



The next wave of targeted therapies in oncology

Corporate Overview
May 2025

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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 first quarter of 2027; the Company's belief that TNG260 may be a first-in-class oral CoREST inhibitor; the potential for TNG462 to have best-in-class tolerability; the Company's belief that TNG462 and TNG456 have the potential to be best-in-class PRMT5 oral inhibitors for multiple common cancers; 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, including in terms of safety and tolerability; the anticipated milestones and timing for the Company's drug programs (including combination studies), including the timing for clinical trial initiation, enrollment, patient dosing, dose escalation, dose expansion, and clinical updates; the Company's expectations regarding a registrational trial for TNG462; the Company's plans for and timing of combination trials for TNG462 and TNG456, including with RAS(ON) inhibitors for TNG462 and with abemaciclib for TNG456; the Company's belief that TNG462 has the potential to transform care in front line pancreatic cancer; the timing of initial, 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 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 Company's expectations around the size and value of the potential patient population for PRMT5 inhibitors (including for lung and pancreatic cancers) and the Company's belief that it has a significant opportunity to treat multiple common cancers; potential combination strategies and uses for PRMT5 inhibitors, including TNG462 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 TNG462, TNG456, or TNG260; 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 TNG462 combination activity for TNG961. 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. 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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
- Potential best-in-class tolerability
- Phase 1/2 clinical update 2H 2025

TNG456

- Key indication is glioblastoma
 - 45% of GBM is MTAP-del (7K pts/yr US)
- CNS penetrant in preclinical studies
- Highly potent and selective
- First patient dose planned 2Q 2025

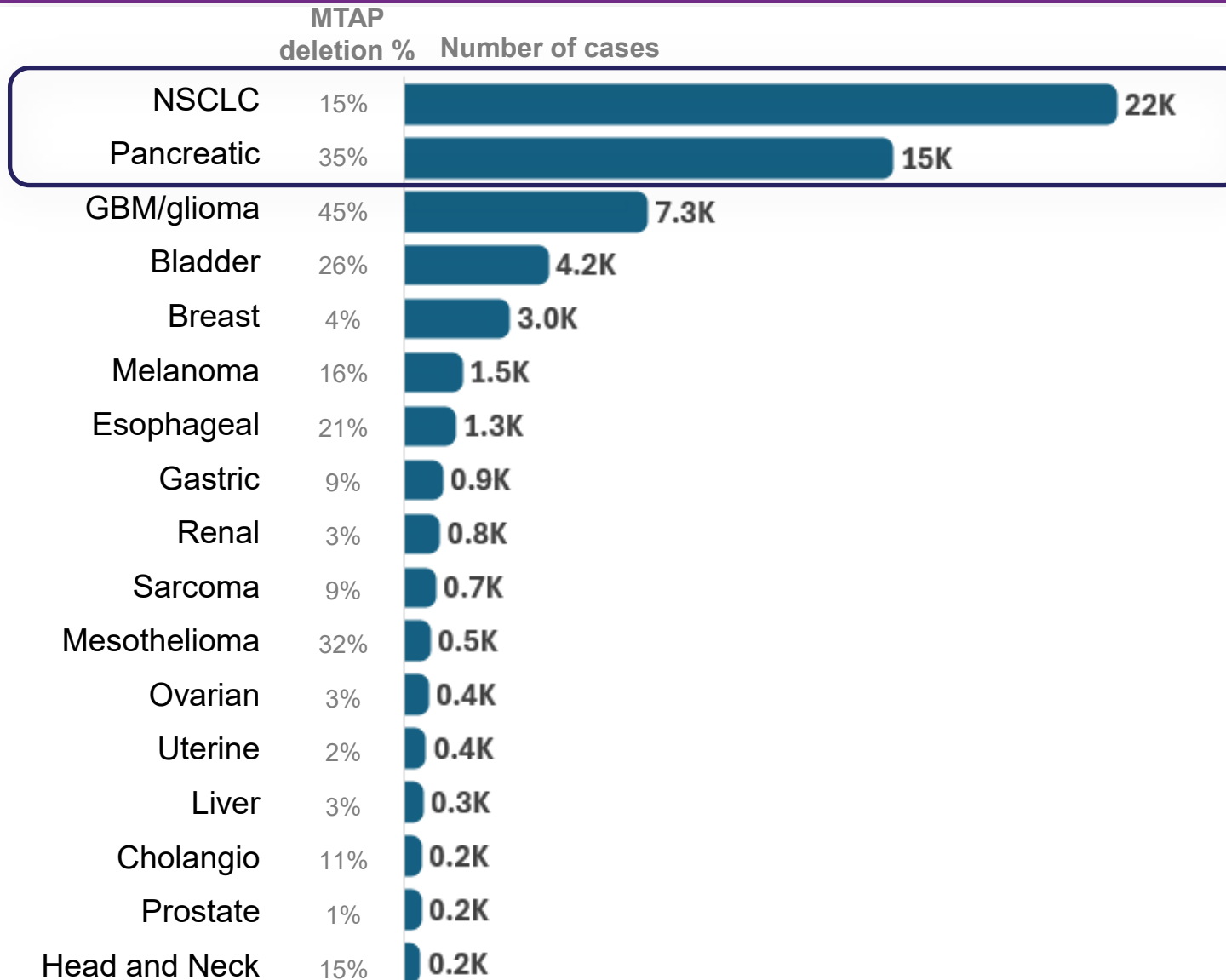
First-in-class oral CoREST inhibitor

TNG260

- Key indication is STK11-mut lung cancer
 - 20% of non-small cell 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 2H 2025

*O’Kane, G.M et al. Cancer Res., 2024

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

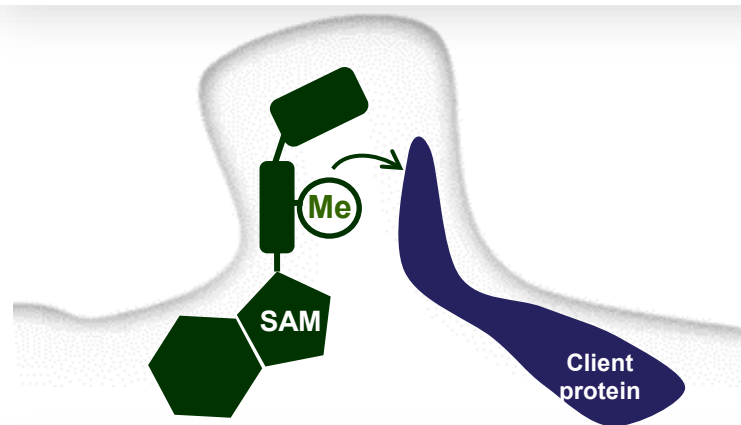


Large unmet need

- MTAP deletion confers sensitivity to PRMT5 inhibitors
- Up to ~37K MTAP-del lung and pancreatic cancer patients/yr (US)

