The next wave of targeted therapies in oncology

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January 14, 2026

TANGO therapeutics™

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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 2028; the potential for vopimetostat to have best-in-class tolerability; the Company's expectations regarding its PRMT5 inhibitors as compared to competitor molecules, including in terms of safety and tolerability; the anticipated milestones and timing for the Company's drug programs (including registrational studies), including the timing for clinical trial initiation, enrollment, patient dosing, dose escalation, dose expansion, and clinical updates; of initial, interim, and final safety and efficacy or clinical activity data and results from clinical trial(s); the Company's expectations regarding a registrational trial for vopimetostat; the Company's plans for and timing of combination trials for vopimetostat and TNG456, including with RAS(ON) inhibitors for vopimetostat and with abemaciclib for TNG456; the Company's belief that vopimetostat has the potential to transform care in front line pancreatic cancer; the Company's expectations regarding the combination study with RAS(ON) inhibitors, including future enrollment, study design, and the ability of early signs of activity and tolerability to translate to positive results; the Company's expectations regarding TNG456's predicted brain exposure may not be realized; the expected benefits of the Company's development candidates and other product candidates (including for combination studies); the Company's expectations around the size and value of the potential patient population for PRMT5 inhibitors (including for lung and pancreatic cancers); potential combination strategies and uses for PRMT5 inhibitors, including vopimetostat and TNG456; the development plans for the PRMT5 franchise (including future single agent and combination clinical trials); future clinical trial designs; TNG260 future clinical trials strategy and implementation; expectations regarding the benefits and success of collaborations and combination clinical trials; and the anticipated benefits of its current and future product candidates; expectations around TNG456's clinical efficacy, including its potential to treat glioblastoma and expectations around the brain exposure required for clinical efficacy; the development and regulatory pathway for vopimetostat, TNG456, or TNG961; the Company's belief that TN961 may be a first-in-class HBS1L degrader; and the Company's belief that there is potential for single agent and vopimetostat combination activity for TNG961. 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Finally, while Tango believes its internal research is reliable, such research has not been verified by any independent source.

