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): January 13, 2025

TANGO THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-39485**	**85-1195036**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

201 Brookline Avenue
Suite 901
Boston, MA 02215
(Address of principal executive offices, including zip code)

Registrant's telephone number, including area code: 857-320-4900

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 $0.001 per share	TNGX	The Nasdaq Global Market

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 January 13, 2025, Tango Therapeutics, Inc. (the "Company") disclosed that its cash, cash equivalents and marketable securities as of December 31, 2024 totaled $257.9 million (unaudited). The information in this Item 2.02 does not present all information necessary for an understanding of the Company's financial condition as of December 31, 2024.

Item 7.01. Regulation FD Disclosure.

On January 13, 2025, the Company updated its corporate presentation to be used from time to time with investors, analysts and other third parties. A copy of the Company's presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information disclosed under Item 2.02 and 7.01, as well as Exhibit 99.1 to the Current Report on Form 8-K, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that Section. Nor shall such document be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, regardless of any general incorporation language in the filing, unless specifically stated so therein.

Note Regarding Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements that are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including the Company's anticipated financial results and cash runway. The use of words such as "anticipate," "believe," "continue," "could," "endeavor," "estimate," "expect," "anticipate," "intend," "may," "might," "plan," "potential," "predict," "project," "seek," "should," "target," "will" or "would" or the negative of such words or other similar expressions can be used to identify forward-looking statements. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement, including (i) the initiation, timing, progress, and cost of our research and development programs and our current and future preclinical studies and clinical trials (including combination clinical trials), enrollment and dosing in our clinical trials (including combination clinical trials), and the timing of initial and interim (and final) safety and efficacy or clinical activity data from our clinical trials may not take place in the timeframe that the Company expects; and (ii) we may be required to utilize our cash resources more quickly than we expect. These and other risks and uncertainties are described in additional detail in the section entitled "Risk Factors" in the Company's Annual Report on Form 10-K filed March 18, 2024 and its other filings made with the SEC from time to time. Although the Company's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by the Company. As a result, you are cautioned not to rely on these forward-looking statements. Any forward-looking statement made in this Current Report on Form 8-K speaks only as of the date on which it is made. Except as required by applicable law, the Company undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future developments, or otherwise.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit	Description
99.1	Presentation, dated January 13, 2025
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

Signature

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.

Dated: January 13, 2025

TANGO THERAPEUTICS, INC.

By: /s/ Douglas Barry
Name: Douglas Barry
Title: General Counsel

TANGO therapeutics™

The next wave of targeted therapies in oncology

Corporate Overview

January 2025

Disclaimer and Safe Harbor Statement

Certain statements in this presentation may be considered forward-looking statements. Forward-looking statements generally relate to future events, Tango's future financial and operating performance, goals, expectations, beliefs, development plans, as well as development and clinical trial objectives for Tango's product pipeline (as individual therapies and combination therapies with other party's drugs). In some cases, you can identify forward-looking statements by terminology such as "may", "should", "expect", "intend", "will", "path", "achievable", "milestones", "goal", "forecast", "estimate", "potential", "anticipate", "believe", "predict", or "continue", or the negatives of these terms or variations of them or similar terminology. For example, express or implied statements concerning the following include or constitute forward-looking statements: the potential for the Company to have best-in-class oral PRMT5 inhibitors; the Company's belief that it has a significant opportunity to treat multiple common cancers; the Company's expected cash runway into the third quarter of 2026; the Company's belief that TNG260 may become a first-in-class oral CoREST inhibitor; the potential for TNG462 to have best-in-class tolerability; the Company's planned and ongoing clinical trials, including the anticipated timing for enrollment and the timing to report results and updates of such trials; the Company's belief that TNG462 has the potential to be a best-in-class molecule for multiple MTAP-deleted solid tumors; the potential for TNG462 activity in cholangiocarcinoma to indicate activity in lung and pancreatic cancer; the Company's expectations regarding its PRMT5 inhibitors as compared to competitor molecules; the anticipated milestones for the Company's drug programs, including the timing for patient dosing, dose escalation, dose expansion, and clinical updates; the timing of initial and interim (and final) safety and efficacy or clinical activity data and results from clinical trial(s); the timing of first-in-human and clinical trials; the timing of IND-enabling or registrational studies; the timing of clinical trial initiation, dose escalation, and dose expansion (including for combination studies); the timing of disclosure for initial, interim, additional and final clinical trial results or safety and efficacy data; the expected benefits of the Company's development candidates and other product candidates (including for combination studies); the potential for a large patient population to be treated with Tango's PRMT5 inhibitors; potential combination strategies and uses for PRMT5 inhibitors, including TNG462 and TNG456; the development plans for the PRMT5 franchise (including future clinical trials); future clinical trial designs; TNG260 future clinical trials strategy and implementation; the significant patient opportunities for the Company's pipeline therapies; the Company's key future milestones; the anticipated benefits of synthetic lethal drugs; expectations regarding the benefits and success of collaborations and combination clinical trials; and the anticipated benefits of its current and future product candidates including those identified in the future through the Tango discovery platform; the potential of TNG462 to have broader and deeper clinical activity in MTAP-deleted solid tumors; expectations around TNG 456's clinical efficacy, including its potential to treat glioblastoma and central nervous system metastases; the development and regulatory pathway for TNG462, TNG456, or TNG260. Such forward-looking statements are subject to risks, uncertainties, and other factors which could cause actual results to differ materially from those expressed or implied by such forward looking statements. These forward-looking statements are based upon estimates and assumptions that, while considered reasonable by Tango and its management at the time of this presentation, are inherently uncertain. Drug development, clinical trials and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Factors that may cause actual results to differ materially from current expectations include, but are not limited to: Tango has a limited operating history and has not generated any revenue to date from drug sales, and may never become profitable; future clinical trial data releases may differ materially from initial or interim data from our current and future clinical trials; Tango has limited experience with conducting clinical trials (and will rely on third parties to operate its clinical trials) and may not be able to commence any clinical trial, enroll and dose patients when expected and may not generate results in the anticipated timeframe (or at all); dosing (including dose expansion) in clinical trials may need be delayed or may be stopped for various reasons, including due to any potential issues at the site, safety issues or supply disruptions; any significant changes required to be made to an applicable IND application or protocol could significantly delay on-going clinical trials); the benefits of Tango pipeline products (stand-alone and as potential combination therapies) that are seen in preclinical experiments may not be present in clinical trials or in use commercially or may not be safe and/or effective in humans (and Tango or a third-party may not be able to obtain approval or commercial sales of any stand-alone or combination therapies); Tango has incurred significant operating losses and anticipates continued losses for the foreseeable future; Tango will need to raise capital in the future and if it is unable to raise capital when needed or on attractive terms, the Company would be forced to delay, reduce, or eliminate or discontinue some development programs or future commercialization efforts; Tango may be unable to advance the preclinical development programs into and through the clinic for safety or efficacy reasons or experience significant delays in doing so as a result of factors beyond Tango's control; the expected benefits of our product candidates in patients as single agents and/or in combination may not be realized; the Company may experience delays or difficulties in the initiation, enrollment, or dosing of patients in clinical trials or the announcement of clinical trial results; Tango's approach to the discovery and development of product candidates is novel and unproven, which makes it difficult to predict the time, cost of development, and likelihood of successfully developing any products; Tango may not identify or discover development candidates (including next generation products) or may expend a portion of its limited resources to pursue a particular product candidate or indications and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success; delays or difficulties in the initiation, enrollment or dosing of patients in clinical trials could delay or prevent receipt of regulatory approvals or reporting trial results; our product candidates may cause adverse or other undesirable side effects that could, among other things, delay or prevent regulatory approval; our dependence on third parties for conducting clinical trials and producing drug product (including the potential impact of the BIOSECURE Act on our supplier of drug substance); our ability to obtain and maintain patent and other intellectual property protection for our technology and product candidates or the scope of intellectual property protection obtained is not sufficiently broad; and delays and other impacts on product development and clinical trials from public health events. Additional information concerning risks, uncertainties and assumptions can be found in Tango's filings with the SEC, including the risk factors referenced in Tango's Annual Report on Form 10-K for the year ended December 31, 2023, as may be supplemented and/or modified by its most recent Quarterly Report on Form 10-Q. You should not place undue reliance on forward-looking statements in this presentation, which speak only as of the date they are made and are qualified in their entirety by reference to the cautionary statements herein. Tango specifically disclaims any duty to update these forward-looking statements.

