

**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): May 15, 2024

THIRD HARMONIC BIO, INC.

(Exact name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction
of Incorporation)

001-41498
(Commission
File Number)

83-4553503
(IRS Employer
Identification No.)

1700 Montgomery Street, Suite 210
San Francisco, California
(Address of Principal Executive Offices)

94111
(Zip Code)

Registrant's Telephone Number, Including Area Code: (209) 727-2457

N/A
(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:

- 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 \$0.0001 per share	THRD	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 2.02 Results of Operations and Financial Condition.

On May 15, 2024, Third Harmonic Bio, Inc. (the “*Company*”) issued a press release reporting the Company’s financial results for the first quarter ended March 31, 2024. A copy of the Company’s press release is attached as Exhibit 99.1 to this report.

The information in this Item 2.02, including Exhibit 99.1 attached to this report, shall not be deemed to be “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 or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended (the “*Securities Act*”). The information contained in this Item 2.02 and in the accompanying Exhibit 99.1 shall not be incorporated by reference into any other filing under the Exchange Act or under the Securities Act, except as shall be expressly set forth by specific reference in such filing.

Item 7.01 Regulation FD Disclosure.

On May 15, 2024, the Company updated its corporate presentation, which it intends to use in conferences and meetings. A full copy of the Company’s corporate presentation is attached as Exhibit 99.2 to this Current Report on Form 8-K. The corporate presentation will also be available on the Company’s website in the Investors & Media section at <https://ir.thirdharmonicbio.com>.

The information in this Item 7.01, including Exhibit 99.2 attached to this report, shall not be deemed to be “filed” for purposes of the Exchange Act, or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act. The information contained in this Item 7.01 and in the accompanying Exhibit 99.2 shall not be incorporated by reference into any other filing under the Exchange Act or under the Securities Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

<u>Exhibit Number</u>	<u>Description</u>
99.1	Press Release issued by Third Harmonic Bio, Inc. dated May 15, 2024
99.2	Corporate Presentation
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

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

THIRD HARMONIC BIO, INC.

Date: May 15, 2024

By: /s/ Christopher M. Murphy
Christopher M. Murphy
Chief Financial & Business Officer

Third Harmonic Bio Announces First Quarter 2024 Financial Results and Provides Business Update

U.S. FDA clears Investigational New Drug application for THB335

Phase 1 SAD/MAD clinical trial initiated and subject screening underway, with results expected during 1H'25

Strengthened leadership team with the appointment of Christopher J. Dinsmore, Ph.D., to Chief Scientific Officer; Dennis Dean, Ph.D., to Chief Non-Clinical Development Officer; and the promotion of Jennifer Dittman to Chief Development Operations Officer

Strong financial position with cash and cash equivalents totaling \$262.8 million as of March 31, 2024

SAN FRANCISCO, CA, May 15, 2024 (GLOBE NEWSWIRE) — Third Harmonic Bio, Inc. (Nasdaq: THRD), a clinical stage biopharmaceutical company focused on advancing the next wave of medicine for dermal, respiratory, and gastrointestinal inflammatory diseases, today announced financial results for the first quarter March 31, 2024, recent business updates, and anticipated milestones.

As part of its business update, the Company announced U.S. FDA clearance of its Investigational New Drug (IND) application to initiate a first-in-human clinical trial of THB335, a potent, highly selective, oral, small molecule KIT inhibitor that is in development for the treatment of mast cell-mediated diseases, with an initial focus in chronic spontaneous urticaria (CSU). The Company has initiated a Phase 1 single and multiple ascending doses (SAD/MAD) clinical trial of THB335 to evaluate safety, pharmacokinetics, and pharmacodynamics in healthy volunteers, and expects to report clinical results from the trial during the first half of 2025. The Phase 1 trial is expected to be followed by a Phase 2 trial in CSU, with planned rapid expansion into additional mast cell-mediated disorders.

“With the initiation of THB335 clinical trials, we are advancing the development of our potentially best-in-class oral KIT inhibitor toward becoming an important treatment for patients living with chronic spontaneous urticaria and other mast-cell mediated inflammatory diseases,” said Natalie Holles, Chief Executive Officer at Third Harmonic Bio. “We are continuing to conduct our development efforts with urgency given the significant unmet need in CSU and the potentially transformative benefit that TBH335 may deliver to patients.”

The Phase 1 SAD/MAD clinical trial of THB335 is being conducted in healthy volunteers to assess safety and tolerability, characterize pharmacokinetics, and to measure the pharmacodynamic effect by reductions in serum tryptase, a biomarker associated with mast cell activation and correlated with clinical response in urticaria studies. Results are expected in the first half of 2025.

Leadership Team Updates

The Company also announced the appointment and promotion of key executive leaders to the organization. Christopher J. Dinsmore, Ph.D., was appointed to Chief Scientific Officer, Dennis Dean, Ph.D., was appointed to Chief Non-Clinical Development Officer, and Jennifer Dittman was promoted to Chief Development Operations Officer.

“We are excited to expand the executive team with the appointments of Chris, Dennis and Jennifer to their respective leadership roles in these critical discovery, research and development functions,” continued Natalie Holles. “In addition to their outstanding collective track record in our industry, all three embody our core operating principles of open collaboration, enterprise-level thinking and drive. I look forward to our future achievements under this outstanding leadership team.”