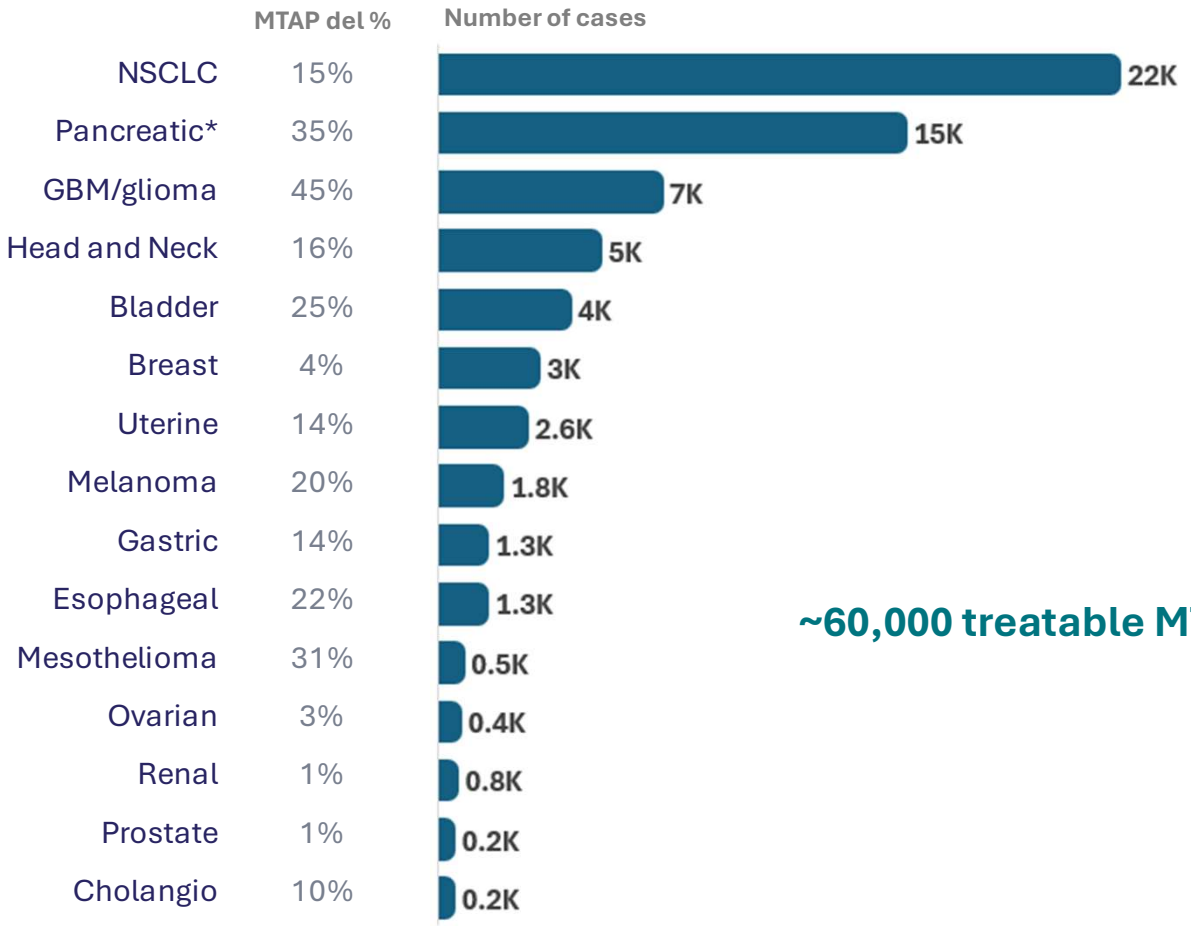
TANGO therapeutics

Malte Peters, MD President and CEO to lead our next phase of growth

Accomplished leader with deep clinical development expertise

- Member of Tango Board of Directors since 2018
- Previous roles
  - Chief Research and Development Officer, MorphoSys AG and member of the Management Board
  - Global Head of Clinical Development, Biopharmaceuticals Business Unit, Sandoz International
  - Global Clinical Head, Oncology Translational Medicine, Novartis Oncology
- Track record of innovative global regulatory approvals in particular of combination regimens

MTAP deletion is one of the most common genetic changes in cancer



*Patient population sizes estimated by Clearview using data from SEER, Kantar, TCGA PanCancer Atlas and other sources.

Large unmet need

- MTAP deletion confers sensitivity to PRMT5 inhibitors
- Large opportunity for development in pancreatic and lung cancer, glioblastoma and multiple other common cancers

~60,000 treatable MTAP del cancers in the US annually

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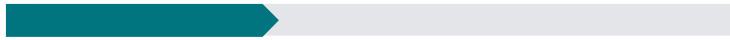
A pipeline targeting multiple high value indications with MTAP deletion

TARGET	MOLECULE	PATIENT SELECTION	INDICATIONS	CLINICAL TRIALS	STATUS
				PRE-CLINICAL / PHASE 1/2 / PHASE 3	
PRMT5	Vopimetostat (TNG462)	MTAP-del cancers	Pancreatic, lung, other non-CNS cancer		Dose expansion ongoing
		MTAP-del/ RAS-mut (+RASi)	Pancreatic, lung cancer		Dose escalation ongoing
	TNG456	MTAP-del cancers	Glioblastoma		Dose escalation ongoing
HBS1L	TNG961	MTAP/ FOCAD-del cancers	Solid tumors		Phase 1 enabled

Key 2025 achievements

Advancing multiple clinical programs
Creating value for patients

Vopimetostat

- Clinical data supporting vopimetostat as a potentially best-in-class PRMT5 inhibitor in multiple MTAP-del cancers
- FDA supportive of pivotal study design in 2L MTAP-del pancreatic cancer
- Vopimetostat + RAS(ON) inhibitors (Revolution Medicines) in MTAP-del/RAS-mut pancreatic and lung cancer initiated

Pipeline

- TNG456 (brain penetrant PRMT5 inhibitor) in phase 1/2 development for MTAP-del glioblastoma
- TNG961 advanced to IND-ready for multiple MTAP-del/FOCAD-del solid tumors

Financial/Corporate

- $225M equity raise
- $343M* cash balance as of December 31, 2025
- Cash runway into 2028

* Financial information as of December 31, 2025 has not yet been audited

Competitive advantage drives 2026 strategic execution

Launch pivotal study in 2L pancreatic cancer

Complete vopimetostat/RASi study to support 1L pivotal study in pancreatic cancer

Expand vopimetostat data in lung/other cancers to support additional pivotal studies

Evaluate TNG456 efficacy in glioblastoma

- Planned pivotal protocol design including dose selection supported by FDA
- MTAP selectivity and potency of vopimetostat provides potentially best-in-class PRMT5 suppression
- Potentially best-in-class safety profile supports combinability with other molecules
- First PRMT5 inhibitor clinical combination with RAS inhibitors may provide an innovative and fast path to front line approvals

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Pipeline poised to deliver meaningful clinical benefit in multiple common cancers with MTAP deletion

Potential best-in-class oral PRMT5 inhibitors

Vopimetostat

- Key indications*
  - ~20K pancreatic cancer
  - ~22K lung cancer
  - ~20K histology selective cluster
- 2L MTAP-del pancreatic ca pivotal study start planned 2026
- RAS(ON) inhibitor combo study ongoing
- Potential best-in-class tolerability