Certain information contained in this Presentation relates to or is based on studies, publications, surveys and Tango's own internal estimates and research. In addition, market data included in this presentation involve assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while Tango believes its internal research is reliable, such research has not been verified by any independent source.

COMPANY OVERVIEW

Significant opportunity to treat multiple common cancers

Potential best-in-class oral PRMT5 inhibitors

TNG462

- Key indications are lung and pancreatic cancer
  - 15% of lung cancer is MTAP-del (22K pts/yr US)
  - ~35% of pancreatic cancer is MTAP-del* (15K pts/yr US)
- Durable responses in multiple cancer types demonstrated in phase I
- Potential best-in-class tolerability
- Actively enrolling 250 mg QD dose expansion cohort
- Phase 1/2 clinical update in 2025

TNG456

- Key indication is glioblastoma
  - 45% of GBM is MTAP-del (7K pts/yr)
- CNS penetrant in preclinical studies
- Highly potent and selective
- First patient dose planned 1H2025

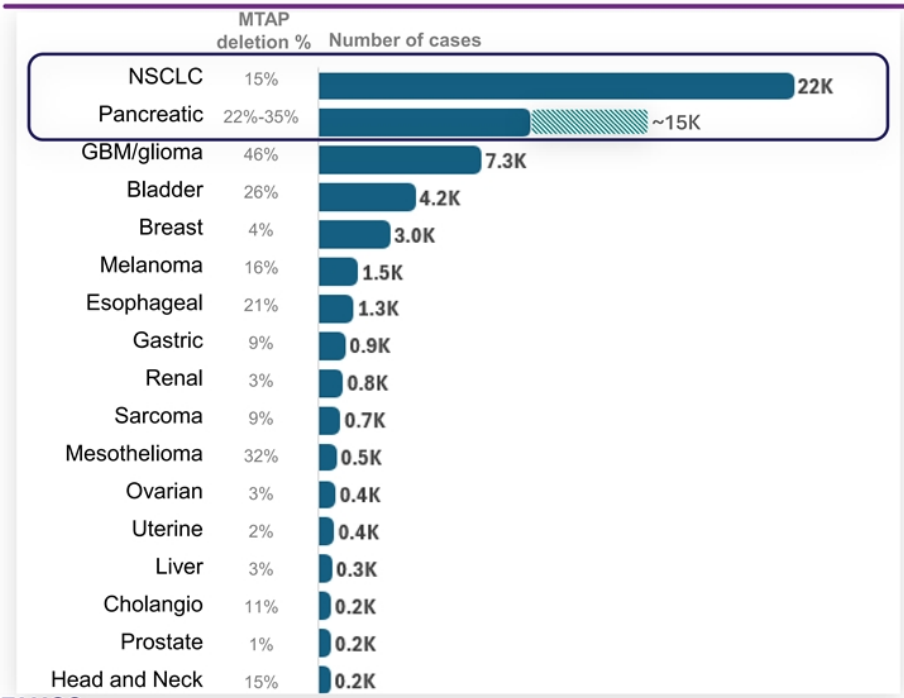
First-in-class oral CoREST inhibitor

TNG260

- Key indication is STK11-mut lung cancer
  - 20% of lung cancer is STK11 mut (25K pts/yr US)
- Proof-of-mechanism demonstrated in lung cancer patients
- Dose expansion cohort ongoing
- Phase 1/2 clinical update in 2025

O'Kane GM et al. Cancer Res, 2024

~50K total treatable MTAP-deleted patients/year (US)



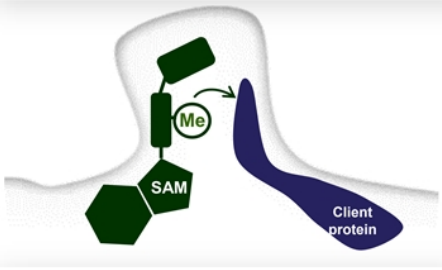
Large unmet need

- MTAP deletion confers sensitivity to PRMT5 inhibitors
- Up to ~37K MTAP-del lung and pancreatic cancer patients/yr (US)
- Recent data from DFCI and others demonstrate MTAP-deletion incidence in pancreatic cancer to ~35% increasing the treatable patients to 15K/year (US)*

O'Kane, G.M et al. Cancer Res., 2024

TNG462 and TNG456 selectively inhibit PRMT5 in MTAP-deleted cancers

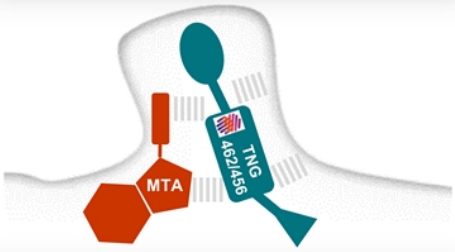
Normal cells



Active PRMT5

- Active SAM-PRMT5 complexes predominate in normal cells
- Non-MTA cooperative PRMT5 inhibitors are equally cytotoxic in normal and MTAP-del cells