TNG462 and TNG456 selectively inhibit PRMT5 in MTAP-del cancers

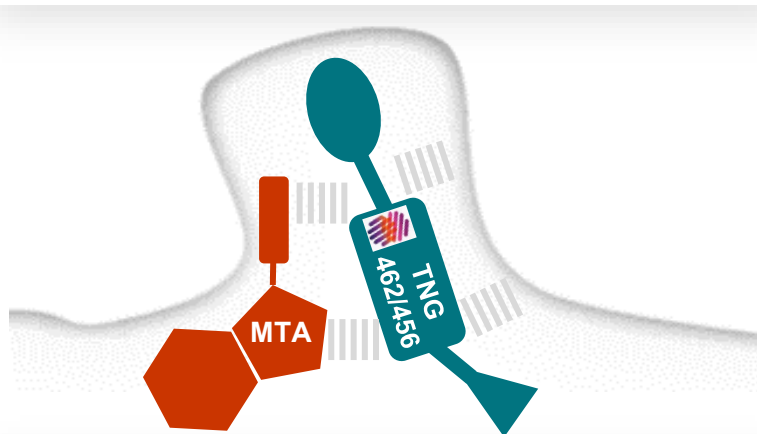
Normal cells



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



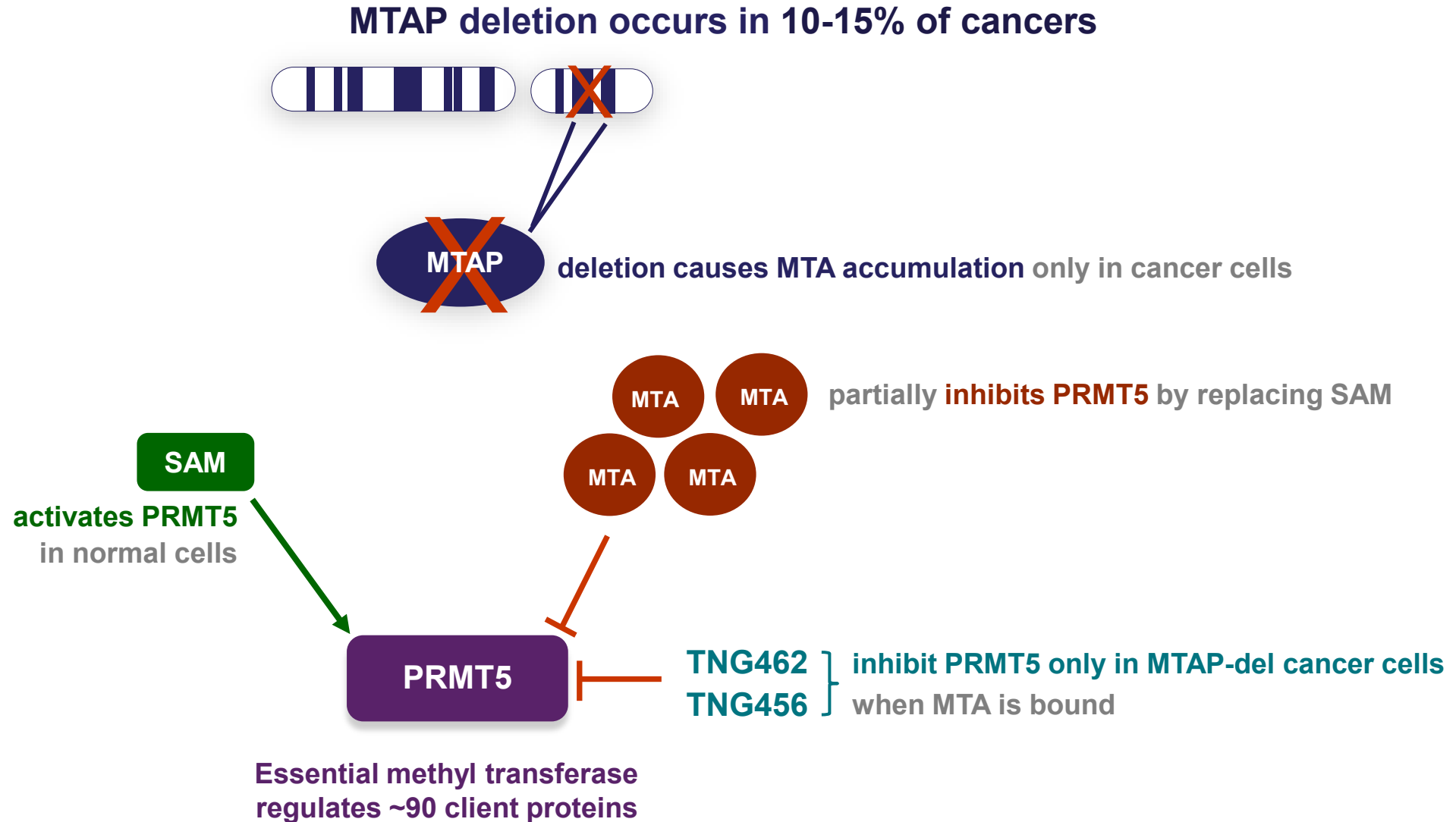
Inactive PRMT5

- 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

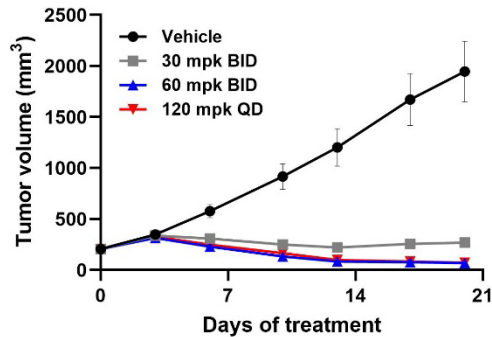


Tango PRMT5 inhibitors have superior preclinical efficacy

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

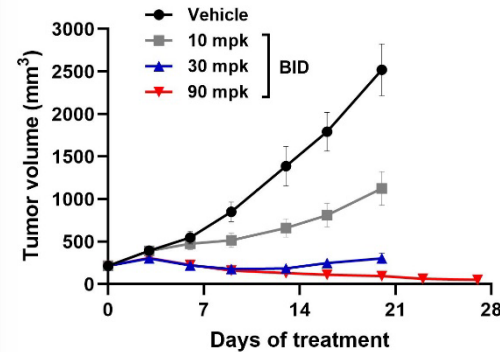
Tango PRMT5 inhibitors

TNG462



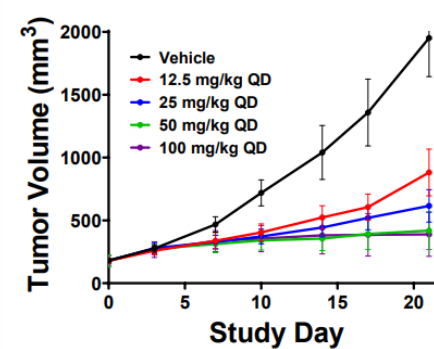
Deep tumor regression

TNG456



Deep tumor regression

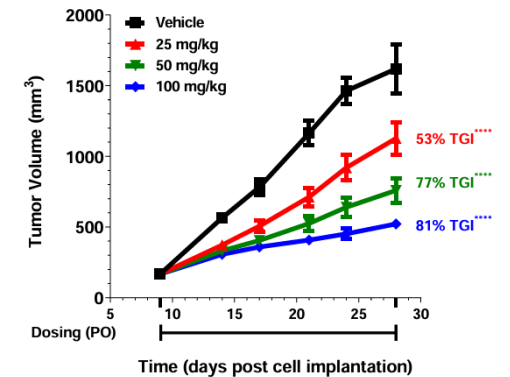
MRTX1719



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 (RevMed)	Pancreatic and lung cancer				Enrollment 2Q2025
	TNG456	MTAP-del cancers	Glioblastoma				Enrollment 2Q2025
CoREST	TNG260	STK11-mut cancers	Lung cancer				Dose expansion ongoing
HBS1L	TNG961	FOCAD deleted cancers	Solid tumors				IND-enabling studies