TNG456

- Brain penetrant PRMT5 inhibitor being developed for glioblastoma
- 45% GBM is MTAP-del (~7K pts/yr US)
- CNS penetrance predicted in preclinical studies
- Dose escalation ongoing
- Abemaciclib combo planned with evidence of single agent activity

TNG961

- HBS1L degrader synthetic lethal with FOCAD deletion
- ~30% of MTAP-del cancers also have FOCAD deletion
- Single agent and vopimetostat combination activity in multiple preclinical models
- Ready for phase 1 in 2026

*MTAP-del pts, US/yr

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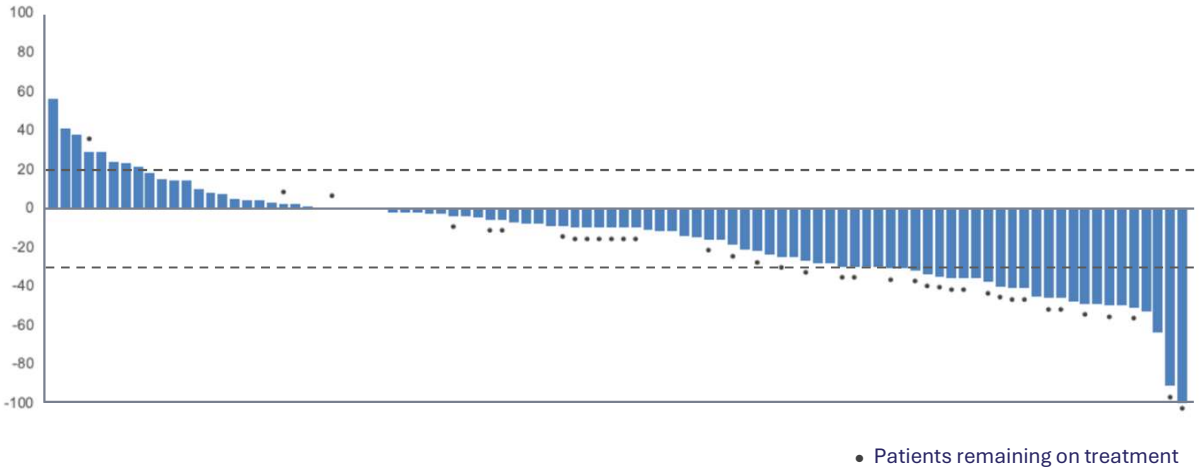
Vopimetostat demonstrates clear monotherapy activity across histologies

Active doses >6 mo follow-up
n=94



Key points

- ORR 27% in 16 different histologies
- mPFS 6.4 months
- DCR 78%
- 37/94 patients ongoing
- Median follow-up 9.4 months
- Good tolerability with no discontinuations for drug related events at 250 mg QD

Data extract 1 Sept 2025.

Includes all tumor evaluable patients receiving 200 mg QD dose or higher more than 6 months prior to the data cutoff, including those remaining on study, progressed or withdrew. ORR/DCR in tumor evaluable patients, BOR rounded to the nearest whole number. Tumor evaluable is defined as MTAP-del patients with at least one scan. ORR defined as confirmed RECIST PR or unconfirmed PR with pending confirmation scan. A lung cancer patient who died of COVID before confirmation scan is included in ORR. Active doses are defined as 200 mg QD and above.

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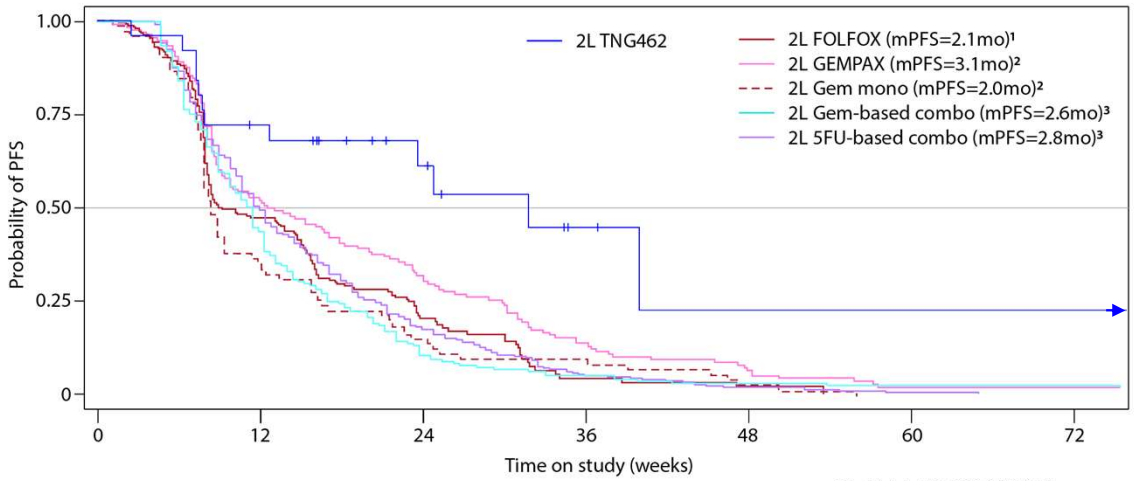
Vopimetostat mPFS in 2L pancreatic cancer more than twice historical SOC trials