Chris is a seasoned leader with a strong track record of advancing early targets to drug candidate identification and through clinical development. In his role as Chief Scientific Officer, he will oversee the Company’s scientific research strategy from discovery through preclinical proof-of-concept, IND filing, and also support early clinical development. Chris joins Third Harmonic Bio from Kronos Bio, where he was Chief Scientific Officer, responsible for the discovery functions, and played a key role in the company’s initial public offering and partnership with Genentech. Prior to Kronos, he served as an Entrepreneur-in-Residence at Third Rock Ventures, focusing on the launch of new biomedical companies. Earlier in his career, he served as Vice President, Head of Chemistry, of Forma Therapeutics, where he oversaw chemistry functions in support of discovery and early development. He began his career at Merck Research Laboratories where he held positions of increasing responsibility in discovery chemistry. He received his Ph.D. in organic chemistry from University of Minnesota, Minneapolis, and was a NIH Postdoctoral Fellow in organic chemistry at Harvard University.

Dennis brings extensive experience across multiple therapeutic areas of drug discovery and development, with a particular focus in DMPK, preclinical safety assessment, clinical pharmacology, biomarkers, and modeling and simulation. In his role as Chief Non-Clinical Development Officer, he will be responsible for leading the selection of high-quality development candidates, including toxicology, DMPK and translation functions. Prior to joining Third Harmonic Bio, Dennis has served as Chief Development Officer of IFM Therapeutics,

where he oversaw preclinical and clinical development, advancing multiple programs into early clinical development leading to three acquisitions by global pharmaceutical companies. Before IFM Therapeutics, he was Senior Vice President, Head of Preclinical Development at Vertex Pharmaceuticals, where he linked key preclinical translational groups, effectively progressed the pipeline, and bridged transition for discovery into development. Earlier in his career, he held positions of increasing responsibility in DMPK at Merck Research Laboratories. He received his Ph.D. in medicinal chemistry at State University of New York, Buffalo, and was a Postdoctoral Fellow at Emory University.

Jennifer joined Third Harmonic Bio in November 2022 as Vice President of Regulatory Affairs. In her expanded role as Chief Development Operations Officer, she is now responsible for regulatory affairs, program management, quality, and CMC. Prior to joining Third Harmonic Bio, Jennifer was Vice President of Regulatory Affairs and Medical Writing at Generation Bio, where she was responsible for platform and pipeline regulatory activities. Before Generation Bio, she held roles of increasing responsibility at Vertex Pharmaceuticals, most recently serving as Executive Director, Therapeutic Area Head, in Regulatory Affairs, where she helped set the global regulatory strategy for multiple pipeline products in development, including small molecule and gene therapy/editing programs. Earlier in her career, Jennifer served in roles of increasing responsibility in Regulatory Affairs at bluebird bio and was Adjunct Faculty in the Regulatory Affairs program at Northeastern University. She holds a M.S. in regulatory affairs for drugs, biologics, and medical devices from Northeastern University.

Summary of Financial Results

Cash Position: Cash and cash equivalents totaled \$262.8 million as of March 31, 2024. Based on the company's current operating plan, Third Harmonic Bio believes that its existing cash and cash equivalents will be sufficient to fund its operating expenses and capital expenditure requirements through at least 2026.

R&D Expenses: Research and development (R&D) expenses decreased to \$6.2 million for the three months ended March 31, 2024, from \$6.7 million for the same period in 2023. The decreases were primarily due to decreases in development costs relating to the termination of the THB001 program, partially offset by increases in research costs relating to the nonclinical development of THB335 and other next-generation discovery efforts.

G&A Expenses: General and administrative (G&A) expenses decreased to \$5.1 million for the three months ended March 31, 2024, from \$5.3 million for the same period in 2023. The decreases were primarily attributable to decreases in non-cash stock-based compensation.

Net Loss: Net loss for the three months ended March 31, 2024, decreased to \$7.9 million from a net loss of \$9.1 million for the same period in 2023. The decreases were primarily due to increases in interest income and decreases in operating expenses.

About Third Harmonic Bio, Inc.

Third Harmonic Bio is a clinical stage biopharmaceutical company focused on advancing the next wave of medicine for dermal, respiratory, and gastrointestinal inflammatory diseases through the development of novel, highly selective, small-molecule inhibitors of KIT, a cell surface receptor that serves as the master regulator of mast cell function and survival. Early clinical studies demonstrate that KIT inhibition has the potential to revolutionize the treatment of a broad range of mast-cell-mediated inflammatory diseases, and that a titratable, oral small molecule inhibitor may provide the optimal therapeutic profile against this target. Third Harmonic Bio's lead product candidate, THB335, is a titratable, oral, small molecule inhibitor that is currently in a Phase 1 clinical trial. For more information, please visit the Third Harmonic Bio website: www.thirdharmonicbio.com.

Forward-Looking Statement

This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding the expected timing for clinical trials and regulatory submissions for THB335, planned clinical and development activities and timelines, and the sufficiency of Third Harmonic Bio's cash and cash equivalents to fund its operating expenses and capital expenditure requirements through at least 2026. Forward-looking statements can be identified by words such as: "anticipate," "intend," "plan," "goal," "seek," "believe," "project," "estimate," "expect," "strategy," "future," "likely," "may," "should," "will" and similar references to future periods. These statements are subject to numerous risks and uncertainties, including risks and uncertainties related to Third Harmonic Bio's cash forecasts, ability to advance its product candidates, the receipt and timing of potential regulatory submissions, designations, approvals and commercialization of product candidates, our ability to protect our intellectual property, the timing and results of preclinical and clinical trials, changes to laws or regulations, market conditions, geopolitical events, and further impacts of pandemics or health epidemics, that could cause actual results to differ materially from what Third Harmonic Bio expects. Further information on potential risk factors that could affect Third Harmonic Bio's business and its financial results are detailed under the heading "Risk Factors" included in Third Harmonic Bio's Quarterly Report on Form 10-Q for the three months ended March 31, 2024, filed with the U.S. Securities and Exchange Commission (SEC) on May 15, 2024, and in Third Harmonic Bio's other filings filed from time to time with the SEC. Third Harmonic Bio undertakes no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