MTAP-del cancer cells



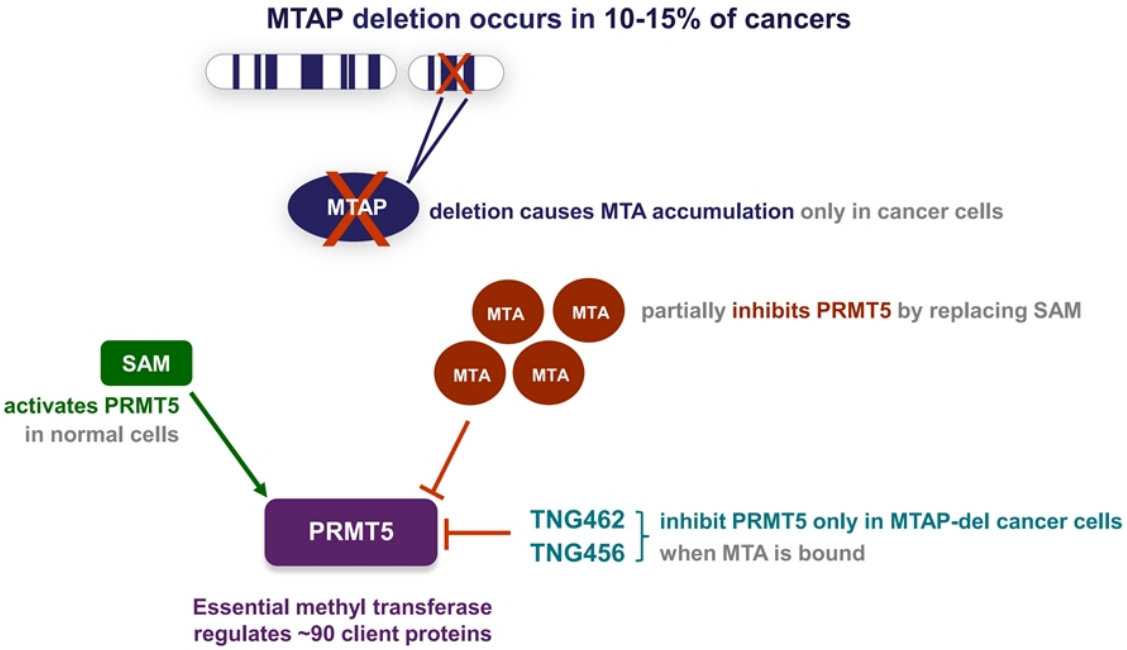
Inactive PRMT5

- Inactive MTA-PRMT5 complexes predominate in MTAP-del cancer cells
- MTA-cooperative PRMT5 inhibitors preferentially kill MTAP-del cells

Key points

- TNG462 and TNG456 selectively kill MTAP-del cancer cells while sparing normal cells
- TNG462 and TNG456 lock PRMT5-MTA into the inactive state (MTA cooperative)

MTAP-del cancers are uniquely sensitive to PRMT5 inhibition

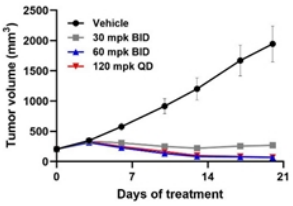


Tango PRMT5 inhibitors have superior preclinical efficacy

LU99 non-small cell lung cancer
MTAP del, KRAS mut

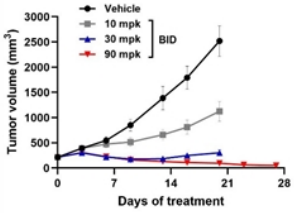
Tango PRMT5 inhibitors

TNG462



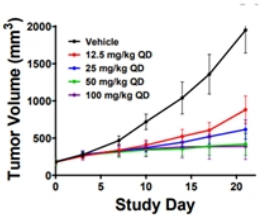
Deep tumor regression

TNG456



Deep tumor regression

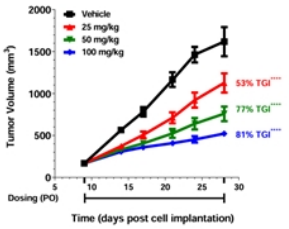
MRTX1719



Engstrom et al., 2023

Tumor stasis

AMG 193



Belmontes et al., 2024

Tumor growth inhibition

A clinical pipeline targeting multiple high-value indications

TARGET	MOLECULE	PATIENT SELECTION	INDICATIONS	CLINICAL TRIALS	STATUS
				Pre-clinical / Phase 1/2 / Phase 3	
PRMT5	TNG462	MTAP-del cancers	Pancreatic, lung, other non-CNS cancer		Dose expansion ongoing
		+ RASi	Pancreatic and lung cancer		Enrollment 1H2025
		+pembrolizumab	Lung cancer		Enrollment 1H2025
		+SOC chemotherapy	Pancreatic and lung cancer		Enrollment 2H2025
	TNG456	MTAP-del cancers	Glioblastoma		Enrollment 1H2025
CoREST	TNG260	STK11-mut cancers	Lung cancer		Dose expansion ongoing

All programs wholly owned by Tango

TNG462

PRMT5 inhibition in MTAP-deleted cancers

TNG462 is a potentially best-in-class PRMT5 inhibitor

Durable clinical responses in late-line lung and pancreatic cancer

- RECIST PRs and durable disease control in multiple cancers
- 24 weeks mPFS in dose escalation cohort of late-line, difficult-to-treat cancers (active doses)
- Excellent safety and tolerability profile
- Phase 1/2 study ongoing, focused enrollment in 250 mg expansion cohort
- Key indication for development - MTAP-deleted lung and pancreatic cancer (~35K patients/yr US)

	Potency	MTAP selectivity	mPFS (dose escalation)	CNS exposure
TNG462	**4 nM**	**45X**	**24 weeks**	**No**
TNG908	110 nM	15X	16 weeks	Yes

Data cutoff 20 October 2024

TNG462 dose expansion enrolling in multiple histologies

DOSE ESCALATION

- Solid tumors with MTAP deletion

- First patient dosed July 2023
- 59 patients enrolled (13 histologies)
- 39 evaluable patients at active doses
- MTD 300 mg

DOSE EXPANSION (ongoing)

Non-small cell lung

Pancreatic

Histology-agnostic solid tumors
Enriched for cholangiocarcinoma, mesothelioma, and bladder cancers

