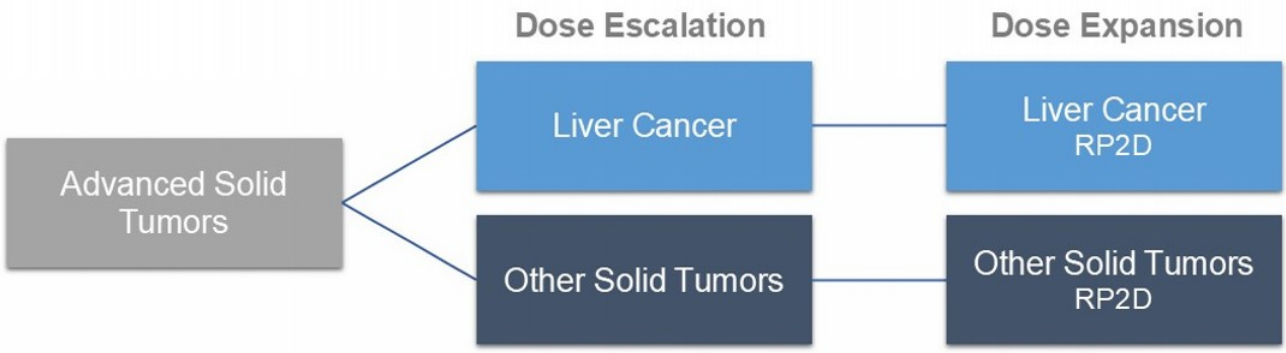
Tumor volume



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

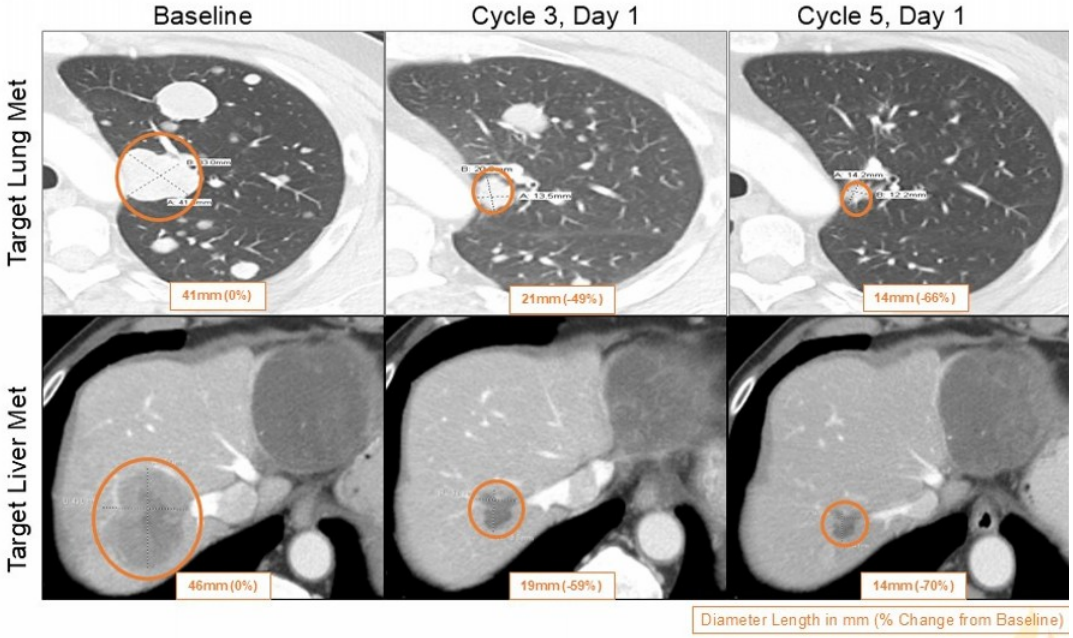
Phase 1 Clinical Trial: TTI-101 Monotherapy Led to Durable Partial Responses in Fibrotic Tumors

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



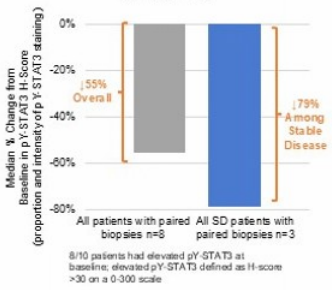
tvardi THERAPEUTICS Tsimberidou et al. *Clin Cancer Res.* 2025