¹Hecht et al., JCO, 2021 (SEQUOIA)
²De La Fouchardiere et al., JCO, 2024
³Liu et al., Canc. Biol. Med., 2024

Vopimetostat (n)	Events	Censored	mPFS (mo)	95% CI (mo)
25[b]	12	13	7.2	2.9 - NR

Key points

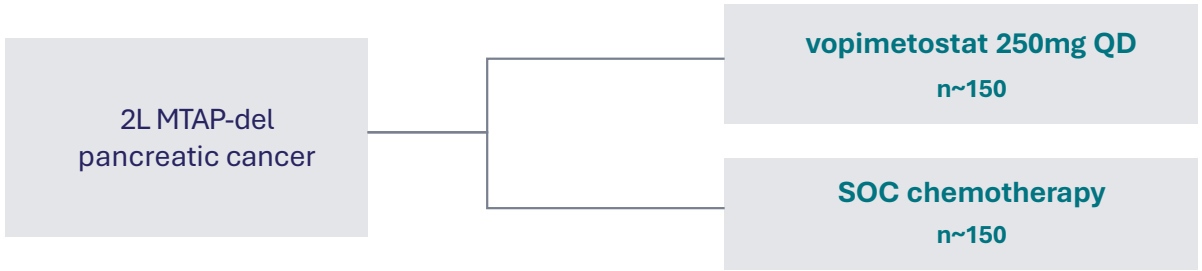
- ORR in 2L PDAC 25% (2/8 evaluable pts)
- Vopimetostat 2L mPFS 7.2 mo
- SOC chemotherapy mPFS 2-3.5 mo
- Vopimetostat pivotal study control arm may have lower mPFS than historical controls, increasing probability of success

Recent studies show MTAP deletion confers poor prognosis due to concurrent CDKN2A deletion[a]

Data extract 1 Sept 2025.
a. Ikushima, ESMO Open, 2025, Rodon et al, ESMO 2025.
b. All tumor evaluable 2L patients at active doses and the only 2L patient at 160 mg QD.
Historical data are derived from different clinical trials at different points in time and head-to-head clinical trials have not been conducted.

Vopimetostat monotherapy pivotal trial in 2L pancreatic cancer

Pivotal study start planned 2026



Planning for 2L registration

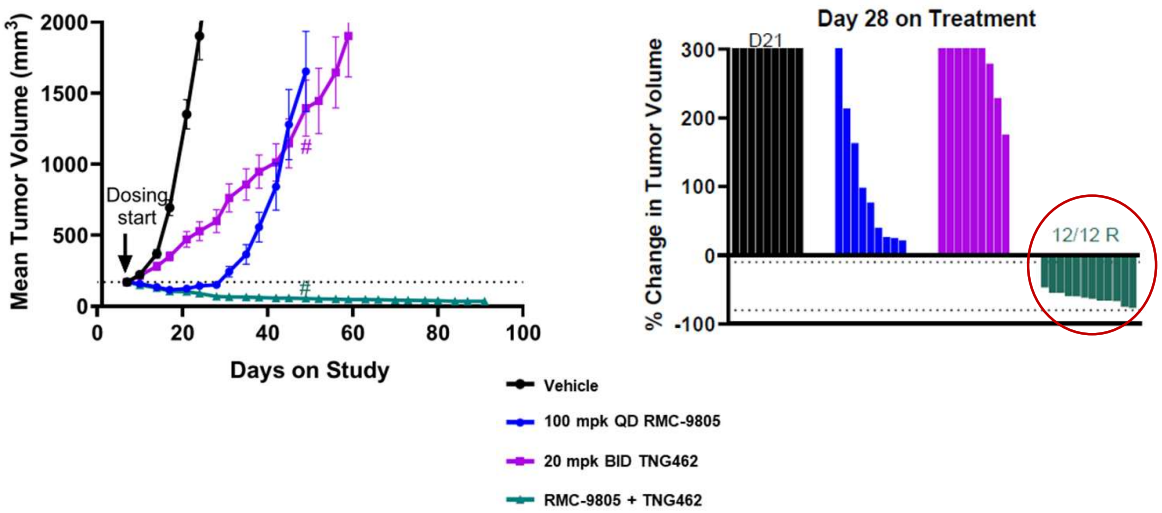
- FDA supportive of study design
- Rapid enrollment of ~300 patients anticipated given high unmet medical need in this patient population