Investor and Media Contact:

Lori Murray
lori.murray@thirdharmonicbio.com

THIRD HARMONIC BIO, INC.
Condensed consolidated balance sheet data
(Unaudited)
(In thousands)

	December 31, 2023	March 31, 2024
Assets		
Cash and cash equivalents	\$ 269,070	\$262,826
Other current assets	3,376	2,771
Non-current assets	5,265	4,924
Total assets	\$ 277,711	\$270,521
Liabilities		
Current liabilities	\$ 5,418	\$ 4,018
Non-current liabilities	3,208	3,002
Total liabilities	8,626	7,020
Stockholders' equity	269,085	263,501
Total liabilities and stockholders' equity	\$ 277,711	\$270,521

THIRD HARMONIC BIO, INC.
Condensed consolidated statements of operations
(Unaudited)
(In thousands of, except per share and share amounts)

	Three Months Ended March 31,	
	2023	2024
Operating expenses:		
Research and development	\$ 6,737	\$ 6,226
General and administrative	5,251	5,064
Total operating expenses	11,988	11,290
Loss from operations	11,988	11,290
Other (income) expense, net	(2,903)	(3,434)
Net loss	\$ 9,085	\$ 7,856
Net loss per share of common stock, basic and diluted	\$ 0.23	\$ 0.20
Weighted-average common stock outstanding, basic and diluted	39,438,572	40,213,158



Third
Harmonic
Bio

FOCUSED

On advancing
the next
wave of
medicine for
inflammatory
diseases



MAY 2024

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Forward Looking Statements

This presentation contains forward-looking statements within the meaning of, and made pursuant to the safe harbor provisions of, the Private Securities Litigation Reform Act of 1995. Any statements made in this presentation that are not statements of historical fact, including statements about our beliefs and expectations, are forward-looking statements and should be evaluated as such. Forward-looking statements include information concerning the anticipated profile, efficacy and target indications of THB335, the expected timing of clinical trials of THB335 and the expected development and timeline for clinical and non-clinical studies of THB335 candidate. These statements often include words such as "anticipate," "expect," "suggests," "plan," "believe," "intend," "estimates," "targets," "projects," "should," "could," "would," "may," "will," "forecast" and other similar expressions. These forward-looking statements are contained throughout this presentation. We base these forward-looking statements on our current expectations, plans and assumptions that we have made in light of our experience in the industry, as well as our perceptions of historical trends, current conditions, expected future developments and other factors we believe are appropriate under the circumstances at such time. As you read and consider this presentation, you should understand that these statements are not guarantees of future performance or results. The forward-looking statements are subject to and involve risks, uncertainties and assumptions, and you should not place undue reliance on these forward-looking statements. Although we believe that these forward-looking statements are based on reasonable assumptions at the time they are made, you should be aware that many factors could affect our actual results or results of operations and could cause actual results to differ materially from those expressed in the forward-looking statements. Factors that may materially affect such forward-looking statements include: our limited operating history and that we have not completed any clinical trials beyond Phase 1 and have not had any product candidates approved for commercial sale; our significant net losses incurred since inception and the likelihood of incurring additional losses for the foreseeable future; our need for substantial additional funding; the early stage of development of our programs and the possibility they may fail in development; our future performance is substantially dependent on our ability to identify and develop future product candidates; legal and regulatory risks; and intellectual property-related risks, among others. Additional risks and uncertainties that could affect our financial results and business are more fully described under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the three months ended March 31, 2024, filed with the SEC on May 15, 2024, and our other SEC filings, which are available on the Investor & Media page of our website at <https://ir.thirdharmonicbio.com/> and on the SEC's website at www.sec.gov. These cautionary statements should not be construed by you to be exhaustive and are made only as of the date of this presentation. We undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise, 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. 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.

Recent Highlights



- THB335 U.S. IND cleared; Phase 1 SAD/MAD trial underway with results expected in 1H'25
- Appointed Chris Dinsmore, Ph.D., to Chief Scientific Officer, Dennis Dean, Ph.D., to Chief Non-Clinical Development Officer and promoted Jennifer Dittman to Chief Development Operations Officer
- Planning rapid advancement to robust Phase 2 study in CSU to support accelerated path to registration studies
- Planned expansion into additional mast-cell mediated inflammatory disorders at Phase 2, including severe asthma
- Next-generation medicinal chemistry efforts continue to support “pipeline-in-a-target” potential
- Cash and cash equivalents of \$262.8M as of March 31, 2024

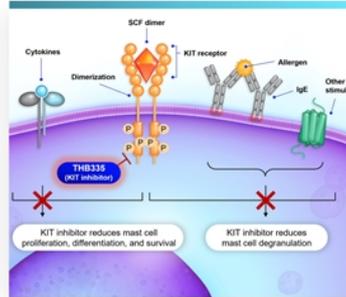
THRD: Focused on KIT to Treat Mast Cell-Mediated Inflammatory Diseases

LARGE ESTABLISHED MARKETS WITH HIGH UNMET NEED



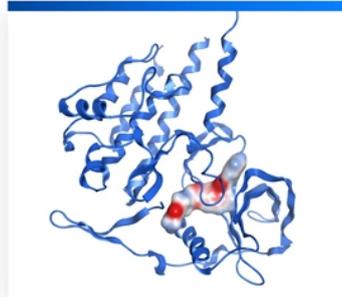
Millions of patients living with severe mast cell-mediated diseases; high residual need despite multiple approved products