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

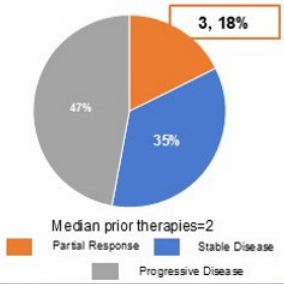
Formulation	F1 N=15		F2 N=47		F3 N=7**	
Grade, n (%)	G1/2	G3	G1/2	G3	G1/2	G3
Diarrhoea	3 (20)	3 (20)	16 (34)	6 (13)	2 (29)	0 (0)
Nausea	4 (26)	0 (0)	6 (13)	1 (2)	0 (0)	1 (14)
Fatigue	6 (40)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)
Elevated ALT/AST***	1 (7)	1 (7)	1 (2)	4 (8)	1 (14)	1 (14)
Dose reduction	3 (20)	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

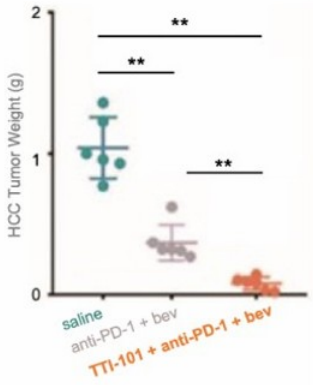


Tsimberidou et al. *Clin Cancer Res.* 2025; *STAT3 IC_{50}: in a controlled system where proliferation is driven by WT STAT3, TTI-101 inhibits cell growth with an IC_{50} of approximately 1.5μM; Kasembeli et al. *Blood.* 2022.
SD: Stable Disease; TRAE : Treatment related adverse events; F1-3: Formulation 1-3

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%**

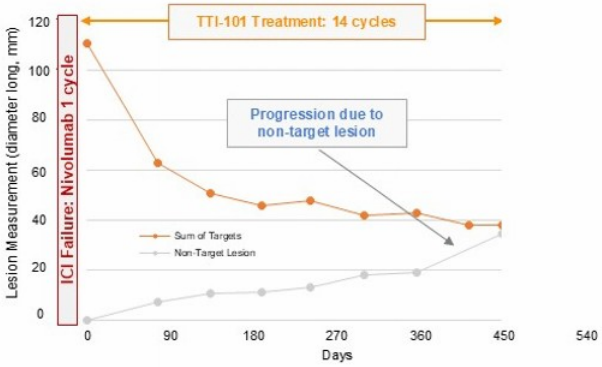
Danvatirsen key limitations:

- 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]



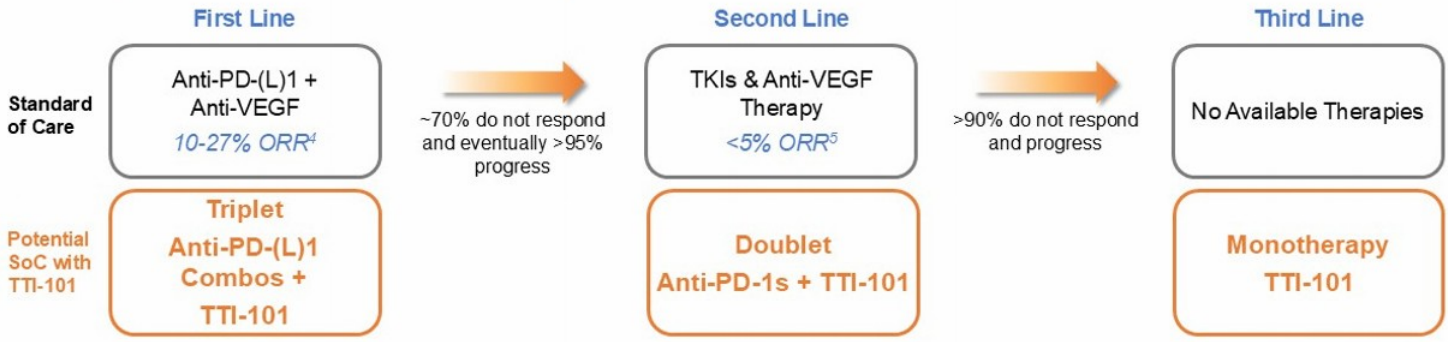
1. Adapted from Zhao, Y et al. *Hepatology*. 2021 2. Cohen et al. *Ann Oncol*. 2018 3. Siu et al. *JAMA Oncol*. 2019. ICI: Immune Checkpoint Inhibition; Bev: Bevacizumab. Certain data on this slide are based on cross-study comparisons and are not based on any head-to-head clinical trials. Cross-study 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