Vopimetostat + zoldonrasib has striking efficacy in preclinical models

Vopimetostat + zoldonrasib

KP4

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

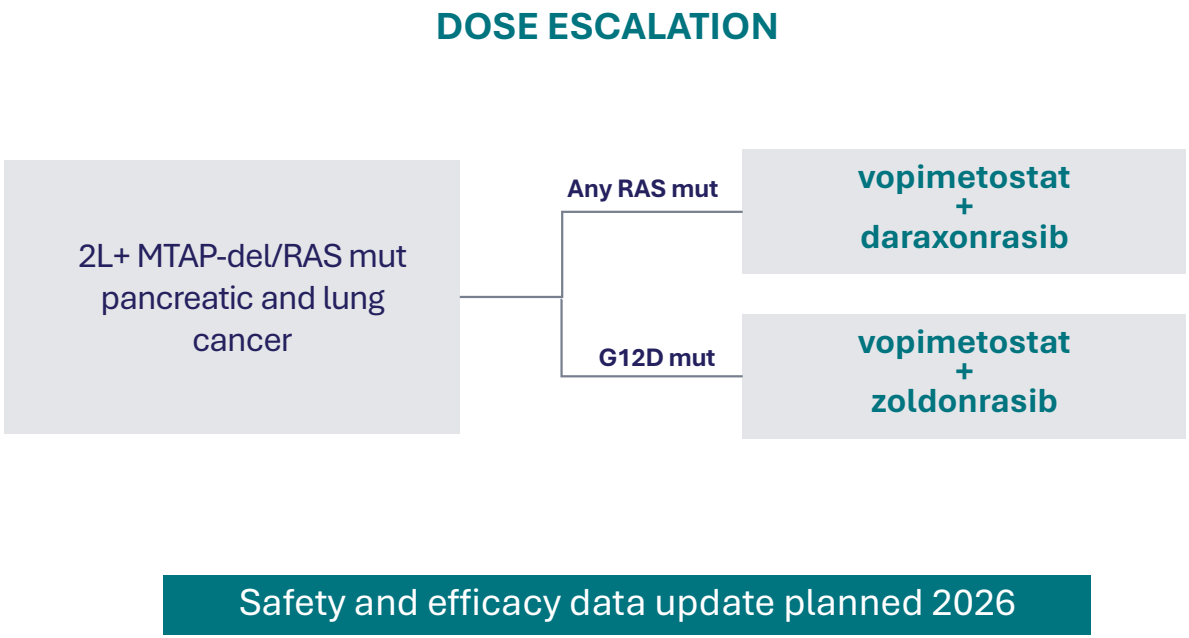


Key points

- Pancreatic cancer is a RAS-addicted cancer
- Almost all MTAP-del pancreatic cancers have a RAS mutation
- ~40% MTAP del pancreatic ca is RAS G12D mut
- Similar preclinical data with daraxonrasib
- Clinical collaboration with Revolution Medicines to evaluate vopimetostat + zoldonrasib (RAS G12D-selective inhibitor) and vopimetostat + daraxonrasib (RAS multi-selective inhibitor)

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

Encouraging early activity in ongoing vopimetostat + RAS(ON) inhibitor clinical study



Safety and efficacy data update planned 2026

Study update

- Ongoing robust enrollment
- 30 patients dosed
  - 14 pts with vopimetostat/daraxonrasib
  - 16 pts with vopimetostat/zoldonrasib
- Both combinations well tolerated at active exposures of all molecules
- No unexpected adverse events
- Early efficacy data encouraging

Enrollment data as of 24 December 2025

Vopimetostat + RASi strategy for 1L pancreatic cancer

RAS inhibitors likely to replace chemotherapy as SOC in 1L pancreatic cancer

- More than 90% of pancreatic cancers are RAS-driven[1]
- Almost all MTAP-del pancreatic cancers have a RAS mutation
  - ~18k pts with MTAP-del and RAS-mut pancreatic cancer annually in the U.S.