KIT: A NOVEL, CLINICALLY VALIDATED TARGET



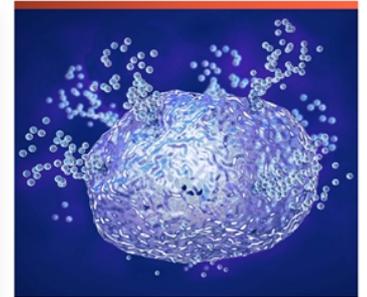
Clinical validation of KIT as potentially transformative target for mast cell-mediated diseases

CLINICAL CANDIDATE: THB335



Highly selective, oral small molecule with potential to optimize therapeutic index and offer patient convenience over injectables

"PIPELINE-IN-A-TARGET" POTENTIAL



Developing a franchise of KIT inhibitors as potential treatment options for a range of dermal, airway, and GI inflammatory diseases

High Disease Burden in Chronic Spontaneous Urticaria

A severe, yet undertreated dermal inflammatory condition

“Out there, it’s a horrible world for urticaria patients”¹



- **Prevalence:** More than 1.5 million patients or 0.5-1% point prevalence; ~70-80% female, mean age ~46 years
- **Disease impact:** CSU severely impairs quality of life, causes significant physical discomfort and emotional distress, including anxiety, depression, insomnia and social isolation
- **Limited treatment options:** Oral anti-histamines effective in only ~50% of patients; single biologic therapy approved for second-line use
- **New treatment options** are imperative to driving disease awareness, diagnosis and treatment

KIT is the Master Regulator of Mast Cell Function and Survival

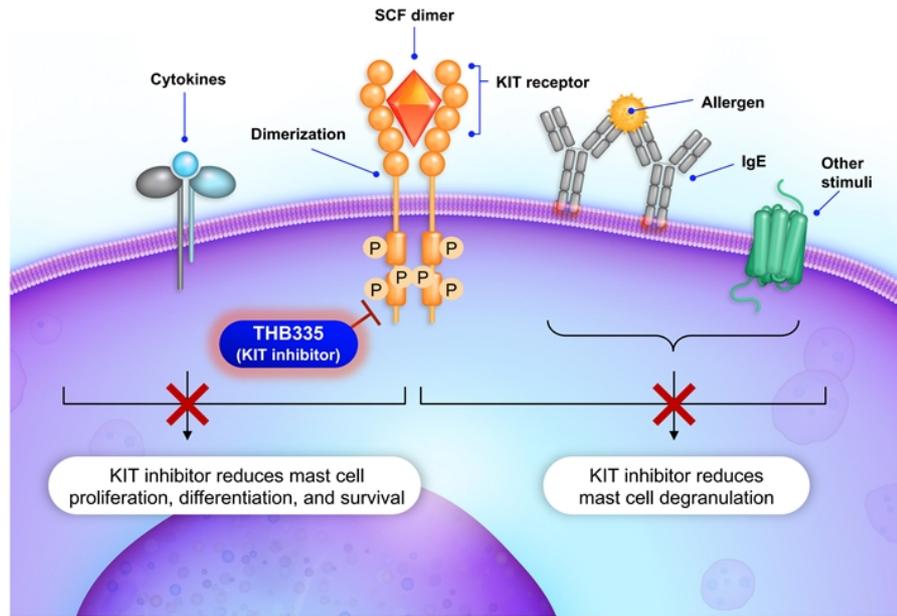
Oral small molecule approach to KIT offers multiple potential therapeutic advantages

KIT

- Targeting mast cell vs specific activating pathways or downstream mediators provides broad approach to addressing disease symptoms
- Emerging clinical validation for potential best-in-disease efficacy in CSU

INTRACELLULAR SMALL MOLECULE INHIBITION

- Potential for therapeutic index optimization
- Patient and medical practice convenience
- Avoids risk of mAb-mediated mast cell activation/anaphylaxis



Early Clinical Proof-Of-Concept Demonstrated With THB001

Discontinued cold inducible urticaria study results

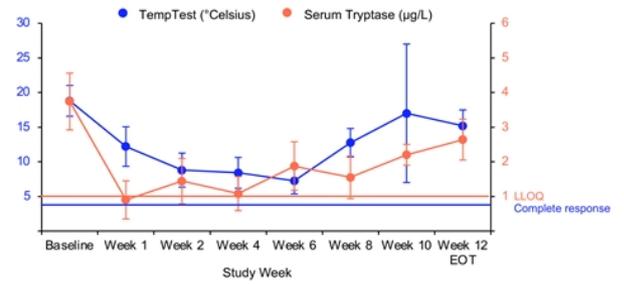
CLINICAL RESPONSES GENERATED AT LOWEST PLANNED DOSE

- Rapid tryptase reduction: -83% mean change from baseline by week 1
- Strong correlation between serum tryptase reduction and clinical response
- 4/5 patients achieved clinical response (2 CRs, 2 PRs) despite early termination of study

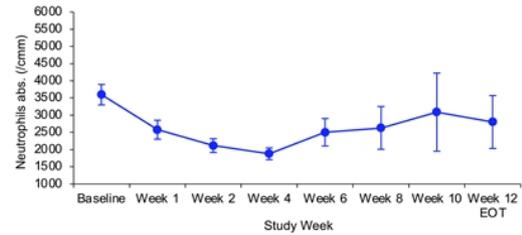
SAFETY SUMMARY

- No serious or severe adverse events (AEs)
- Two moderate AEs of transaminitis which resolved at weeks 17 and 25 of follow-up
- All other AEs were mild, reversible, and consistent with KIT biology