First patient dosed July 2024

PHASE 1/2 STUDY

- Durable activity in multiple cancer types with excellent tolerability profile
- Dose expansion ongoing at 250 mg QD
- First monotherapy registration trials planned in 2L pancreatic and lung cancer

TNG462 phase 1 study demonstrates durable clinical activity and better tolerability than other PRMT5 programs

Demonstrated best-in-class potential

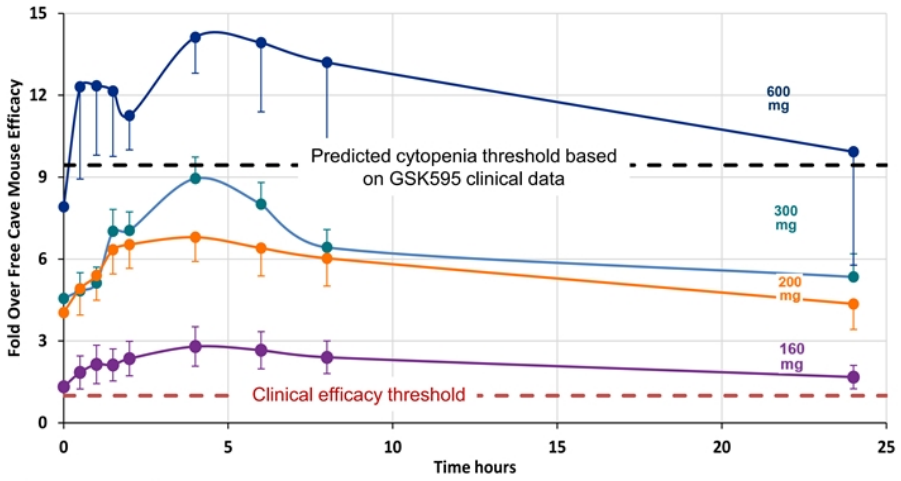
- RECIST partial responses in multiple tumor types, including NSCLC and pancreatic cancer*
- Median time to RECIST response 16 weeks
- 24 weeks mPFS in escalation cohort (AMG193 16 weeks, BMS not disclosed)
- Data continue to mature, with longest follow up in cholangiocarcinoma subset
  - 43% TNG462 ORR in cholangiocarcinoma (n=7) compares favorably to competitor molecules
    - 18% BMS-504 (n=11)
    - 15% AMG193 (n=13)
- Excellent tolerability profile with less fatigue and GI toxicity than competitors
- Ongoing enrollment focused on lung and pancreatic cancer
- TNG462 combinations with RAS inhibitors and multiple standard of care regimens this year

*59 patients enrolled, 13 histologies
39 evaluable patients at active doses (160-300 mg QD)

Data cutoff 20 October 2024

TNG462 on-target cytopenias occur at predicted exposures

Efficacious TNG462 exposure at clinically active doses



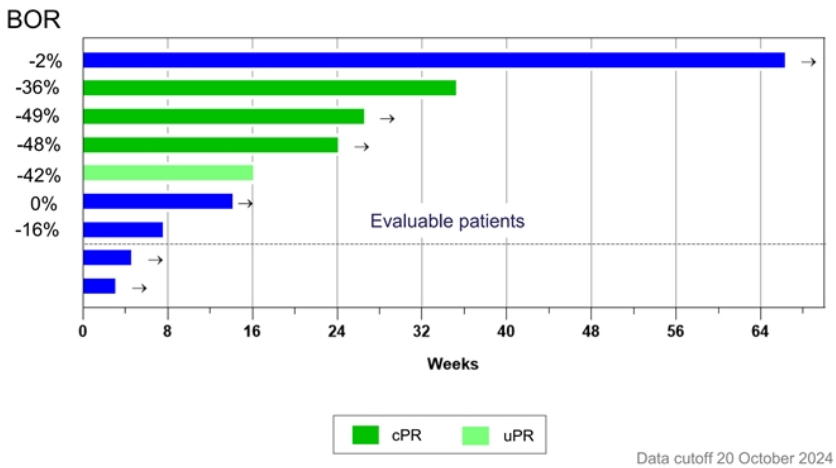
Dose limiting cytopenias observed

Clinically active and well-tolerated

Error bars represent SEM

TNG462 activity in cholangiocarcinoma as a potential indicator of activity in lung and pancreatic cancer

TNG462 ORR 43%



Data cutoff 20 October 2024

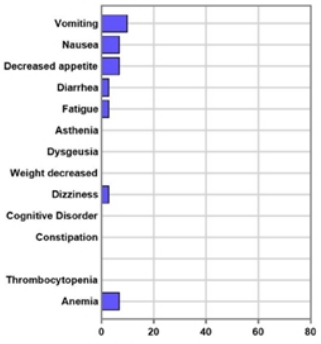
Key points

- 3/7 evaluable patients treated at active doses with RECIST PRs
  - TNG462 43%
  - BMS-504 18% (2/11)
  - AMG 193 15% (2/13)
- Compares favorably to previously treated cholangiocarcinoma patients receiving 2L chemotherapy*
  - ORR ~7% (standard of care)
  - PFS 14 weeks

*Amonkar et al, Future Oncology, 2024

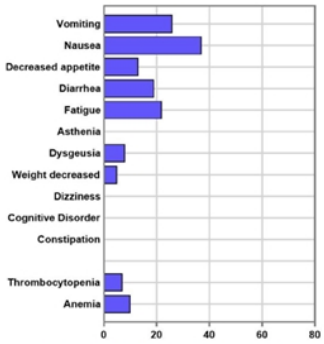
TNG462 safety and tolerability profile is superior to competitors

TNG462
200 mg*



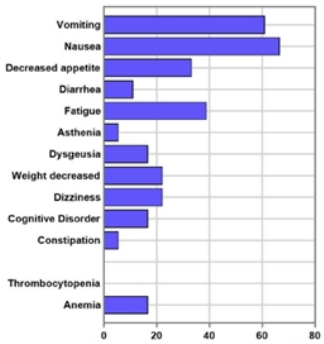
0/30 dose reductions (0%)
No thrombocytopenia
Minimal nausea and fatigue
No dysgeusia

BMS-504
200-600 mg



Dose reductions unknown
Frequent GI side effects
10% dysgeusia
ENA 2024

AMG 193
1200 mg



6/18 dose reductions (33%)
Significant nausea, vomiting, decreased appetite, fatigue, dysgeusia and CNS effects
ESMO 2024