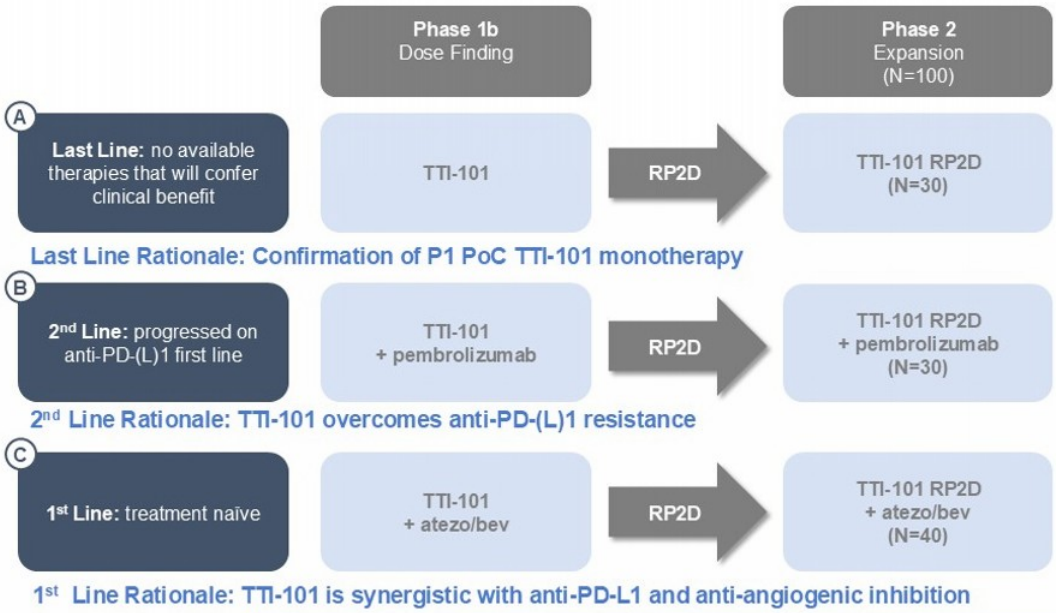
- HCC is 3rd leading cause of cancer deaths in the world[1]
- Annually in the US, >42,000 new cases of HCC and ~32,000 deaths recorded[2]
- Incidence has more than tripled since 1980[3]

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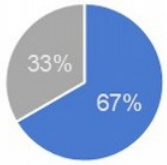
NCT05440708; Dayyani et al. JCO. 2024; Data as of April 2025

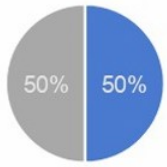
REVERT$_{\text{Liver Cancer}}$: Interim Phase 1b/2 Data

Cohort A:
TTI-101 Monotherapy at RP2D



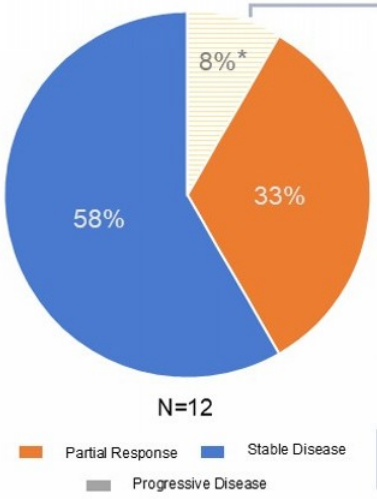
N=21

Cohort B:
TTI-101 (RP2D) + Pembro



N=8

Cohort C:
TTI-101 + Atezo/Bev



*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 $REVERT_{LIVER\ CANCER}$ trial expected in 2H:2026

Our Pipeline

Program	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
TTI-109	Healthy Volunteers (HV)		Phase 1			• Topline data reported July 2026
TTI-109	Dermatology and/or Gastroenterology			Phase 2*		• Study initiation expected 2027*
TTI-101	Hepatocellular Carcinoma (HCC)			Phase 1b/2		• Phase 1b/2 topline data 2H:2026

Diversified Pipeline With Multiple Data Catalysts Driving Long-Term Value

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

Financial Overview and Milestones

Select Corporate Information	
Ticker	TVRD
HQ	Houston, TX
Shares Outstanding[1]	9,381,344
Cash / Cash Equivalents / ST Investments[1]	$25.0 M

Milestones	
July 2026	Data Reported from TTI-109 Phase 1 Healthy Volunteer Trial
2H 2026	Topline Data from TTI-101 Phase 1b/2 HCC Trial