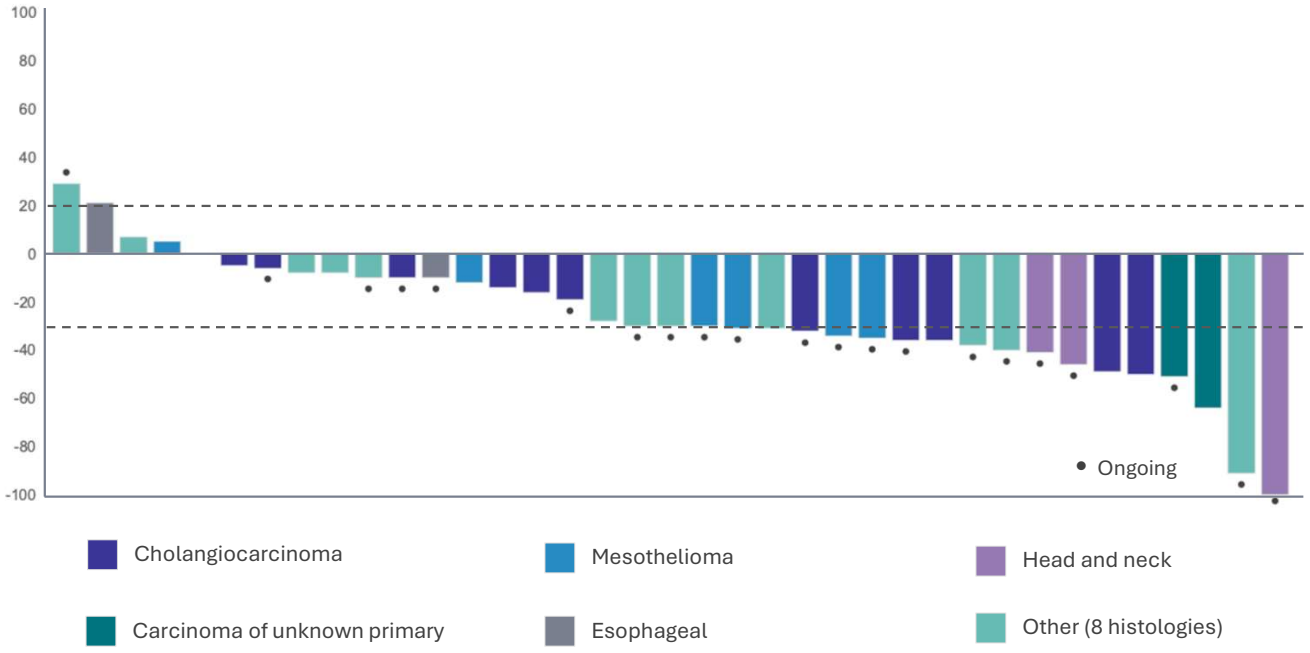
Potential path to vopimetostat 1L pivotal study with chemo-sparing RASi combinations

- Encouraging early activity and robust enrollment in ongoing study in 2L+ pancreatic and lung cancer
- Addition of 1L pancreatic cancer cohort to ongoing study planned 2026
- Phase 1/2 combo data in 2026 could support rapid move into 1L pancreatic cancer pivotal study
  - Single agent daraxonrasib 2L pancreatic ca ORR 29%, 1L pancreatic ca 47%, 2L+ lung ca 39%[2]
  - Single agent zoldonrasib 2L+ pancreatic ca ORR 30%[2]
- First PRMT5 inhibitor being clinically evaluated in combination with RAS inhibitors

1. TCGA PanCancer Atlas (Cerami et al. 2012 and Gao et al., 2013)
2. Revolution Medicines corporate deck November 2025

Vopimetostat 49% ORR in histology selective cohort

Tumor evaluable pts at active doses with >6 months follow-up (n=37)