Currently evaluating 250 mg QD in lung and pancreatic cancer

*Includes dose escalation patients at 160 mg QD
Data cutoff 20 October 2024

TNG462 combinations enable use in first line indications

Multiple combinations to start 2025

First line standard of care combinations

- Pembrolizumab in lung cancer
- FOLFIRINOX in pancreatic cancer
- Gemcitabine/abraxane in pancreatic cancer
- Carboplatin/pemetrexed in lung cancer (adeno)
- Carboplatin/paclitaxel in lung cancer (squamous)

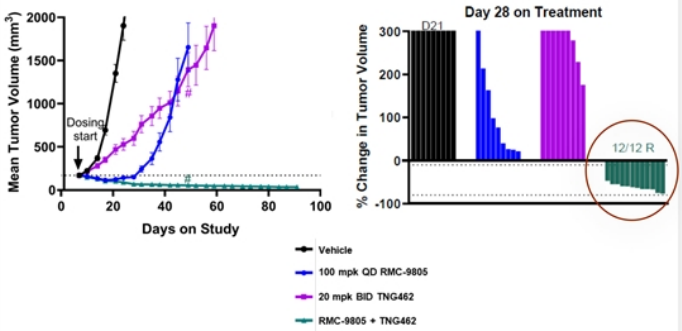
Targeting RAS-mut/MTAP-del cancers in collaboration with Revolution Medicines

- TNG462 + RMC-6236 in RAS-mut and MTAP-del lung and pancreatic cancer
- TNG462 + RMC-9805 in RAS G12D-mut and MTAP-del lung and pancreatic cancer

TNG462 + KRAS inhibition is very active in preclinical models

TNG462 + RMC-9805

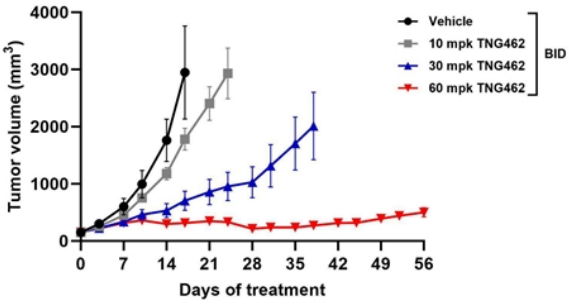
KP4
MTAP-null, $KRAS^{G12D}$ PDAC CDX



*TNG462 exposure in combination formulation predicted equivalent to 30 mpk monotherapy

TNG462 monotherapy

KP4
MTAP-null, $KRAS^{G12D}$ PDAC CDX



- 40% of pancreatic cancers have a KRAS G12D driver mutation
- Clinical collaboration with Revolution Medicines to evaluate TNG462 + RMC-9805 (RAS G12D-selective) and TNG462 + RMC-6236 (RAS multi-selective)

TNG908

Clinically active CNS-penetrant PRMT5 inhibitor replaced by next-gen molecule TNG456

TNG908 is a clinically active PRMT5 inhibitor

Discontinued in favor of TNG462 and TNG456 (CNS)

- Effective in multiple cancers including lung and pancreatic cancers
- 16 weeks mPFS in dose escalation cohort of late-line, difficult-to-treat cancers
- No evidence of activity in glioblastoma, CNS exposure below efficacy threshold
- Phase 1/2 study stopped enrollment November 2024

	Potency	MTAP selectivity	mPFS (dose escalation)
TNG908	**110 nM**	**15X**	**16 weeks**
TNG462	4 nM	45X	24 weeks
TNG456	20 nm	55X	NA

TNG908 is active and well-tolerated in non-CNS solid tumors

All patients

- TNG908 dose escalation began August 2022, dose expansion began April 2024
- 110 patients enrolled

All non-CNS solid tumors

- 77 patients enrolled, 39 evaluable at active doses (24 histologies)
- 8 partial responses observed (4 confirmed, 3 yet to confirm, 1 failed to confirm)
- Median time on study in escalation at active doses* 16 weeks (24 weeks for TNG462)

Pancreatic cancer

- 4/11 patients with partial responses (ORR 36%), 3/11 patients with stable disease
- Longest time on study 84 weeks+

Glioblastoma

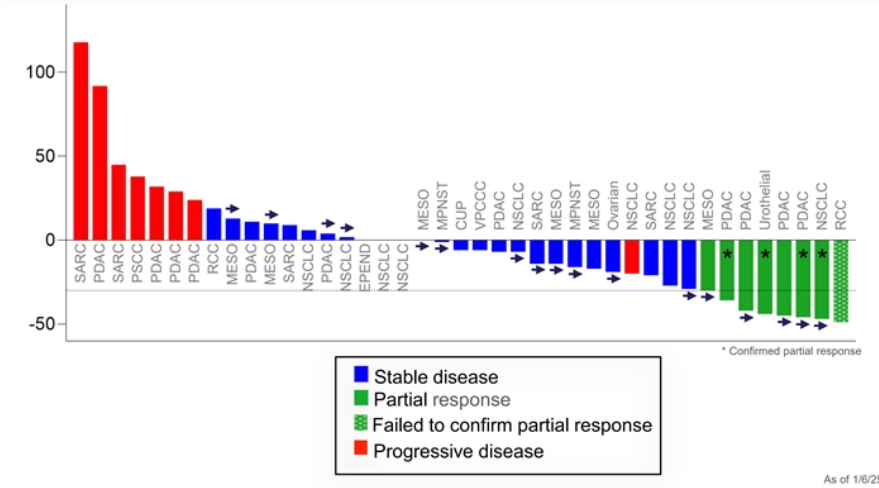
- 33 patients enrolled, 23 evaluable at active doses
- Median time on study less than 8 weeks
- CSF exposure ~30% of plasma exposure is below efficacy threshold

* active dose range 400-900 mg BID

TNG908 is active across histologies

TNG908 400-900 mg QD

(n=41)



As of 1/6/25

Histology-specific activity

Pancreatic cancer (36% ORR)

- n=14, 11 evaluable
- 4 PR (3 ongoing)
- 3 SD (1 ongoing)

NSCLC (11% ORR)

- n=12, 9 evaluable
- 1 PR (ongoing)
- 7 SD (3 ongoing, 2 near PR)

CCC – clear cell carcinoma; CUP – carcinoma of unknown primary; EPEND – ependymoma; MESO – mesothelioma; MPNST – malignant peripheral nerve sheath tumor; NSCLC – non-small cell lung cancer, RCC – renal cell carcinoma; SARC – sarcoma; PSCC – pancreatic spindle cell carcinoma; VPCCC – velopalatine clear cell carcinoma