All programs wholly owned by Tango

TNG462

PRMT5 inhibition in MTAP-del cancers

TNG462 is a potentially best-in-class PRMT5 inhibitor

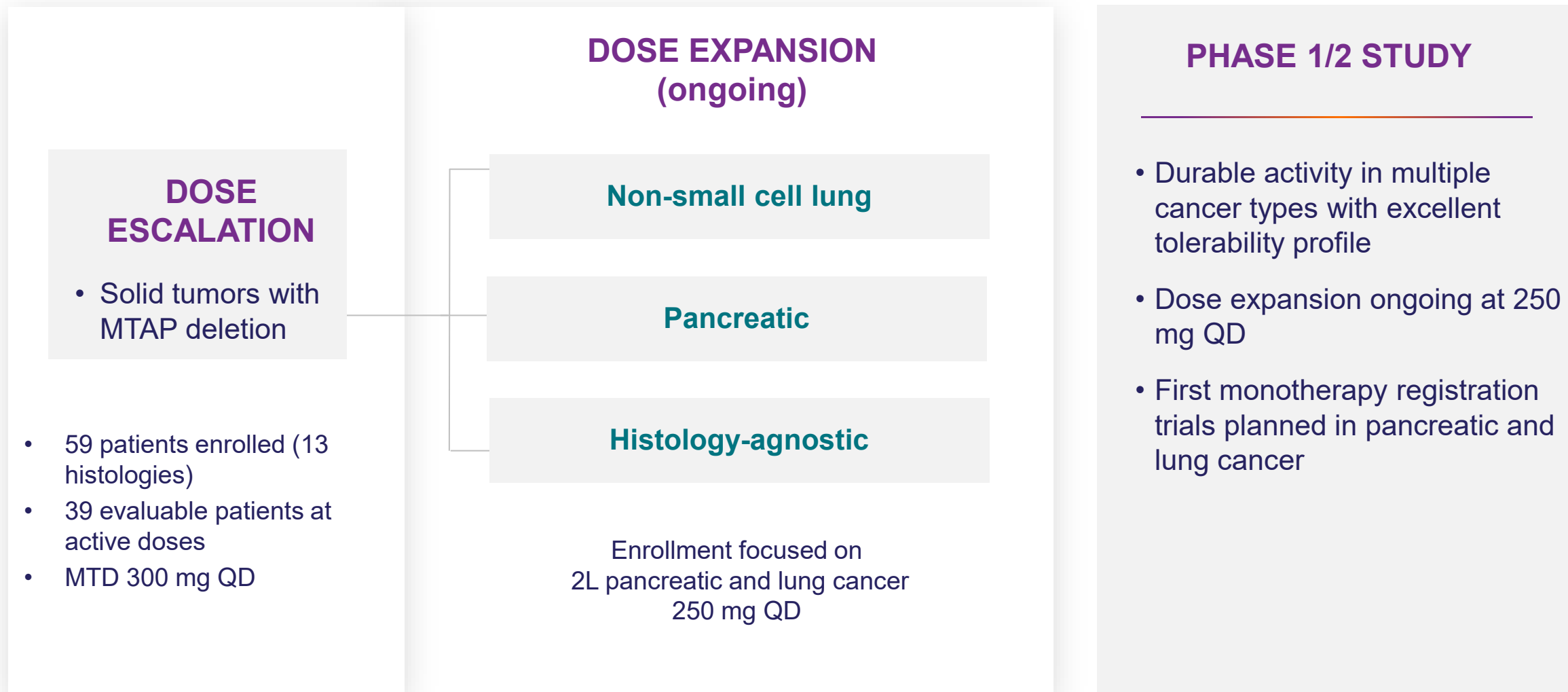
Durable clinical responses in late-line lung and pancreatic cancer

- RECIST partial responses and durable disease control in multiple cancer types
- 24 week mPFS in dose escalation cohort at active doses in late-line, difficult-to-treat cancers
- Excellent safety and tolerability profile
- Phase 1/2 monotherapy study enrolling at 250 mg QD with focus on 2L pancreatic and lung cancer
- MTAP-del pancreatic and lung cancer are priority indications for development (~37K pts/yr US)

	Potency	MTAP del selectivity	mPFS (dose escalation)	CNS penetrance
TNG462	4 nM	45X	24 weeks	No

Data cutoff 20 October 2024

TNG462 dose expansion enrolling pancreatic and lung cancer



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

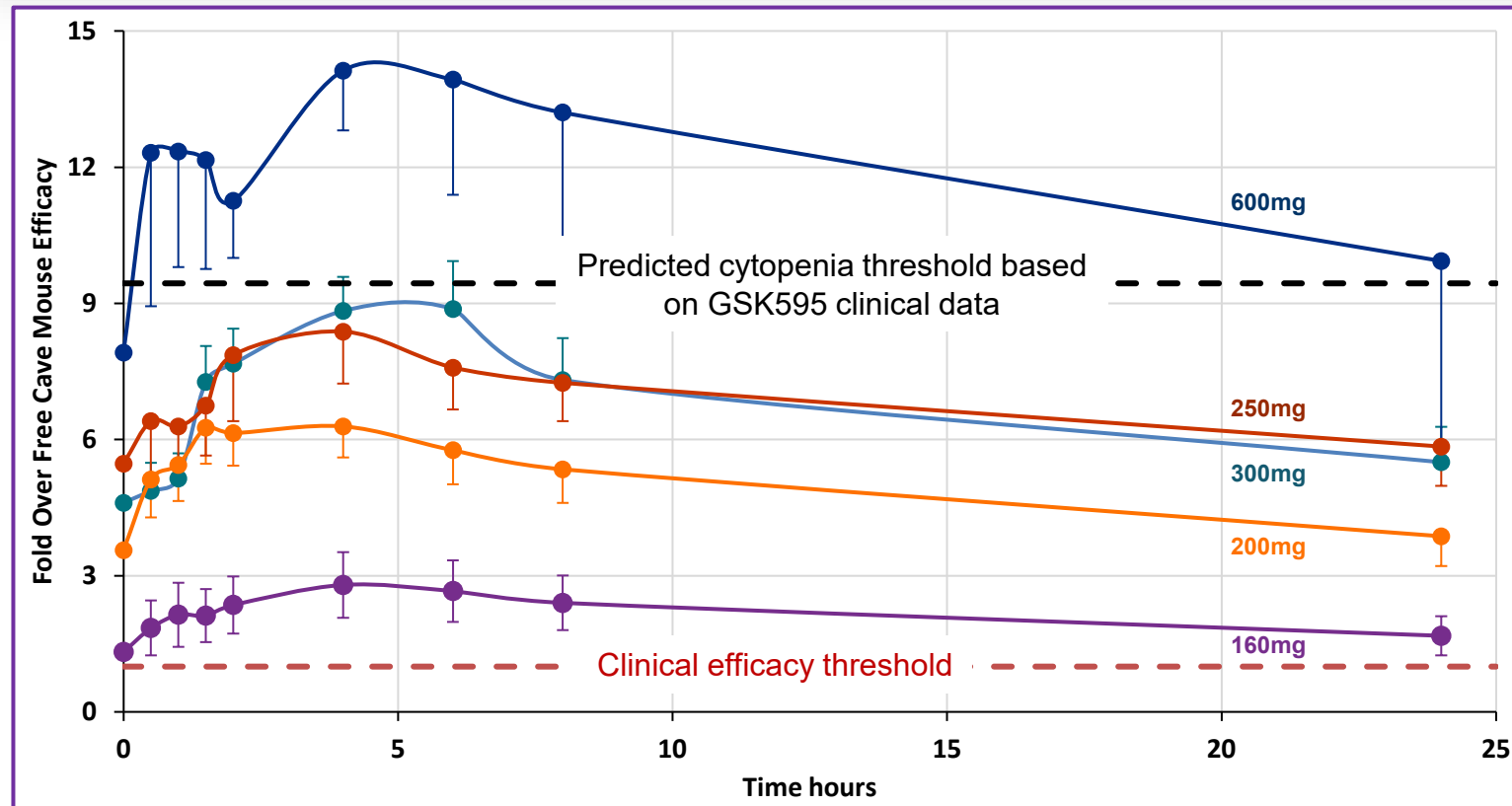
Demonstrated best-in-class potential

- RECIST partial responses in multiple tumor types, including lung 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 pancreatic and lung cancer
- TNG462 combinations with RAS inhibitors 2Q 2025