Anticipated Cash Runway Expected to Fund Tvardi's Operating Plan into Q4 2026

1. As of March 31, 2026

Appendix A.
Preclinical Support

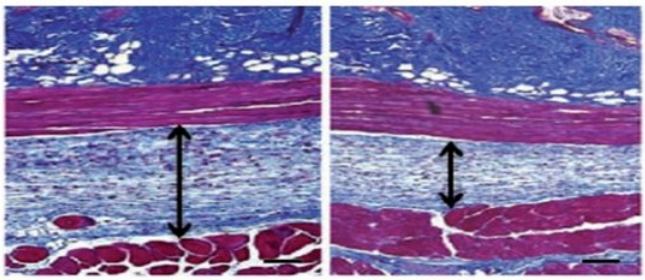
TTI-101 Attenuated *Growth Factor* Driven Fibrosis and Dermal Thickening

Genetically-induced proliferative skin model

Therapeutic treatment with TTI-101 significantly reduced dermal thickness…

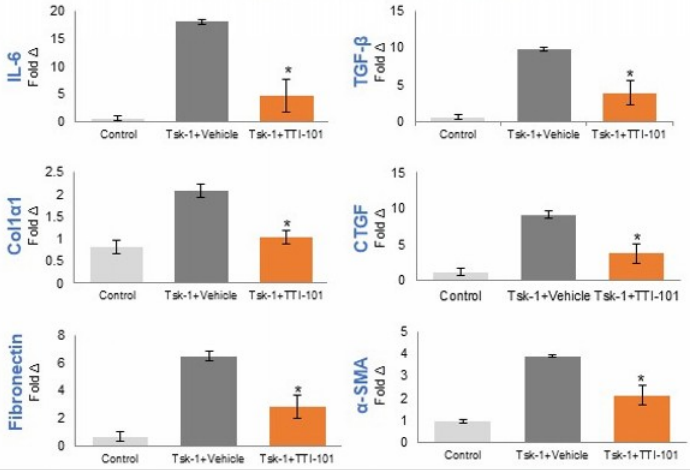
Tsk-1 mice + Placebo

Tsk-1 mice + TTI-101



* p ≤0.05 for all TTI-101 arms relative to Tsk-1 + vehicle

…and significantly reduced key drivers of inflammation and proliferation



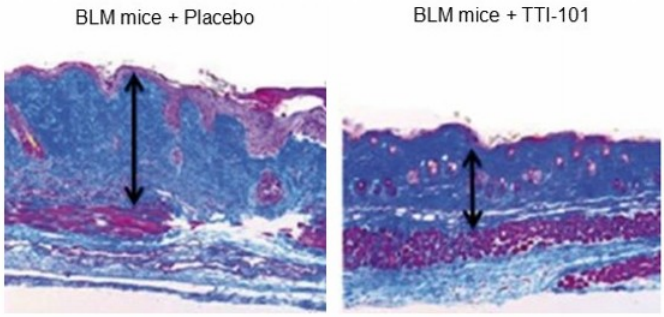
TTI-101 reversed both dermal thickening and inflammatory/pro-fibrotic hallmarks of skin fibrosis

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

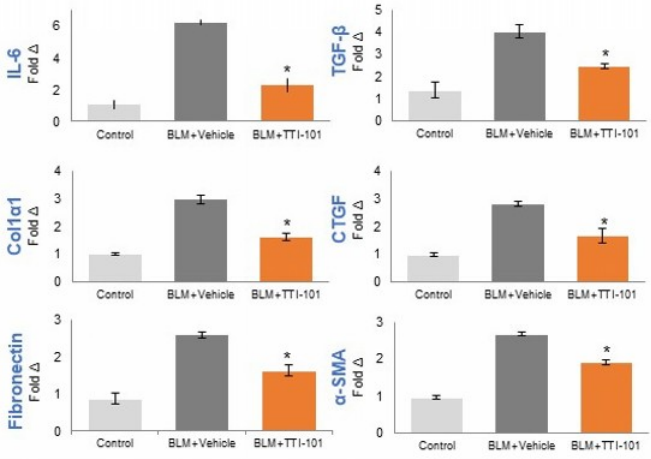
Chemically-induced inflammatory skin model

Therapeutic treatment with TTI-101 significantly reduced dermal thickness



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

…and significantly reduced key drivers of inflammation and proliferation



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

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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

TVRD STAT3 Inhibition Demonstrated Activity Across Multiple Validated IBD Immune Axes

Model Systems and Select Therapies Approved or Developed for IBD		TVRD STAT3i	Anti-TNFa	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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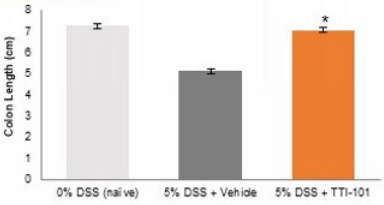
Tvardi data generated with CRO: WuXi; Comparative targets in the IBD space and select therapies approved or developed for IBD used for demonstrative purposes; DSS: dextran sodium sulfate ulcerative colitis (UC) model; TNBS: 2,4,6-trinitrobenzene sulfonic acid Crohn's disease (CD) model; OXA: oxazolone ulcerative colitis (UC) model