THB001 MEAN TEMPTTEST AND SERUM TRYPTASE¹



THB001 MEAN ANC BY VISIT¹

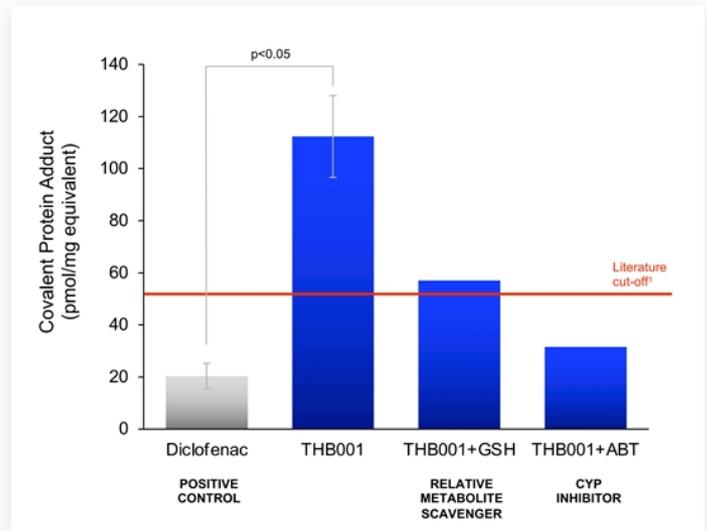
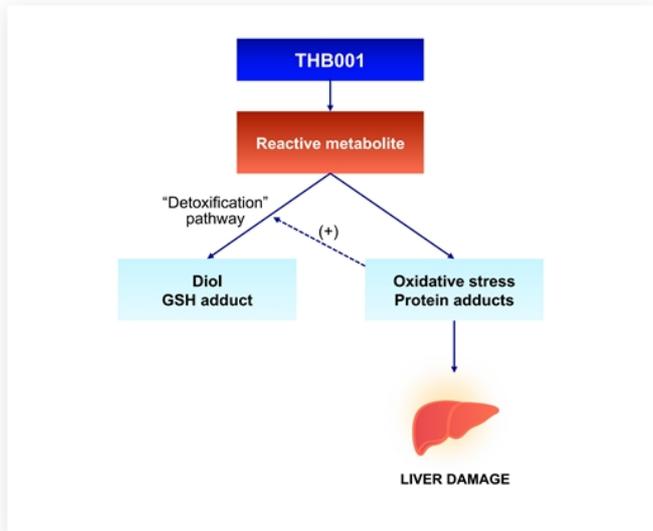


¹ Data are mean +/- SE
ANC = absolute neutrophil count; CR = complete response; EOT = end of treatment; LLOQ = lower limit of quantitation; PR = partial response
Note: Individual subject data available in appendix

THB001 Showed Evidence of Reactive Metabolite Formation

Mechanistic studies provide potential basis for observed transaminitis

[¹⁴C] THB001 COVALENT PROTEIN ADDUCT FORMATION IN HUMAN LIVER MICROSOMES IS REDUCED IN THE PRESENCE OF GSH OR CYP INHIBITION



THB335: A Next-Generation, Potent, and Highly Selective Wild-Type KIT Inhibitor

U.S. IND cleared with Phase 1 trial underway



THB335 Product Profile

- Low nanomolar KIT potency with excellent kinome selectivity in biochemical and cell-based assays
- Peripherally restricted biodistribution
- Structural and metabolic improvements vs THB001 to address DILI risk
- Favorable nonclinical pharmacokinetic profile, including high oral bioavailability, metabolic stability, and long circulating half-life
- No off-target toxicology findings in IND-enabling studies, consistent with THB001 experience through chronic studies in rodent and non-rodent species
- New composition of matter IP; base patent term through 2043

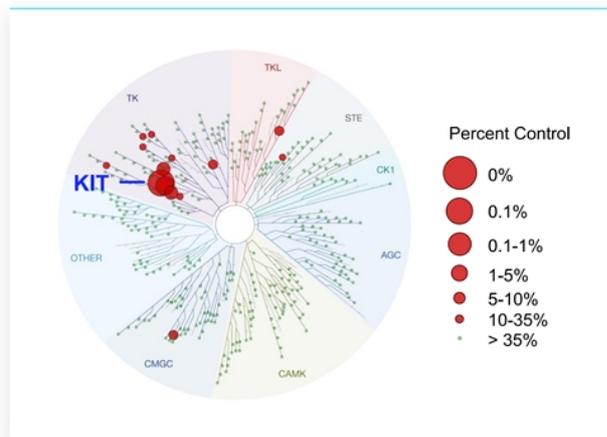


DILI = drug-induced liver injury

THB335 In Vitro Pharmacology Overview

Potent, selective, reversible KIT kinase inhibitor

DiscoverX KinomeSCAN @ 1 μ M



Kinase Target	BIOCHEMICAL		CELLULAR
	K _D (nM)	HTRF KIT IC ₅₀ (nM)	Multiple (nM)
KIT	1.5	16.1	5.0 ¹ – 7.9 ²
CSF1R	33	56	>3000 ³ – >10000 ²
PDGFR α	NT	2710	NT
PDGFR β	34	737	>3000 ⁴
ABL1	NT	NT	>10000 ²
DDR1	NT	NT	7800 ²
FLT3	>1000	NT	NT