Data cutoff 20 October 2024

TNG462 on-target cytopenias occur at predicted exposures

TNG462 exposure at clinically active doses



DLT

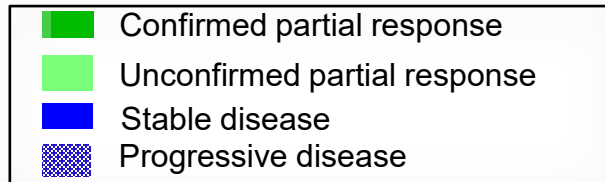
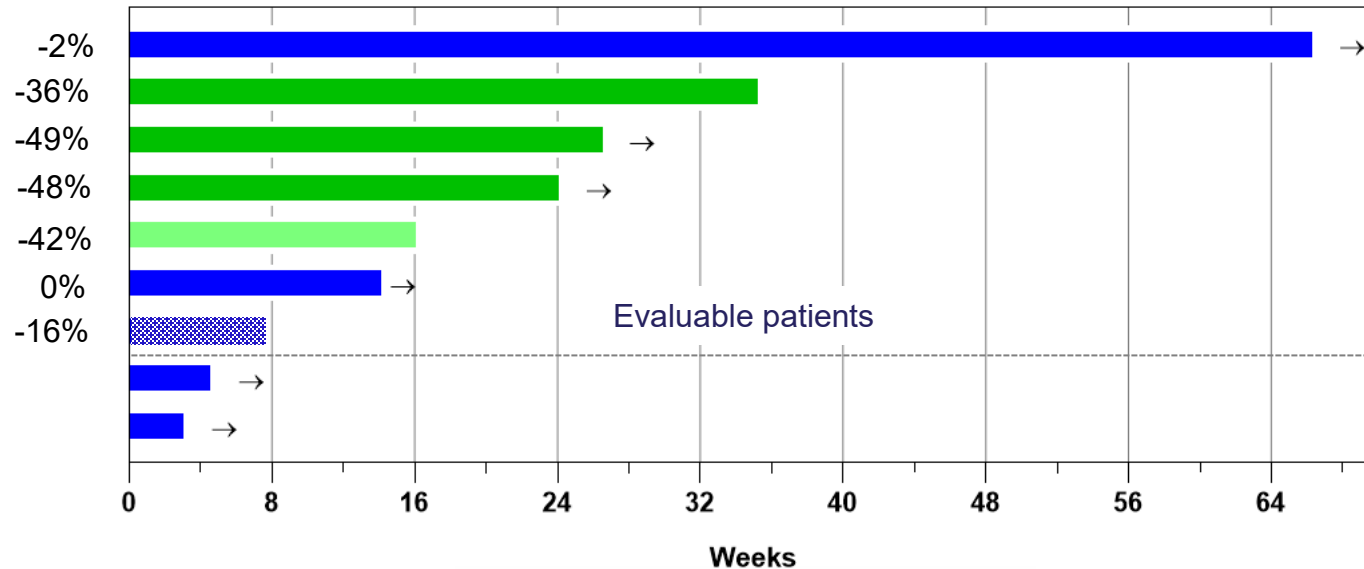
Clinically active and well-tolerated

Error bars represent SEM

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

TNG462 ORR 43%

BOR



Data cutoff 20 October 2024

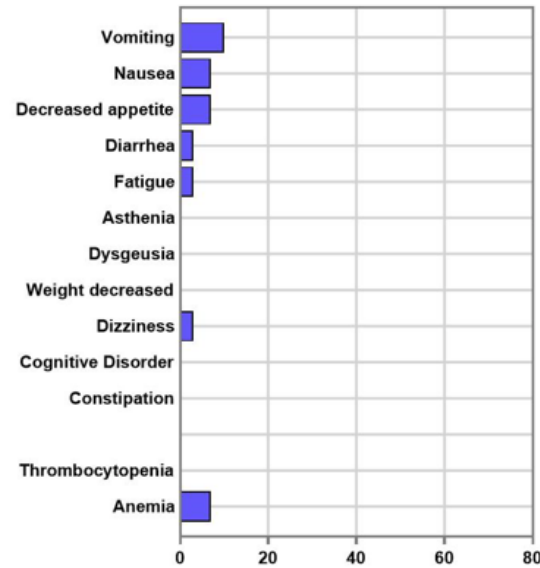
Key points

- 3/7 RECIST PRs in evaluable patients at active doses
- ORR compares favorably to other treatment options
 - TNG462 43%
 - 2L chemotherapy 7%*
 - BMS-504 18% (2/11)
 - AMG 193 15% (2/13)

*Amonkar et al, Future Oncology, 2024

TNG462 safety and tolerability profile is superior to competitors

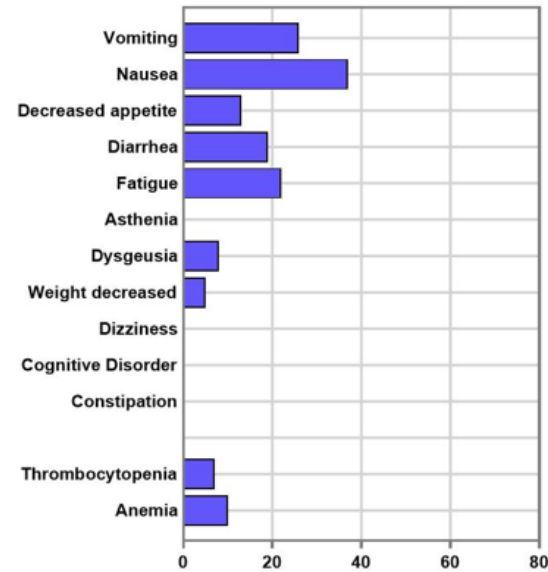
TNG462 200 mg*



0/30 dose reductions (0%)

No thrombocytopenia
Minimal nausea and fatigue
No dysgeusia

BMS-504 200-600 mg

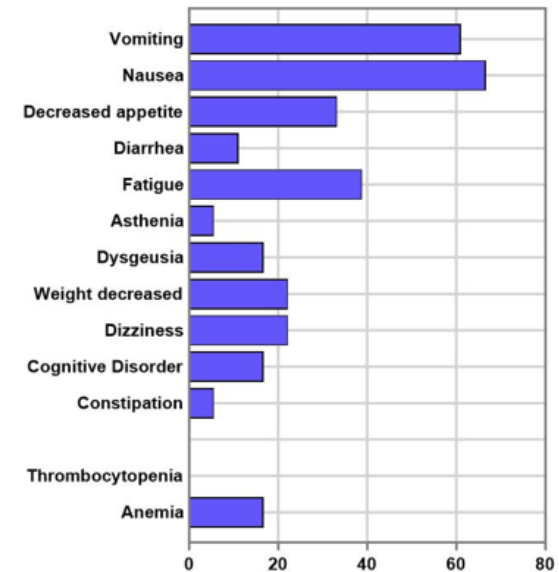


Dose reductions unknown

Frequent GI side effects
10% dysgeusia

ENA 2024

AMG 193 1200 mg



6/18 dose reductions (33%)