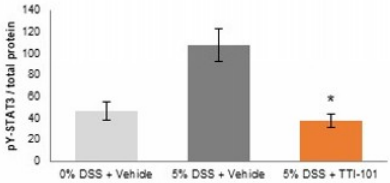
TVRD STAT3 Inhibitors in the DSS-UC Model

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

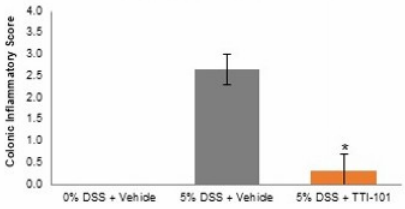
Colon Morphology and Length



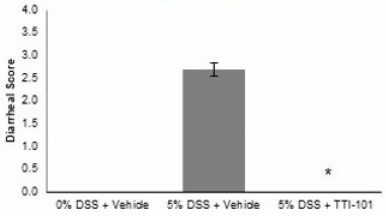
pY-STAT3



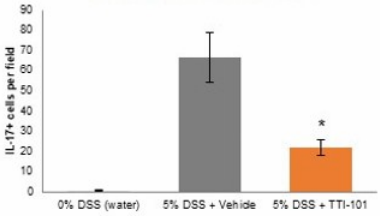
Colonic inflammation



Diarrhea



Colonic IL-17⁺ Cells



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

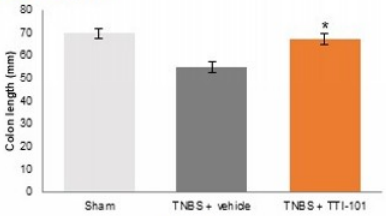
TTI-101 treatment in DSS model normalized all hallmarks of UC

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

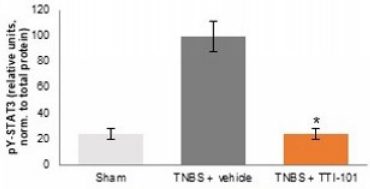
TVRD STAT3 Inhibitors in the TNBS-CD Model

TNBS UC Model with TTI-101[1]

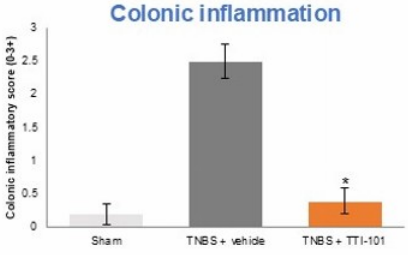
Colon Morphology and Length



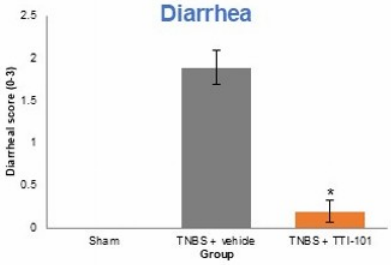
pY-STAT3



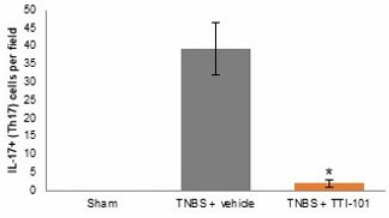
Colonic inflammation



Diarrhea



Colonic IL-17⁺ Cells



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

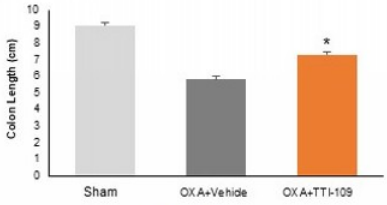
TTI-101 treatment in TNBS model normalized all hallmarks of CD

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

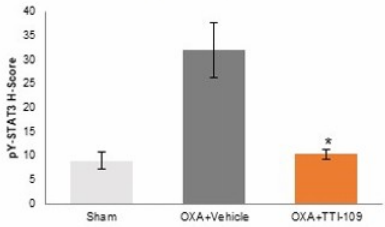
TVRD STAT3 Inhibitors in the OXA-UC Model

OXA UC Model with TTI-101[1]