TNG908 is clinically active, TNG462 has the potential to be best-in-class

TNG462

- TNG462 target coverage is 2-4X better than TNG908
- TNG462 median time on treatment of 24 weeks is notably longer than TNG908 (16 weeks)
- TNG462 tolerability profile is superior to TNG908 with less nausea, vomiting and fatigue
- Clinical activity of TNG908 in lung and pancreatic cancer highlights the potential for TNG462 to be best-in-class

Preliminary clinical data suggest TNG462 will be more active in MTAP-deleted solid tumors than TNG908 and AMG193

TNG456

PRMT5 inhibition in MTAP-deleted cancers

TNG456 is a next-generation CNS-penetrant PRMT5 inhibitor

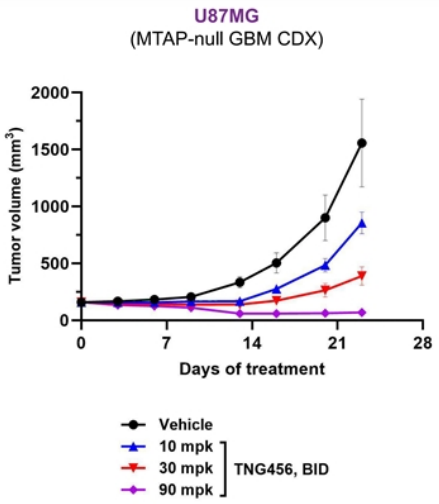
Replaced TNG908 for CNS cancers

- Enhanced potency and MTAP selectivity
- Predicted CNS exposure well above efficacy threshold
- Key indication for development - MTAP-deleted glioblastoma (7,000 patients/yr US)
- First patient dose planned 1H2025

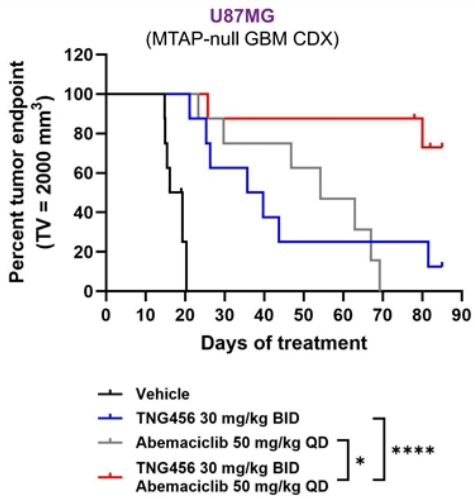
	Potency	MTAP selectivity
TNG456	**20 nM**	**55X**
TNG908	110 nM	15X

TNG456 is active as monotherapy and in combination with CDK4/6i in a glioblastoma xenograft

TNG456 monotherapy



TNG456 + abemaciclib drives additional survival benefit

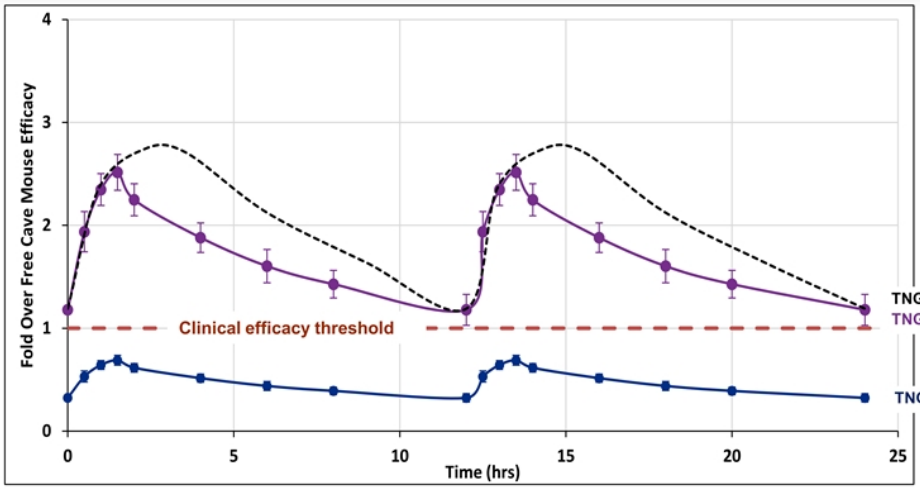


Summary

- TNG456 preclinical Kpuu 0.5-1.1 in NHP CSF and dog brain
- TNG456 + abemaciclib median survival ≥67 days
- Reported survival benefit in orthotopic models
  - Avastin 37 days
  - Temozolomide 23 days

TNG456 CSF exposure predicted to be above clinical efficacy threshold

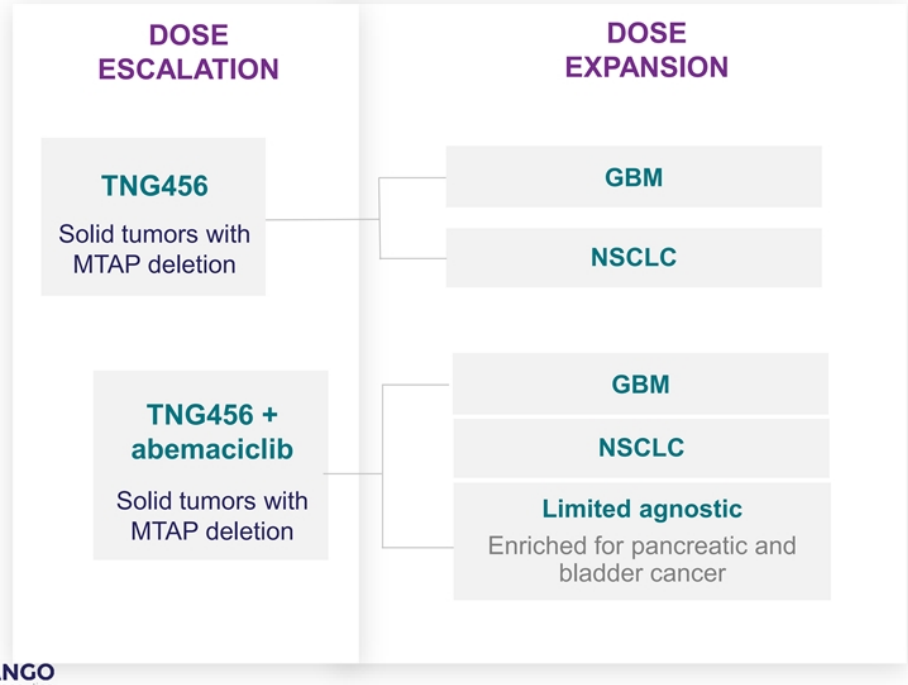
Steady-state clinical exposure in plasma and CSF