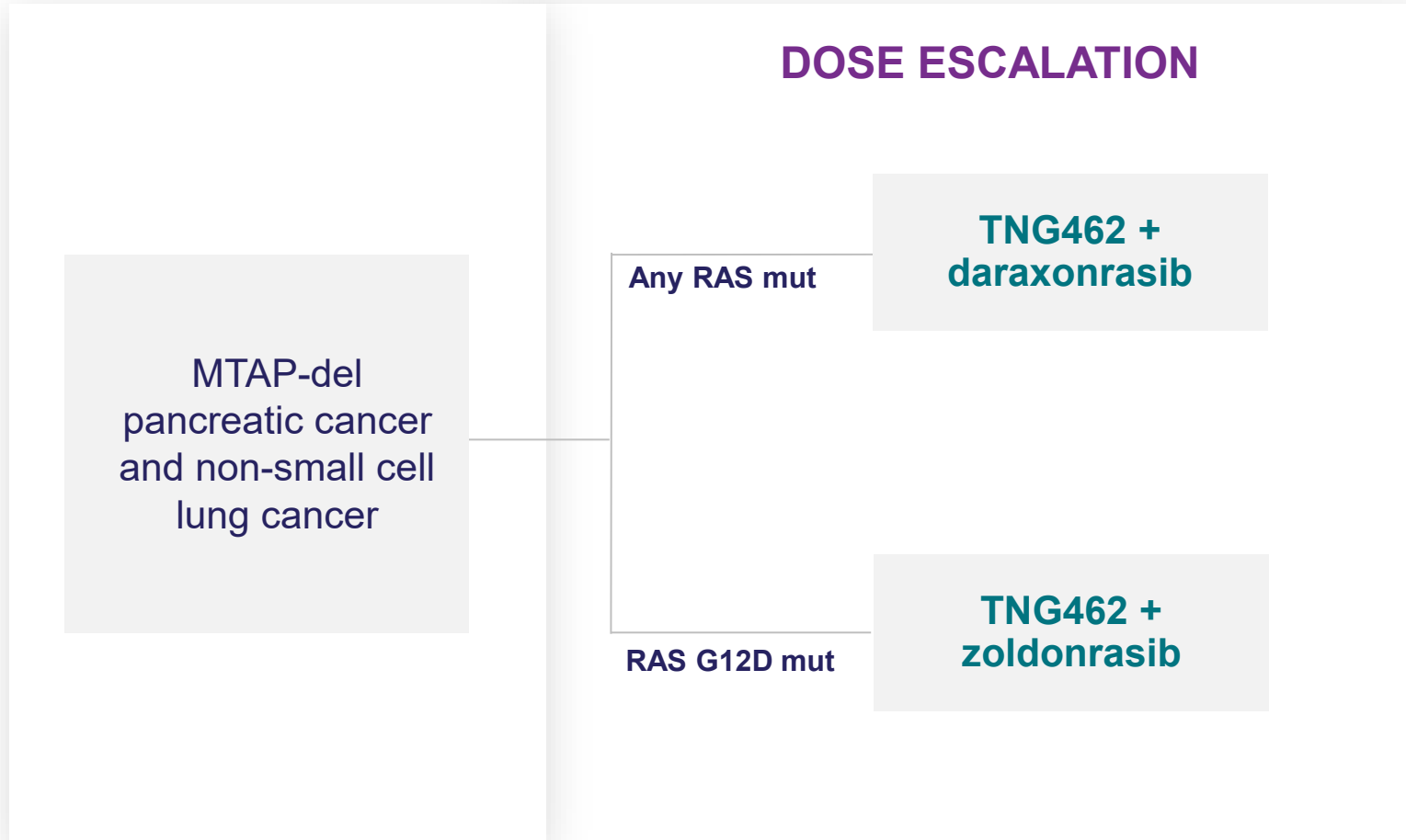
Significant nausea, vomiting,
decreased appetite, fatigue,
dysgeusia and CNS effects

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 + RASi trial design



PHASE 1/2 STUDY

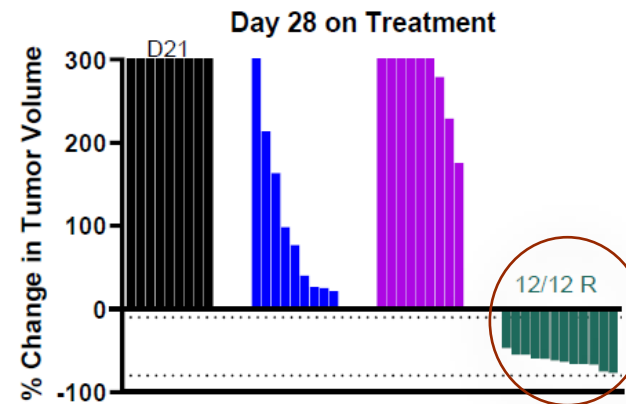
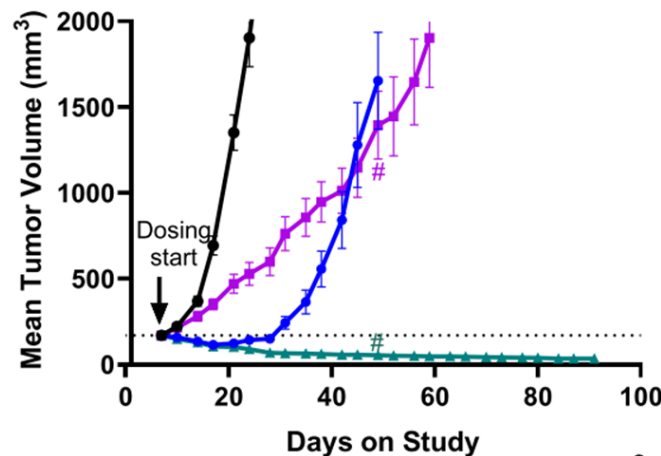
- Potential to transform care in front line pancreatic cancer
- Escalation starting at active dose ranges for all drugs
- Enrollment planned 2Q 2025

TNG462 + RAS inhibition is very active in preclinical models

TNG462 + Zoldonrasib (RMC-9805)

KP4

MTAP-null, KRAS^{G12D} PDAC CDX



● Vehicle
■ 100 mpk QD RMC-9805
▲ 20 mpk BID TNG462
◆ RMC-9805 + TNG462

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

Key points

- 40% of pancreatic cancers have a RAS G12D mutation
- Clinical collaboration with Revolution Medicines to evaluate TNG462 + zoldonrasib (RAS G12D-selective inhibitor) and TNG462 + daraxonrasib (RAS multi-selective inhibitor)