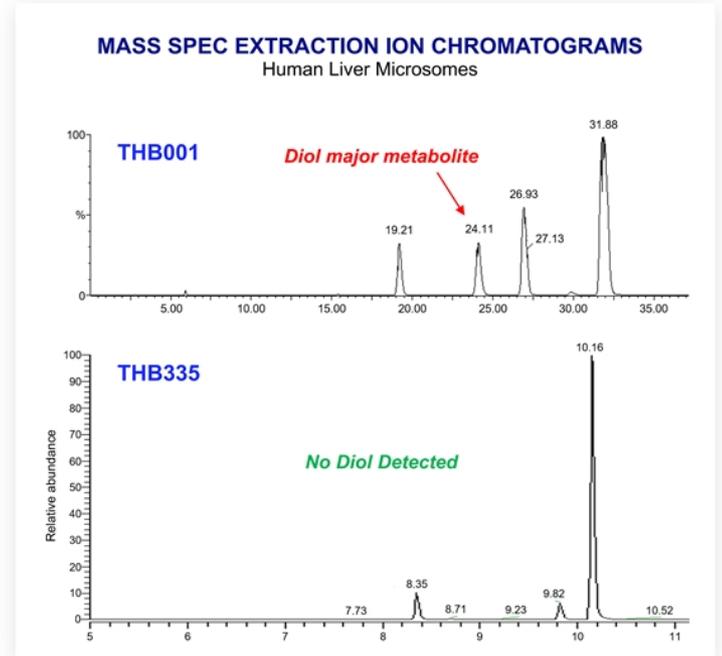
¹ M-07e pKIT IC₅₀ (KIT)
² HEK293 nanoBRET EC₅₀ (KIT, CSF1R, ABL1, DDR1)
³ M-NFS-60 EC₅₀ (CSF1R)
⁴ A10 EC₅₀ (PDGFR β)

THB335 is Metabolically Distinct from THB001

Next-generation structural modifications functionally block the site of reactive metabolite formation

- Diol formed via a reactive epoxide identified as major metabolite of THB001
 - GSH adduct formation associated with detoxification pathways
- Next-generation structural modifications functionally block the reactive metabolic pathway
 - No evidence of diol or GSH adduct formation across species and test systems

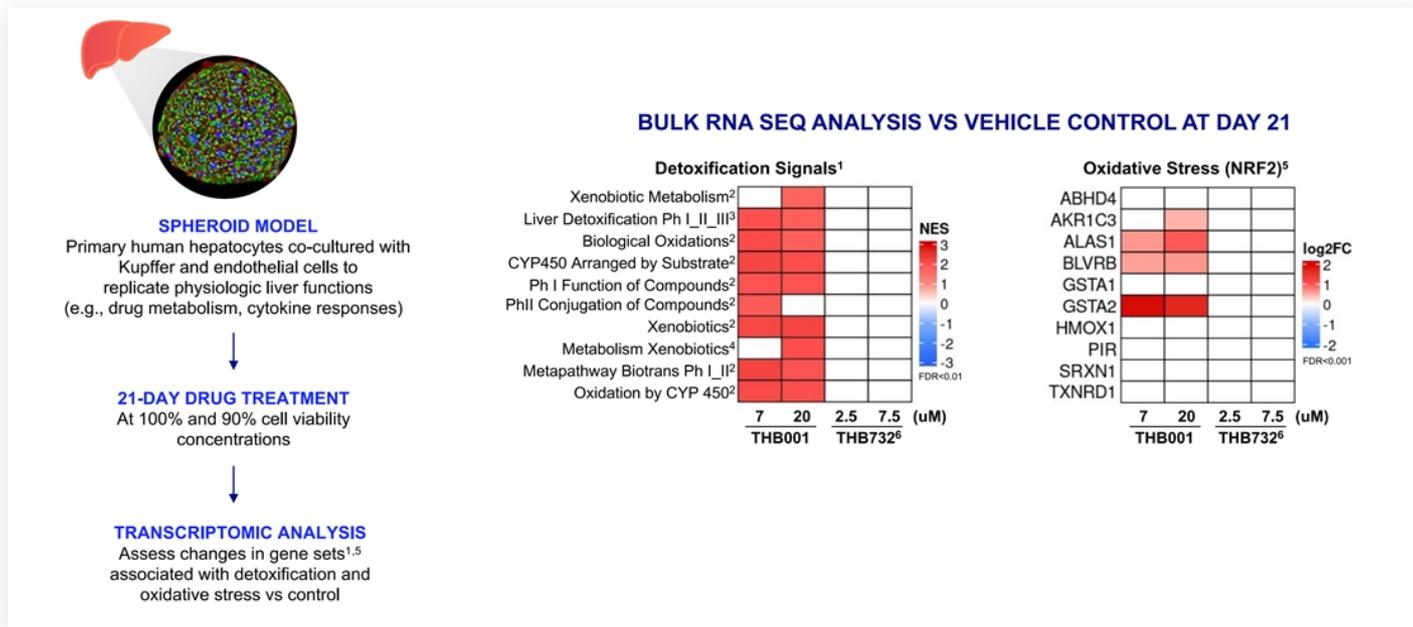
SYSTEM	SPECIES	ASSAY	THB001		THB732 ¹		THB335	
			GSH	Diol	GSH	Diol	GSH	Diol
<i>In vitro</i>	human	human liver microsomes	+	+	-	-	NT	-
	rat	plasma	+	+	-	-	-	-
<i>In vivo</i>	dog	plasma	+	+	-	-	-	-
	human	plasma	+	+				



¹ THB732 is a next-generation tool compound with high structural similarity to THB335

Next-Gen is Phenotypically Distinct from THB001 in Human Hepatocyte Culture

No evidence for induction of oxidative stress pathways with next-generation analog of THB335