- TNG456 is 5X more potent and 3X more selective than TNG908
- TNG908 CSF exposure 0.3X plasma
- TNG456 CSF exposure predicted to be 2X efficacy threshold at 0.3X plasma exposure

Error bars represent SEM

TNG456 phase 1/2 clinical study



SUMMARY

- Safety, PK/PD and efficacy as primary endpoints
- Combination with abemaciclib to start at pharmacologically active TNG456 dose
- Enrollment planned 1H 2025

PRMT5 program development plans

Potential best-in-class PRMT5 inhibitors for multiple common cancers

TNG908

- Active and well-tolerated
- Development discontinued in favor of TNG462 (non-CNS cancers) and TNG456 (glioblastoma)

TNG462

- Monotherapy expansion cohorts focused on lung and pancreatic cancer ongoing
- Combination with KRAS inhibitors and multiple standard of care regimens 2025
- Registration trials in 2L lung and pancreatic cancer planned 2026
- Roche/Ventana selected for IHC CDx

TNG456

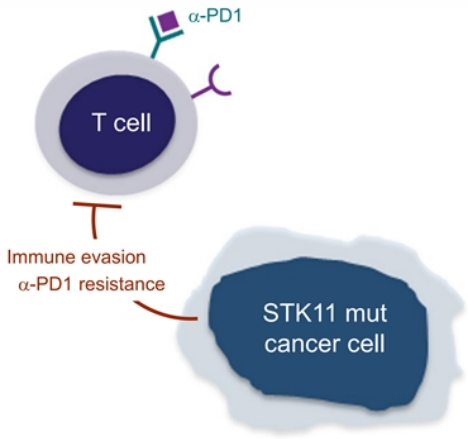
- Monotherapy dose escalation to begin 1H2025
- Combination with abemaciclib planned 2H2025 (pending monotherapy data)

TNG260

CoREST inhibition in STK11-mutant cancers

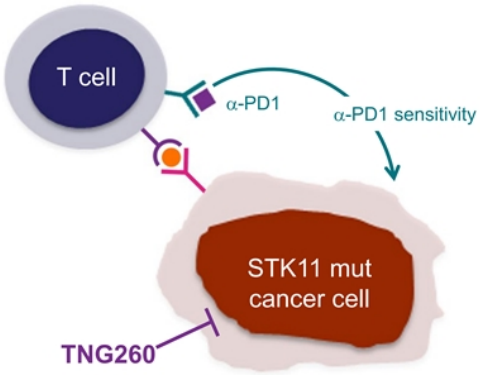
TNG260 reverses immune evasion caused by STK11 mutations

Immune evasion driven by tumor suppressor gene loss



STK11 re-activation is not feasible

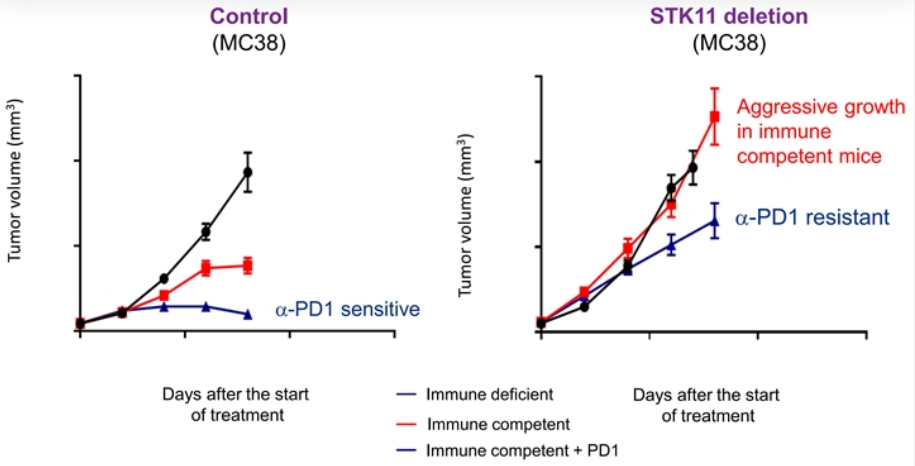
TNG260 reverses tumor-intrinsic immune evasion



Selective CoREST inhibition in cancer cells enables immune-mediated cytotoxicity

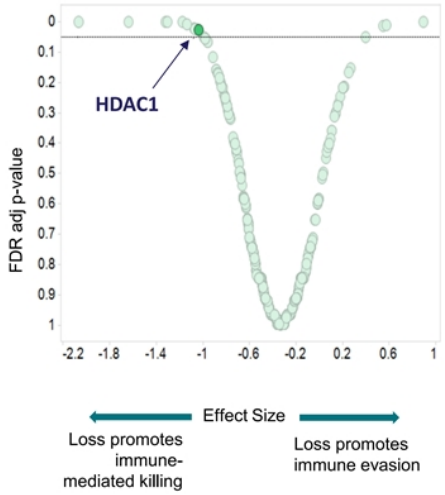
STK11 loss-of-function mutations drive immune evasion

STK11 deletion causes α-PD1 resistance

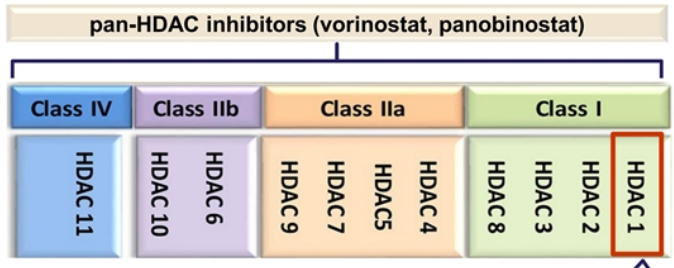


STK11 loss-of-function mutations are associated with clinical immune checkpoint inhibitor resistance

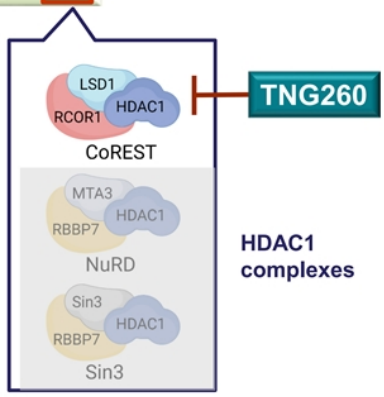
In vivo CRISPR screening identifies mediators of immune evasion reversion



TNG260 is a highly selective CoREST complex inhibitor



- **TNG260** alters expression of ~400 genes, predominantly those important for immune response
- **Pan-HDAC inhibitors** alter the expression of ~3000 genes (~12% of the genome)