TNG456

PRMT5 inhibition in MTAP-deleted cancers

TNG456 is a next-generation CNS-penetrant PRMT5 inhibitor

Superior preclinical profile to address high unmet need in glioblastoma

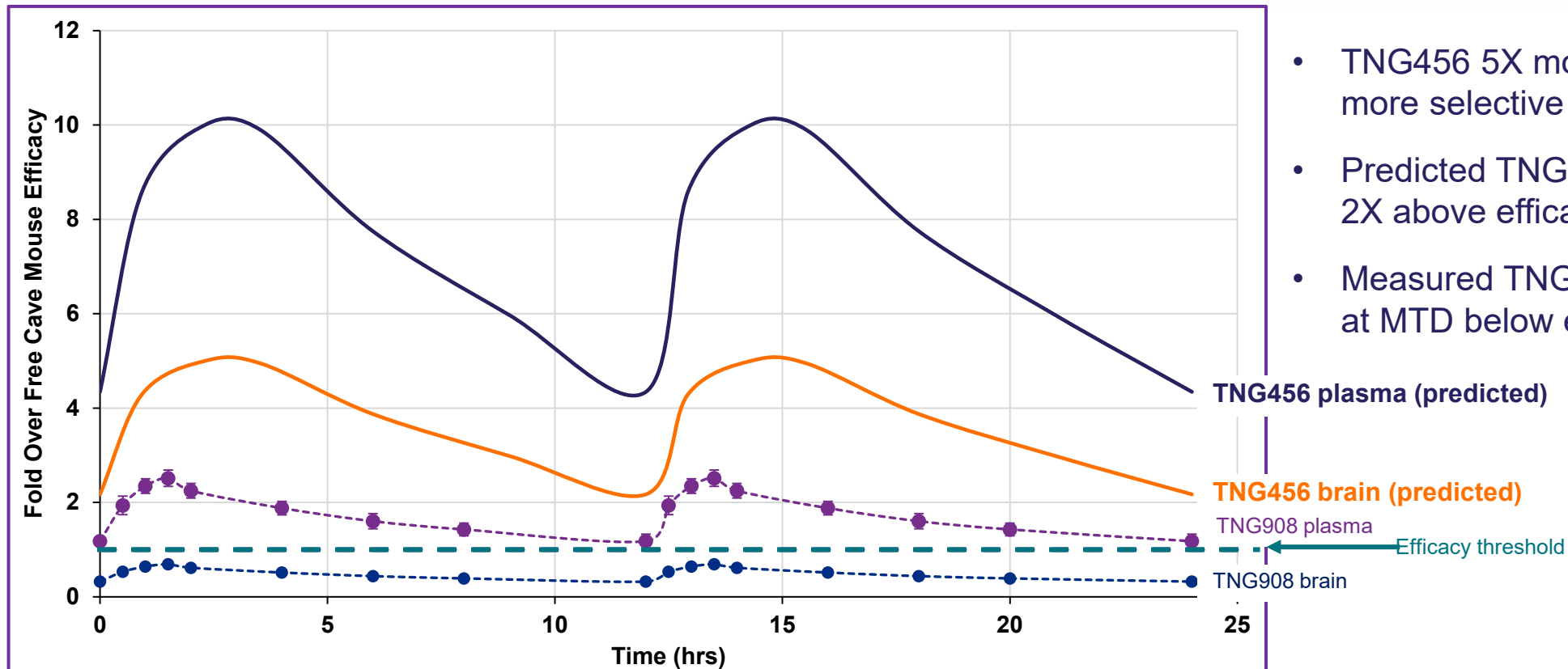
- Enhanced potency and MTAP selectivity
- Predicted brain exposure well above efficacy threshold
- Key indication for development is MTAP-del glioblastoma (7,000 patients/yr US)
- First patient dose planned 2Q 2025

	Potency	MTAP selectivity	CNS exposure
TNG456	20 nM	55X	0.5-1X plasma
TNG462	4 nM	45X	-
TNG908	110 nM	15X	0.3X plasma

- TNG456 modeled from NHP data
- TNG908 measured in patients

TNG456 brain exposure predicted to be above clinical efficacy threshold

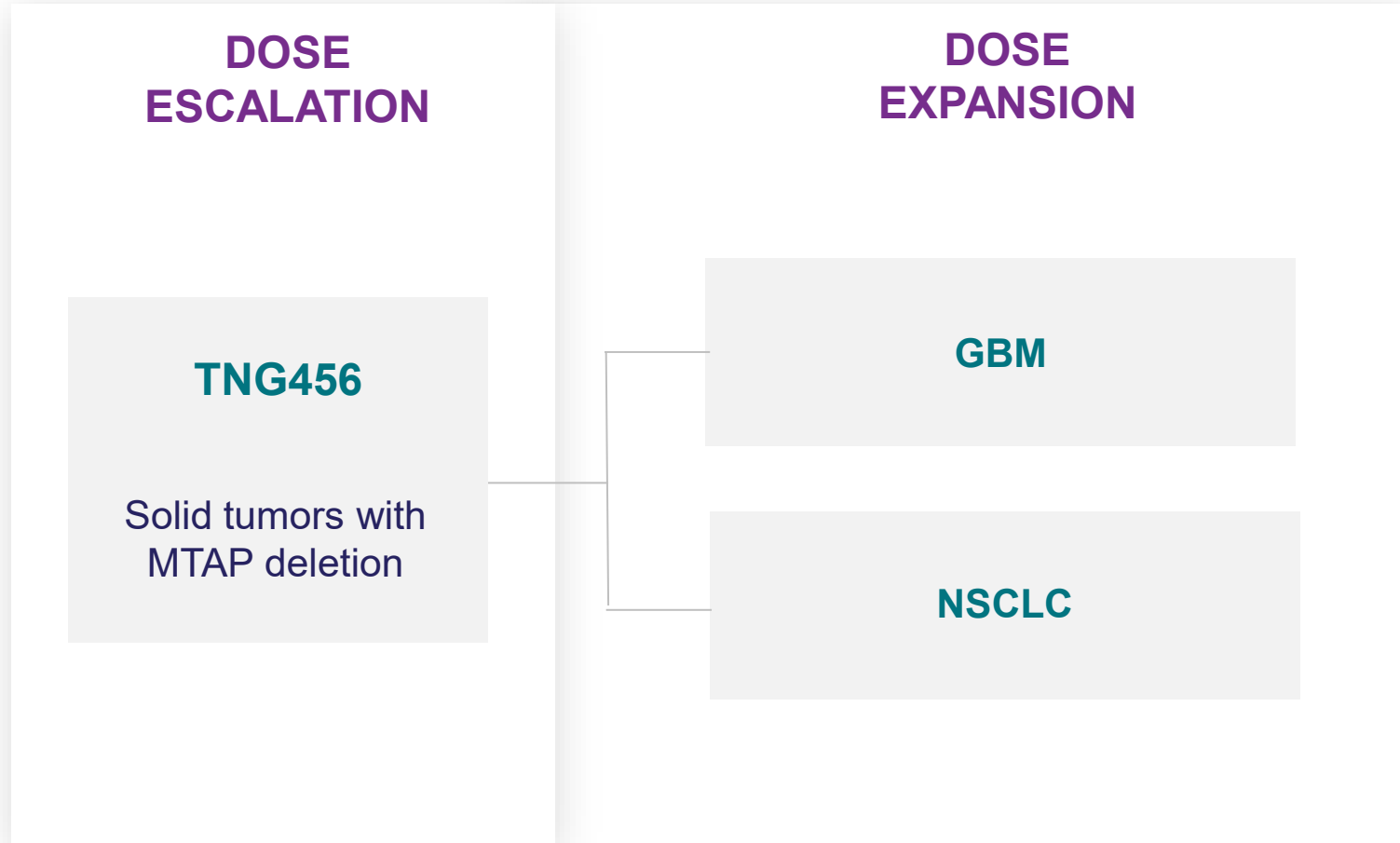
Predicted TNG456 exposure in plasma and brain



- TNG456 5X more potent and 3X more selective than TNG908
- Predicted TNG456 brain exposure 2X above efficacy threshold
- Measured TNG908 brain exposure at MTD below efficacy threshold

TNG456 brain exposure modeled at 50% of plasma
Error bars represent SEM

TNG456 phase 1/2 clinical study



SUMMARY

- 10% lung cancer patients have brain mets at diagnosis, up to 40% will develop over time
- Abemaciclib combination to start with evidence of single agent TNG456 activity in GBM

PRMT5 program development plans

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

TNG462

- Monotherapy enrollment focused on lung and pancreatic cancer at 250 mg QD
- Combination with KRAS inhibitors enrollment 2Q 2025
- Registration trials in pancreatic and lung cancer planned 2026
- Companion diagnostic development ongoing