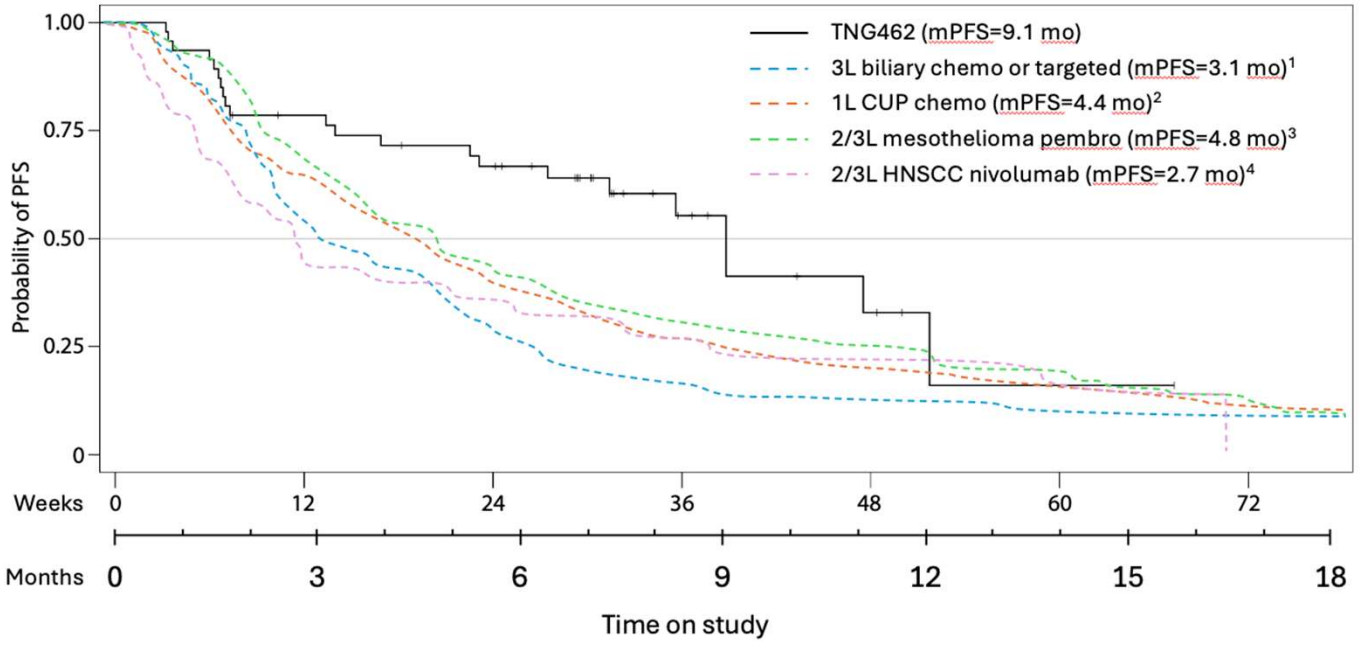


Key points

- ORR 49%
- mPFS 9.1 months
- DCR 89%
- 21/37 patients ongoing
- Median follow-up 9.5 months
- Excludes sarcoma, pancreatic and lung cancer

Data extract 1 Sept 2025.
ORR in tumor evaluable patients, BOR rounded to the nearest whole number.

Vopimetostat 9.1 mo mPFS more than twice historical SOC trials in multiple indications



[1]Gray et al., Cancers, 2023
[2]Kang et al., Sci.Rep.,2021
[3]Ahmadzada et al., JTO Clin. Res. Rep., 2020
[4]Du et al., Curr. Oncol., 2023

mPFS (95% CI)
9.1 months (6.5 – 12.0)

Durable activity in multiple late line, difficult to treat cancers provides:

- Further evidence of robust single agent activity
- Additional optionality for development in large patient population with high unmet need

Data extract 1 Sept 2025.
Historical data are derived from different clinical trials at different points in time and head-to-head clinical trials have not been conducted.

TNG456

PRMT5 inhibition being developed for MTAP-deleted glioblastoma

TNG456 is a next-generation CNS-penetrant PRMT5 inhibitor

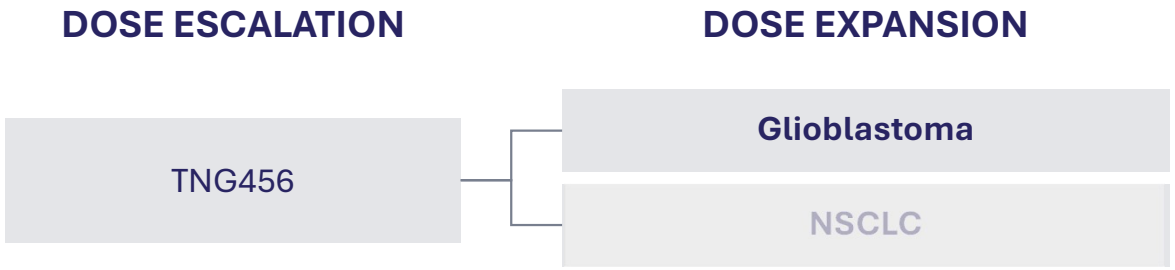
Brain penetrance provides potential to address high unmet need in glioblastoma

- Enhanced potency and MTAP selectivity
- Predicted brain exposure well above efficacy threshold
- In development for MTAP-del glioblastoma (7,000 patients/yr US)[1]

	Potency	MTAP selectivity	CNS exposure
TNG456	**20 nM**	**55X**	**0.5-1X plasma**
Vopimetostat	4nM	45X	-
TNG908	110 nM	15X	0.3X plasma