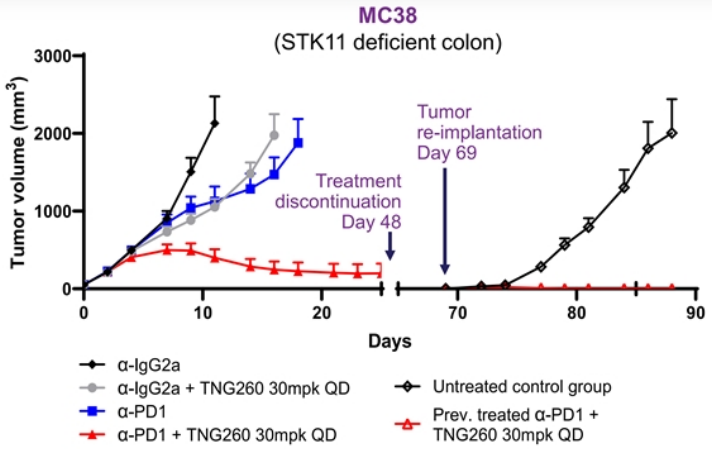


Key points

- CoREST-mediated deacetylation regulates transcription of a specific set of immune response genes
- Sin3 is the predominant HDAC1 complex involved in hematopoiesis
- Pan-HDAC inhibitors target all 11 HDAC isoforms
- HDAC3 is an essential gene and likely a primary contributor to pan-HDACi toxicity

TNG260 + α-PD1 induces complete regression and prevents re-implantation in STK11-mutant xenografts

TNG260 IC50 100nM, 10X CoREST complex selectivity

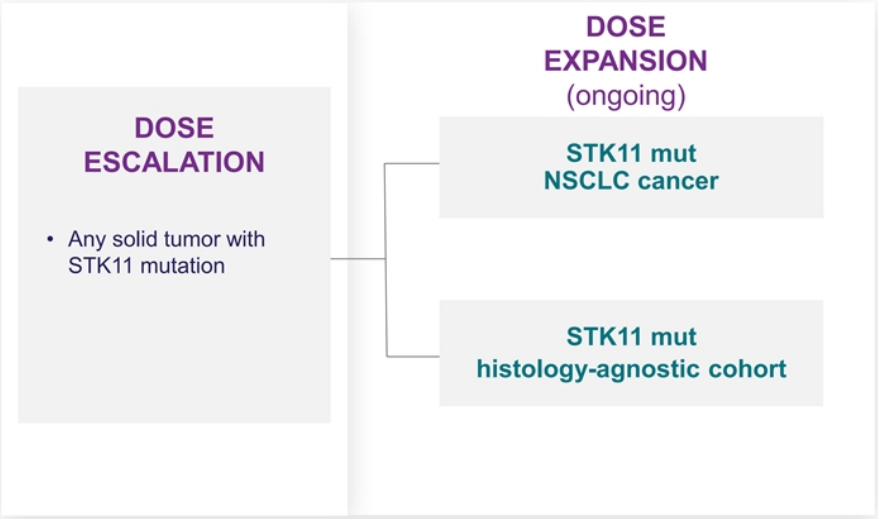


- 5/8 mice had complete tumor regression at day 34, treatment discontinued at day 48
- All mice with complete regression remained tumor free off treatment for 21 days
- 5/5 mice with complete regression rejected tumor reimplantation

TNG260

- Potent, highly selective molecule with good pharmacologic properties
- Marked in vivo efficacy in combination with α-PD1 antibody
- Induces immune memory and renders treated mice resistant to tumor re-implantation

TNG260 + pembrolizumab first-in-human trial

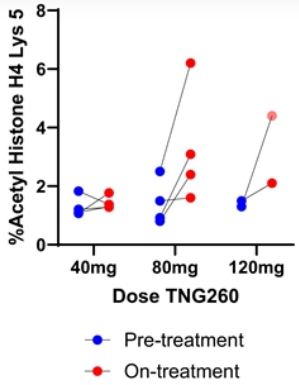


PHASE 1/2 STUDY

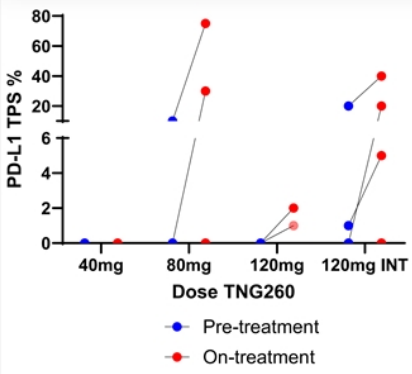
- STK11 mutations occur in ~15% NSCLC, 15% cervical, 10% carcinoma of unknown primary, 5% breast and 3% pancreatic cancers
- Combination with pembrolizumab to assess safety, PK/PD and efficacy as primary endpoints
- FDA Fast Track designation

TNG260 proof-of-mechanism in phase 1 study

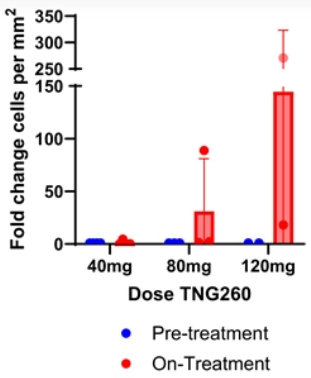
Increased histone acetylation



Increased tumor PD-L1 staining



Increased Intra-tumoral cytotoxic T cells



"Turning cold tumors hot" validates immune evasion hypothesis

TNG260 summary

PROGRAM	PATIENT SELECTION	DISCOVERY	IND-ENABLING	CLINICAL TRIALS		STATUS
				Phase 1/2	Phase 3	
CoREST TNG260	STK11-mut cancers					Dose expansion ongoing, clinical data 2025

- STK11 mutations are associated with checkpoint inhibitor resistance in lung cancer patients
- TNG260 is a novel, highly selective CoREST complex inhibitor
- TNG260 reverses checkpoint inhibitor resistance in preclinical STK11-mut models and induces immune memory that prevents tumor regrowth in responders
- Phase 1/2 clinical study ongoing evaluating efficacy in combination with pembrolizumab in STK11-mutant cancers

FINANCIAL HIGHLIGHTS AND MILESTONES

Multiple projected key milestones and strong balance sheet

Clinical milestones

- ☐ TNG462 clinical data update 2025
- ☐ TNG462 combination trials enrollment begin 1H 2025
- ☐ TNG456 phase 1/2 trial enrollment begin 1H 2025
- ☐ TNG260 clinical data 2025

Cash balance

- $258M cash, cash equivalents and marketable securities as of December 2024
- Cash runway into Q3 2026, including additional TNG462 and TNG456 clinical trials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