TNG456

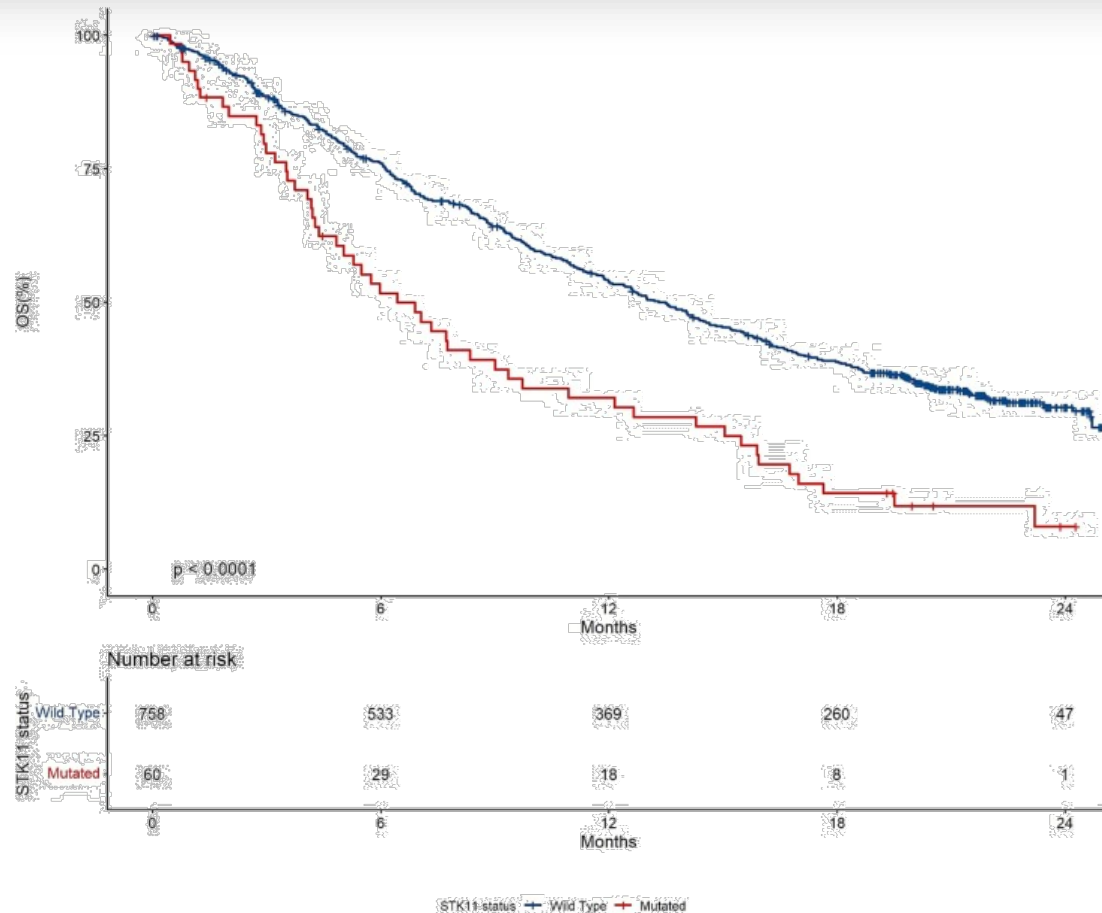
- Dose escalation in MTAP-del solid tumors with focus on glioblastoma to begin 2Q 2025
- Abemaciclib combination to start with evidence of single-agent activity in GBM

TNG260

CoREST inhibition in STK11-mutant cancers

STK11 mutant lung cancer responds poorly to standard of care

Overall survival in 1L lung cancer is significantly lower in STK11 mut vs. WT patients

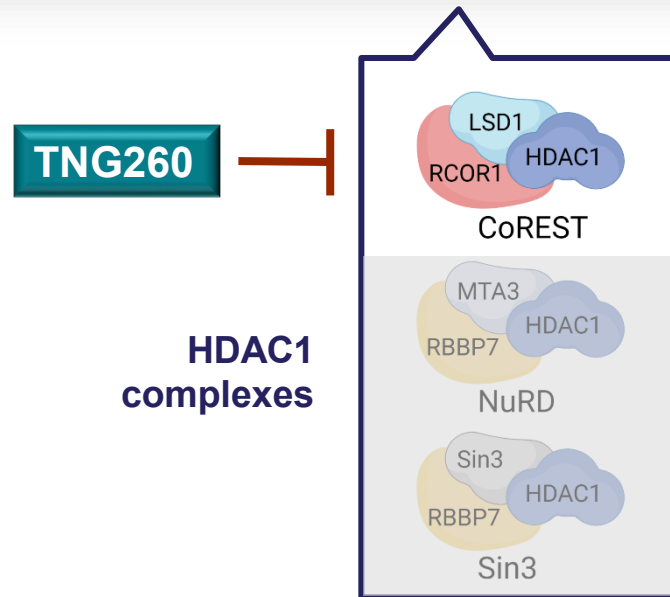


Summary

- ~20% of non-small cell lung cancer is STK11 mut
- STK11 included on all commercial NGS panels
- Median OS 6.4 vs 12.7 mo for STK mut vs WT patients

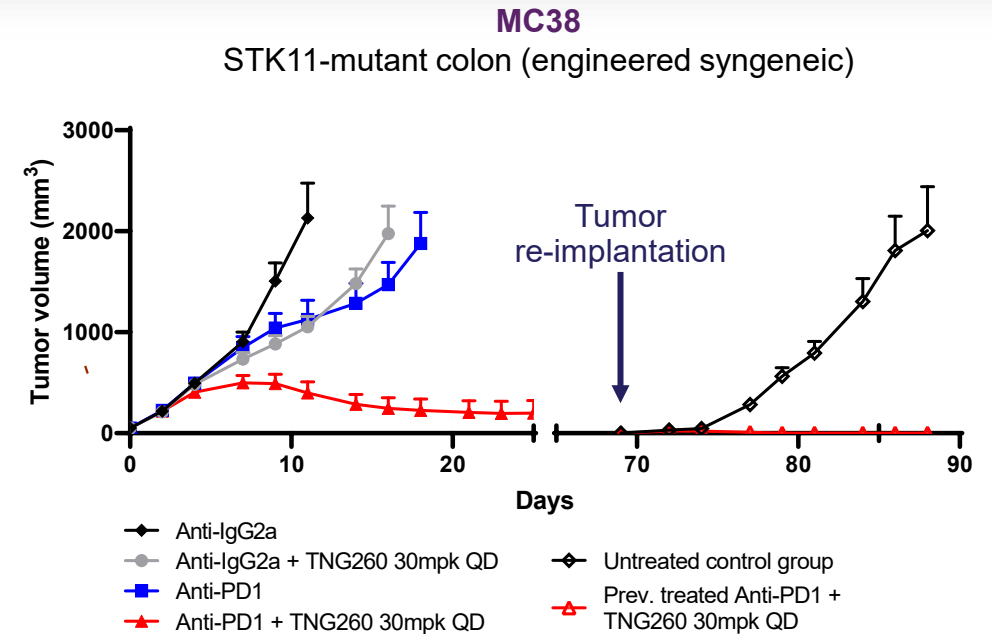
TNG260 restores α -PD-1 responsiveness to STK11-mutant cancers

Selective CoREST complex inhibition



CoREST complex selectivity provides large therapeutic index

TNG260 restores α -PD1 efficacy in syngeneic models

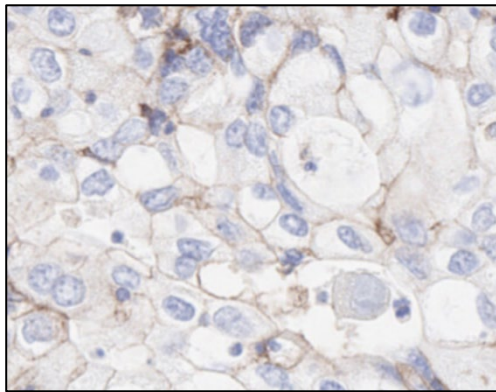


- 5/8 mice complete tumor regression at day 34
- All mice with complete regression rejected tumor re-implantation

Clinical data demonstrate TNG260 converts STK11-mut immune microenvironment from unresponsive to responsive