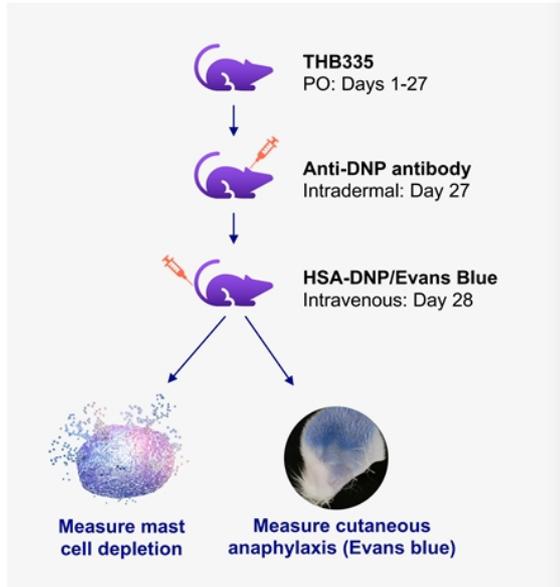


¹Gene sets derived from ²Molecular Signatures Database (MSigDB), ³Insphero and ⁴Toxicogenomics.
⁵Kang, W., et al., Toxicol Sci, 2020, 177(1): p. 121-139.
⁶THB732 is a next-generation tool compound with high structural similarity to THB335

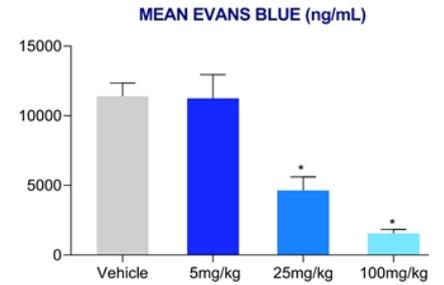
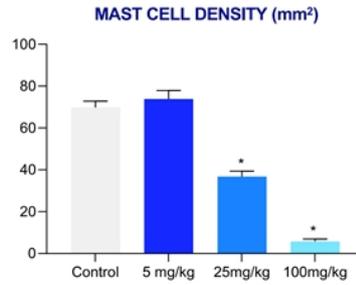
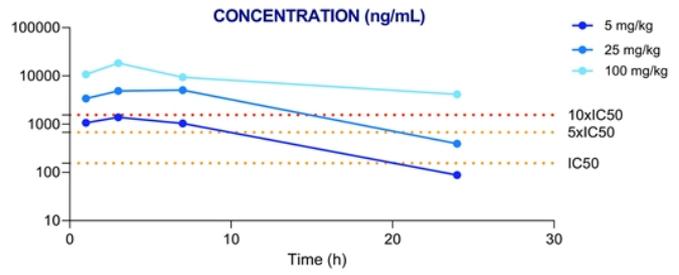
NES = normalized enrichment score
FDR = false discovery rate
FC = fold change

THB335 Drives Dose-Dependent Mast Cell Depletion and Efficacy In Vivo

Rat passive cutaneous anaphylaxis (PCA) model supports PK/PD correlation across species and test systems



RAT THB335 PCA DAY 27



Error bars indicate SEM
* P < 0.0001

Nonclinical Findings of KIT Inhibition Are Well-Characterized Across Programs

Subchronic and chronic toxicology studies of THB001 completed at up to $\geq 10x$ clinical exposures

- No evidence of pharmacologically relevant activity against other kinases
- Demonstrated reversibility of all effects

Reproductive toxicology studies completed for THB001

- No functional effect on fertility in either sex at all doses tested

Improved solubility of THB335 enables more rigorous nonclinical toxicology assessments

- IND-enabling studies included doses at $>30x$ predicted exposure margin to clinical doses

Leveraging our experience to prioritize speed to Phase 2 with THB335

- Initiating reproductive and chronic toxicology studies to support rapid advancement toward late-stage clinical development

THB335 Phase 1 SAD/MAD in Healthy Participants

U.S. IND cleared, and trial initiated with data expected in 1H'25

Study Design

- Randomized, placebo-controlled, double-blind, single and 14-day multiple ascending dose design

Key Objectives

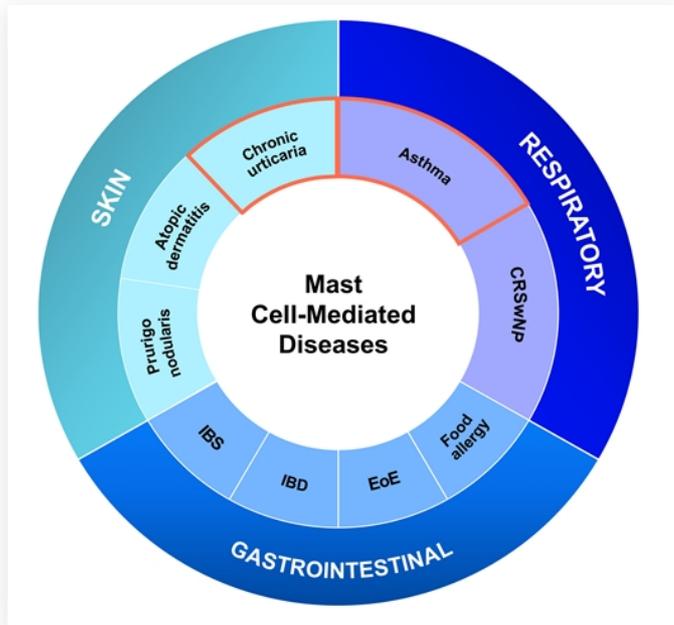
- Assess safety and tolerability
- Characterize pharmacokinetics
 - PK modeling based on nonclinical studies completed to-date supports QD dosing
- Measure pharmacodynamic effect characterized by reduction in serum tryptase
 - Highly correlated with clinical response in urticaria studies