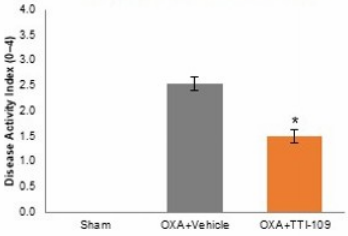
Colon Morphology and Length



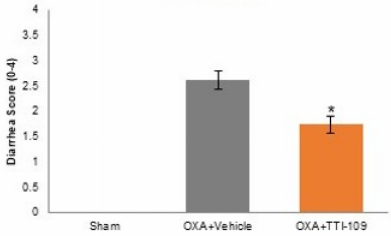
pY-STAT3



Colonic inflammation



Diarrhea



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

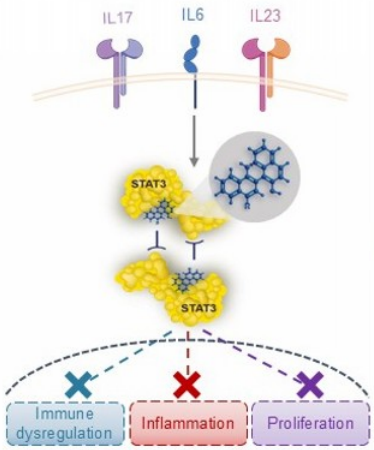
TTI-101 treatment in OXA model normalized all hallmarks of UC

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

Appendix B.
TTI-101 in IPF

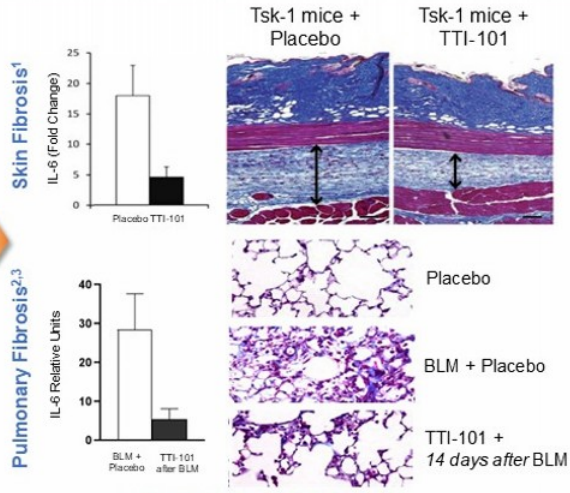
Our STAT3 Inhibitors are Designed to Address the Unmet Need in Inflammatory and Proliferative Diseases

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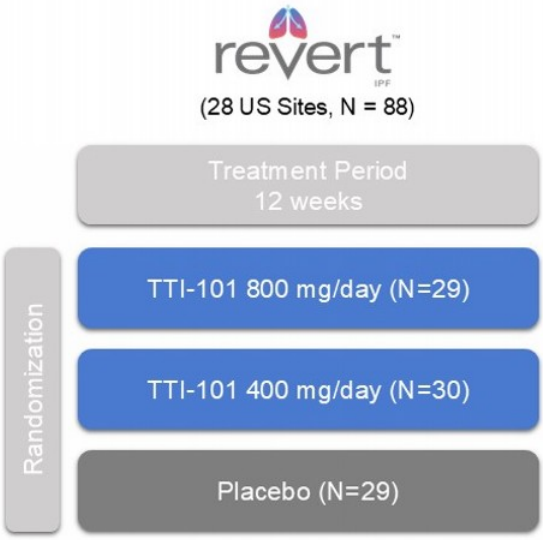
1. Pedroza et al. *Rheum.* 2017: Genetically engineered model of Tight skin (Tsk-1) mice which spontaneously develop fibrosis as a result of a duplication in the fibrillin-1 gene; 2. Pedroza et al. *FASEB J.* 2016; 3. Kauh et al. *CHEST.* 2024. Pulmonary fibrosis bleomycin (BLM) model

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

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

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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