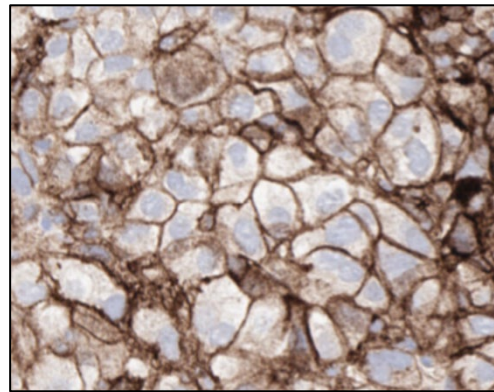
PD-L1 tumor score

Pre-treatment



10%

On treatment

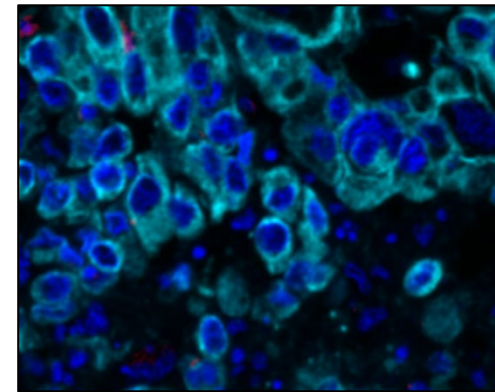


75%

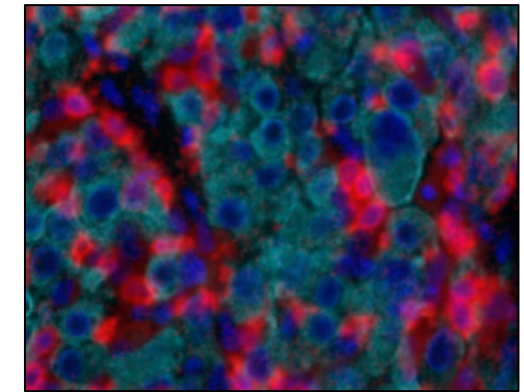
Increased tumor cell surface PD-L1
at 80 mg TNG260

Intra-tumoral cytotoxic T cells

Pre-treatment



On treatment



■ Tumor cells ■ Cytotoxic T cells

Increased tumor T cell infiltration
at 80 mg TNG260

TNG260 + pembrolizumab in checkpoint inhibitor refractory STK11-mutant non-small cell lung cancer

DOSE ESCALATION

Solid tumors with
STK11 mutation

DOSE EXPANSION (ongoing)

STK11 mut
NSCLC cancer

PHASE 1/2 STUDY

- STK11 mutations associated with checkpoint inhibitor resistance in NSCLC
- 20% NSCLC is STK11-mut
- Enrolling dose expansion at 80 mg QD
- Clinical data 2H 2025

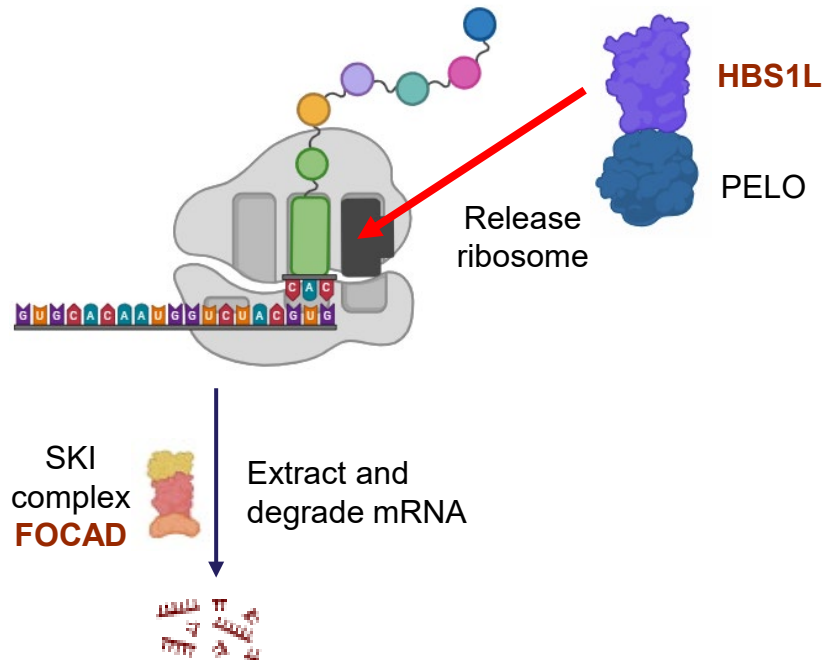
Parekh, D., et al. J. Clin. Oncol. 42, 8032 (2024)

TNG961

HBS1L degrader for FOCAD-del cancers

FOCAD deletion occurs in 20-40% of MTAP-del cancers

HBS1L degradation and FOCAD deletion are synthetic lethal



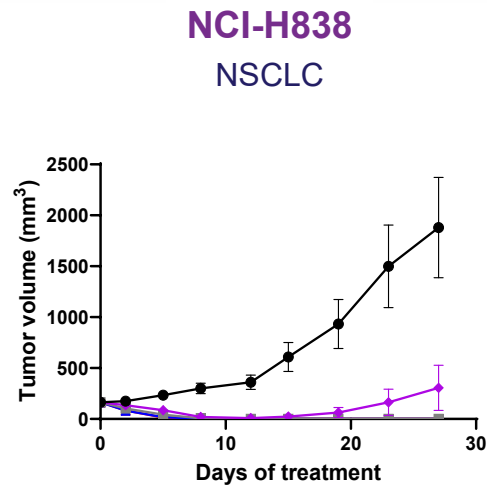
FOCAD-del cancers require HBS1L for protein production

TNG961 is a potential first-in-class HBS1L degrader

- ~7% non small cell lung cancer is FOCAD-del
- FOCAD deletion accurately detected by IHC
- All FOCAD-del cancers also have MTAP-deletion
- Potential for single agent and TNG462 combination activity

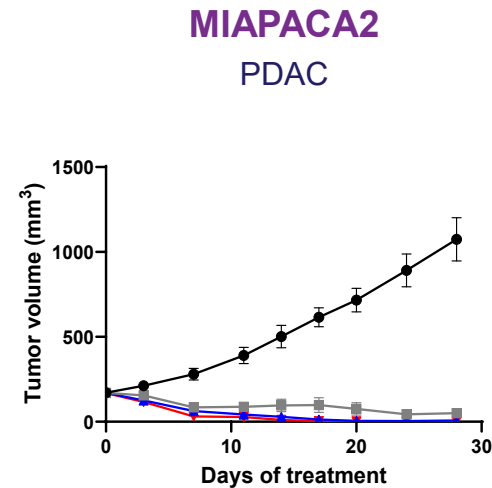
TNG961 drives tumor regression in FOCAD-del preclinical models

Strong xenograft activity across lineages



● Vehicle BID
◆ 2 mpk BID
■ 6 mpk BID
▲ 20 mpk BID
▼ 60 mpk BID

} TNG961



● Vehicle BID
■ 6 mpk BID
▲ 20 mpk BID
▼ 60 mpk BID

} TNG961

TNG961

- Potent and selective HBS1L degrader
- IC50 110 nM
- 100X selectivity for FOCAD del vs WT cells
- IND-enabling studies ongoing

FINANCIAL HIGHLIGHTS AND MILESTONES

Multiple projected key milestones and strong balance sheet

Clinical milestones

- TNG456 phase 1/2 trial enrollment 2Q 2025
- TNG462 clinical data update 2H 2025
- TNG462 + daraxonrasib and TNG462 + zoldonrasib (Revolution Medicines) enrollment 2Q 2025
- TNG260 clinical data 2H 2025

Cash balance

- \$217M cash, cash equivalents and marketable securities as of March 2025
- Cash runway 1Q 2027



TANGO
therapeutics™