Results expected in the first half of 2025



SAD = Single ascending dose; MAD = Multiple ascending dose

“Pipeline-in-a-Target” Potential with KIT Inhibition



- Robust Phase 2 CSU study to support planned direct advancement to Phase 3 registrational studies
- In parallel with CSU, planning to initiate Phase 2 studies in additional mast-cell mediated inflammatory disorders
 - Meaningful opportunity in severe asthma, where mast cells play a central role in pathophysiology and clear need exists for new oral therapies
- Discovery and medicinal chemistry efforts continue to support KIT inhibition franchise expansion
 - Developing differentiated target product profiles to address multiple disease/tissue targets

Third Harmonic Bio Next Steps

Advancing THB335 into the clinic with a longer-term view toward franchise expansion



- THB335 U.S. IND cleared; Phase 1 SAD/MAD trial underway with results expected in 1H'25
- Planning rapid advancement to robust Phase 2 study in CSU to support accelerated path to registration studies
- Planned expansion into additional mast-cell mediated inflammatory disorders at Phase 2, including severe asthma
- Next-generation discovery and medicinal chemistry efforts continue to support “pipeline-in-a-target” potential
- Cash and cash equivalents of \$262.8M as of March 31, 2024

APPENDIX

Previously Presented Data

First-Generation THB001 Phase 1b CINDU¹ Study Overview

Discontinued dose escalation study designed to interrogate potential for therapeutic index optimization

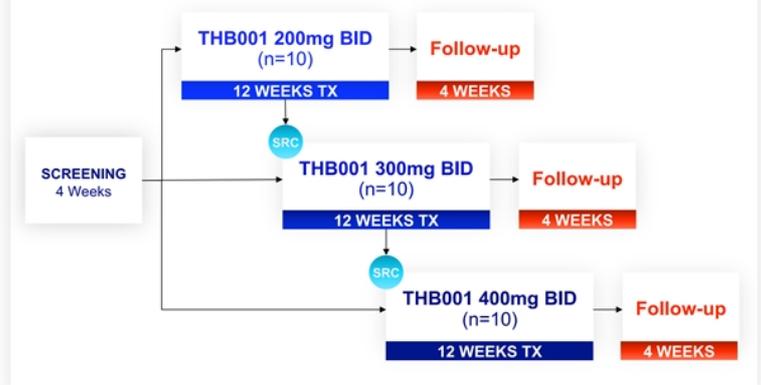
DESIGN AND OBJECTIVES

- 3 doses (1:1:1) of THB001 (total N=30) for 12 weeks
- Pharmacokinetics and serum tryptase levels
- Mean reduction in critical temperature threshold (CTT)

STUDY DISPOSITION

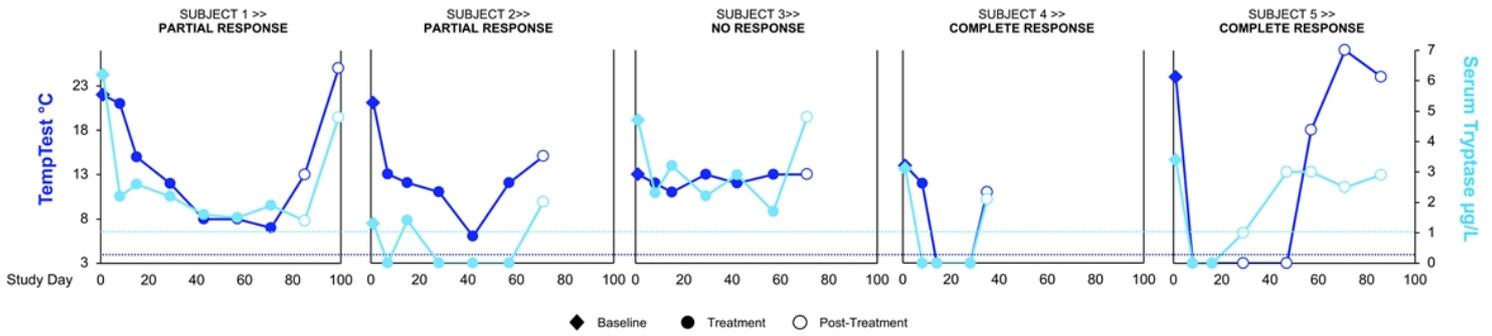
- Enrolled 5 subjects in 200mg BID dose cohort before study discontinuation
- 1 subject completed 12 weeks of treatment
- 2 subjects discontinued at week 8 due to DILI AEs
- 2 remaining subjects were discontinued from study drug at weeks 3 and 4 and were followed for safety

STUDY SCHEMATIC



First-Generation THB001 Phase 1b CINDU Study Efficacy Summary

4 of 5 subjects reached partial (n=2) or complete (n=2) responses at lowest planned dose of 200mg BID



- Rapid tryptase reduction: -83% mean change from baseline by week 1
- Strong correlation between serum tryptase reduction and clinical response consistent with other published urticaria clinical data
- 4/5 patients achieved clinical response despite early termination of study



Note: Negative TempTest results (complete response) are shown at 3° C.
Serum Tryptase values below lower limit of quantitation are shown at 0 µg/L. Empty circles indicate results post treatment.

TempTest complete response ≤ 4°C
Serum lower limit of quantitation = 1 µg/L

First-Generation THB001 Phase 1b CINDU Study Safety Summary

- No serious or severe AEs
- Two moderate AEs of transaminitis which resolved at weeks 17 and 25 of follow-up
- All other AEs were mild
 - Overall profile consistent with on-target effects of KIT inhibition observed in the Phase 1a study (e.g., hair color change)
 - Hematologic profile similar to Phase 1a and trend toward stabilization of values observed as expected

THB001 HEMATOLOGY
Hemoglobin and neutrophil count by subject over time