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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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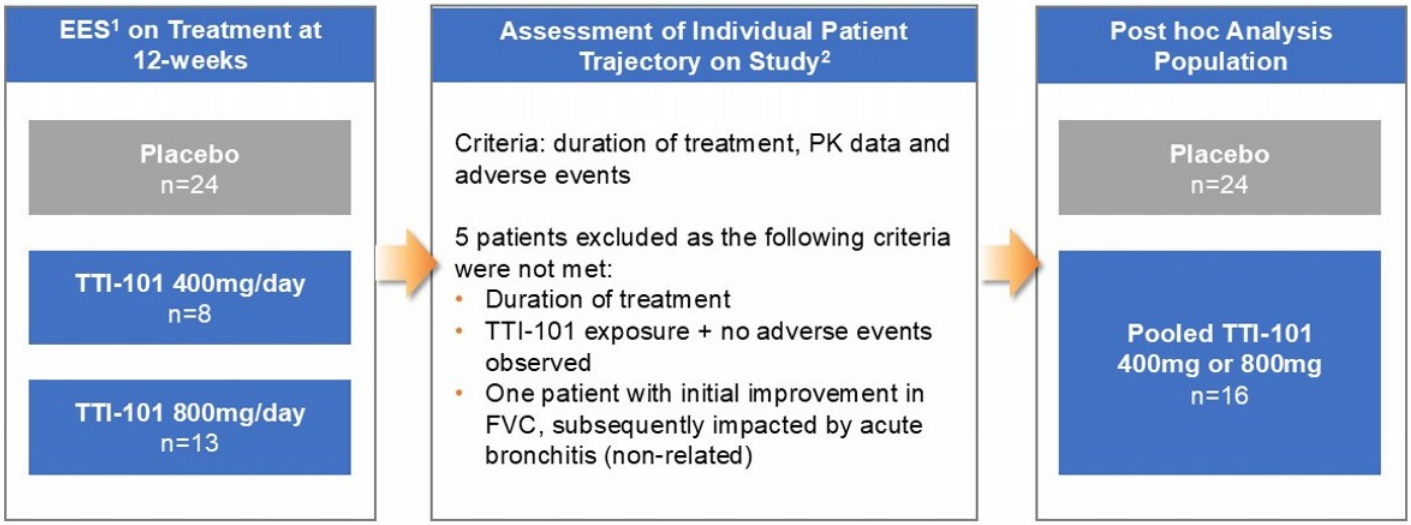
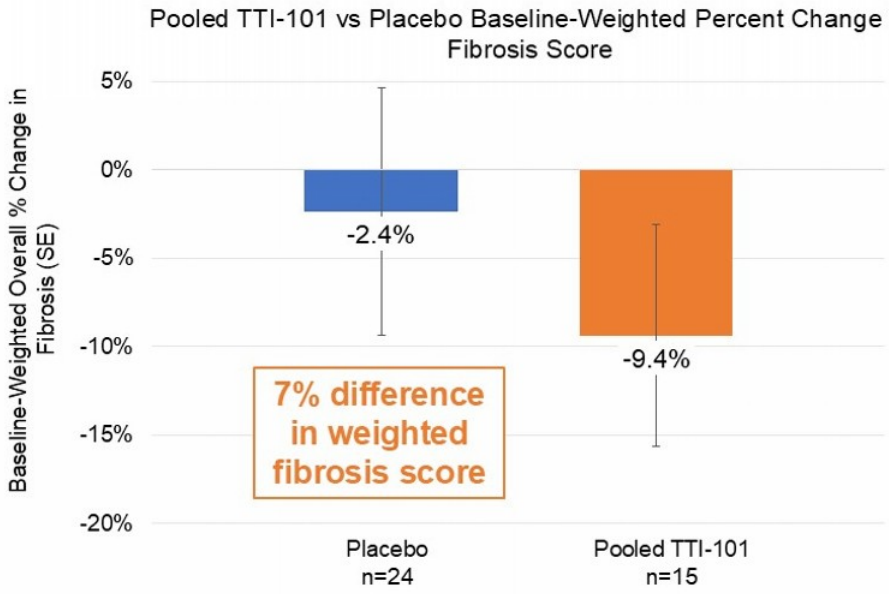
Adverse events selected to align with INPULSIS categories; safety analysis performed on all patients treated with at least one dose of TTI-101. Certain data on this slide are based on cross-study comparisons and are not based on any head-to-head clinical trials. Cross-study comparisons are inherently 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

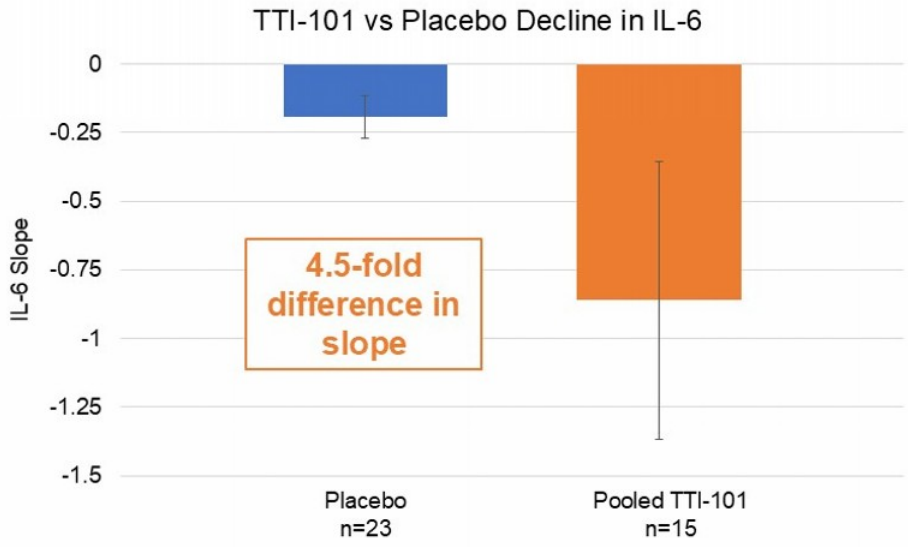
TTI-101-treated Patients Demonstrated Greater Decline in Fibrosis Score (Baseline to 12 Weeks) vs Placebo



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).