1. SEER;CBTRUS, TCGA PanCancer Atlas

TNG456 phase 1/2 clinical study in MTAP-del solid tumors



Summary

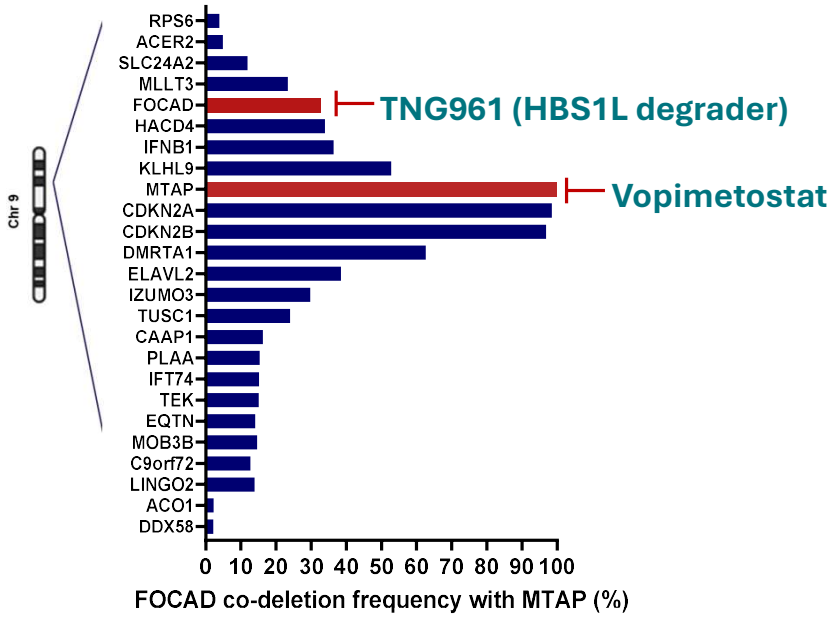
- Dose escalation ongoing
- Abemaciclib combination to start with evidence of single agent activity in GBM
- FDA Fast Track designation
- FDA Orphan Drug Designation for glioblastoma

TNG961

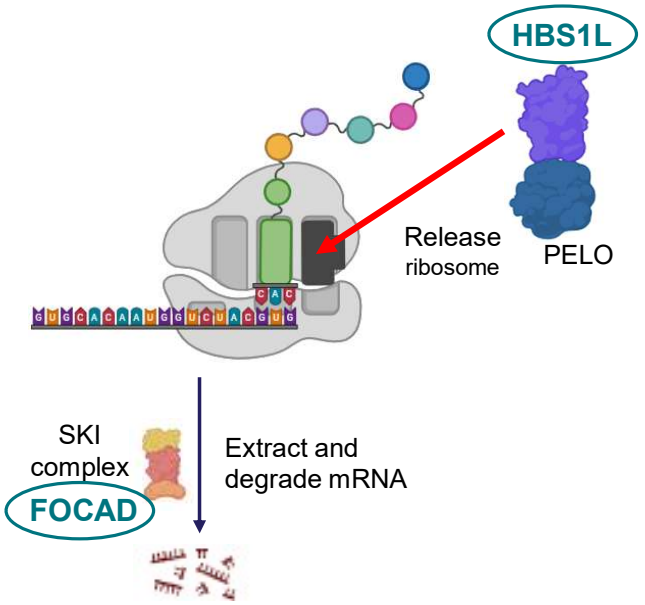
HBS1L degrader for FOCAD-del/MTAP-del cancers

FOCAD deletion and HBS1L are a synthetic lethal pair

FOCAD deletion occurs in one third of MTAP-del cancers



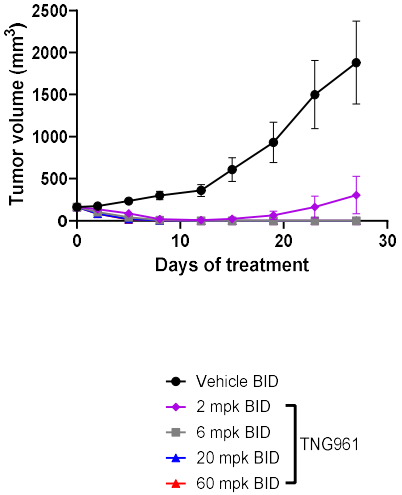
FOCAD deletion confers HBS1L dependency for RNA stability



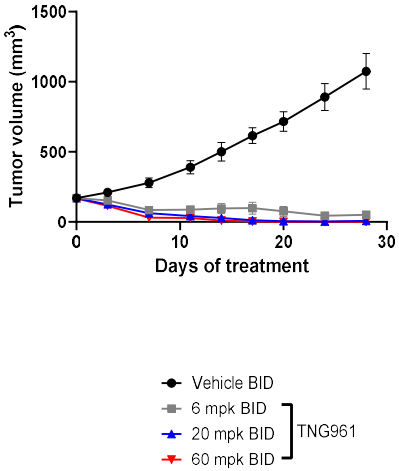
TNG961 drives tumor regression in FOCAD-del/MTAP-del preclinical models

Strong xenograft activity across lineages

NCI-H838
NSCLC



MIAPACA2
PDAC



TNG961

- Potent and selective HBS1L molecular glue degrader
- IC50 110 nM
- 100X selectivity for FOCAD del vs WT cells
- IND-enabling studies complete with very clean safety profile
  - Starting dose within the predicted active range supported

Multiple projected key milestones and strong balance sheet

Clinical milestones

- ❑ Vopimetostat lung ca data 2026
- ❑ Vopimetostat + daraxonrasib/zoldonrasib data 2026
- ❑ 2L PDAC pivotal study start 2026
- ❑ TNG456 data 2026

Cash balance

- $343M cash, cash equivalents and marketable securities as of December 31, 2025*
- Cash runway into 2028

* Financial information as of December 31, 2025 has not yet been audited

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