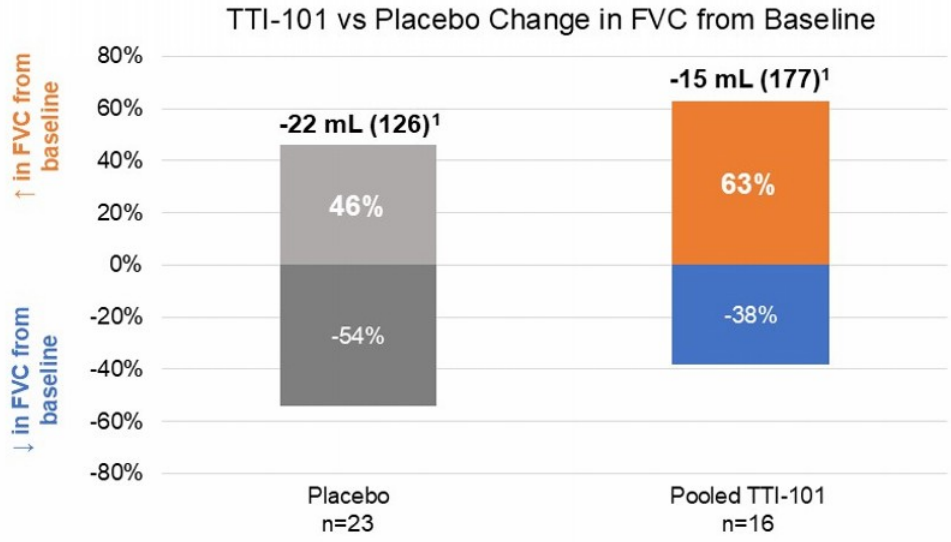
TTI-101-treated Patients Demonstrated Greater IL-6 Decline vs Placebo



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

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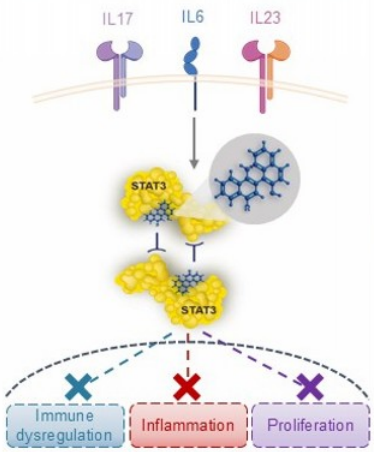

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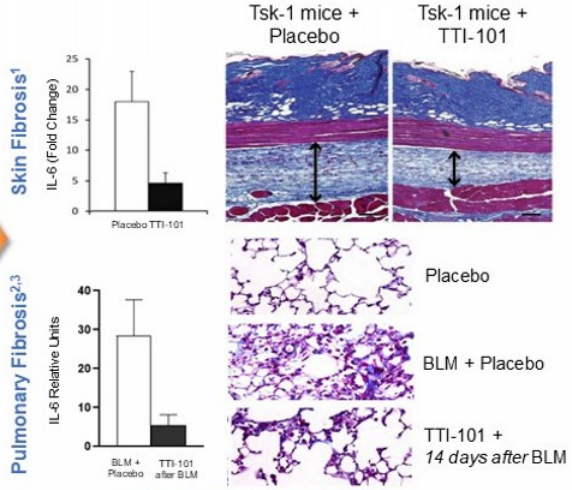
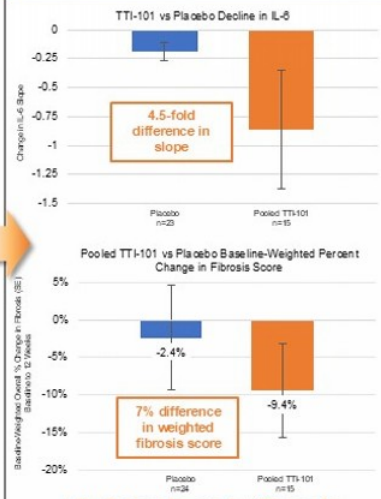
Preclinical Biological Activity



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

Clinical Proof of Mechanism



↓ IL-6 levels and ↓ fibrosis in humans

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