The next wave of targeted therapies in oncology

Corporate Overview

January 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 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. 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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

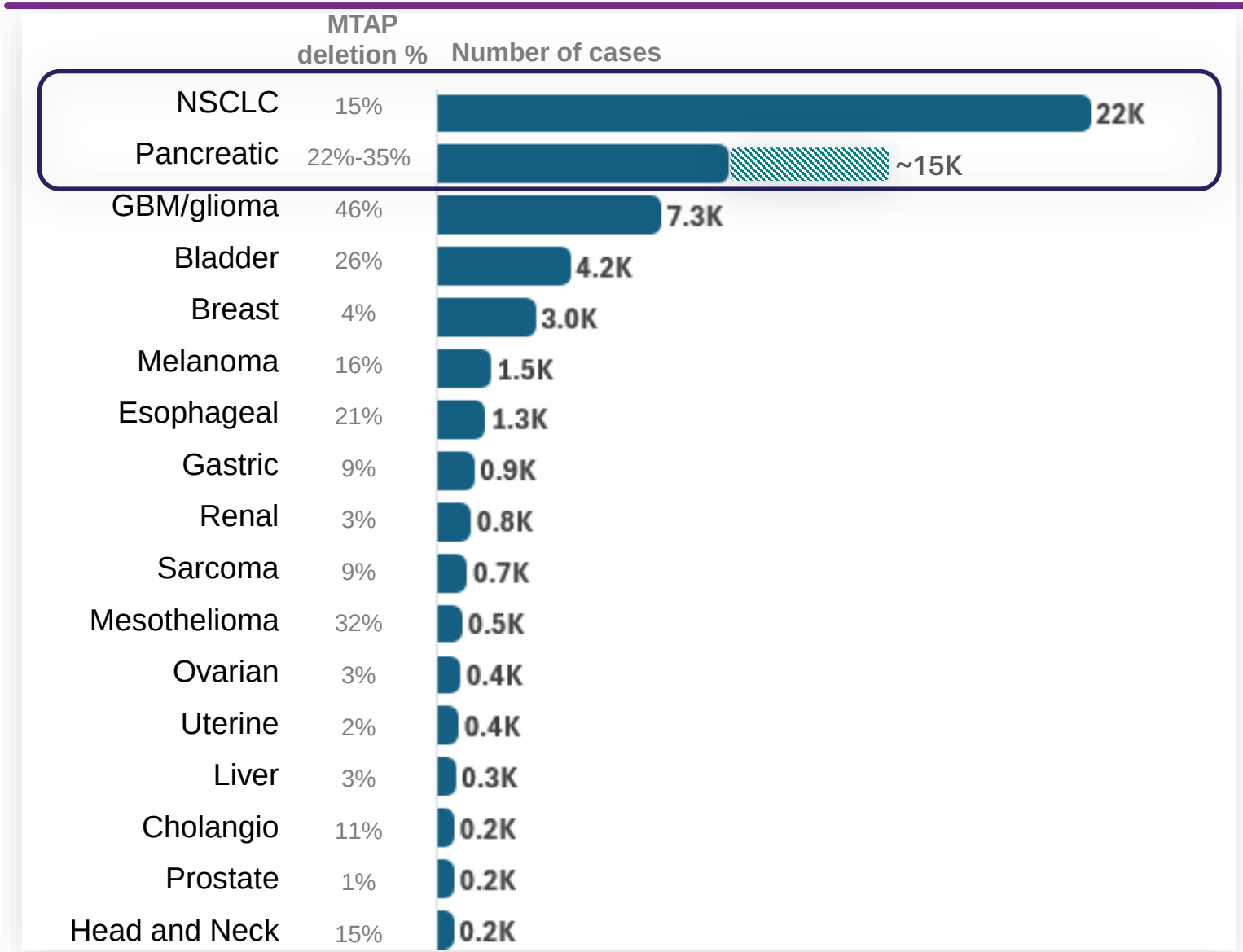
First-in-class oral CoREST inhibitor

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)



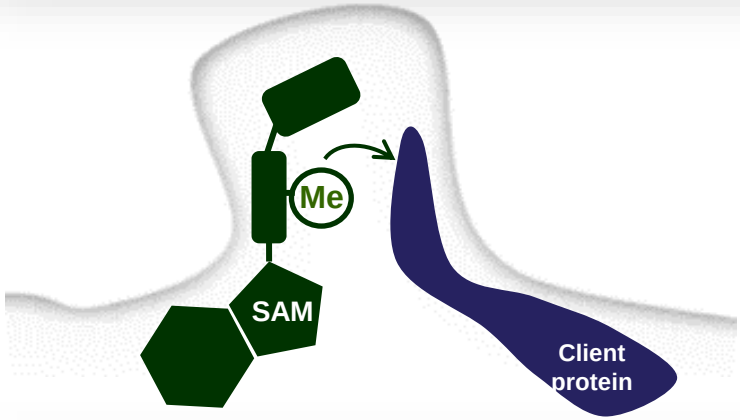
Large unmet need

- 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

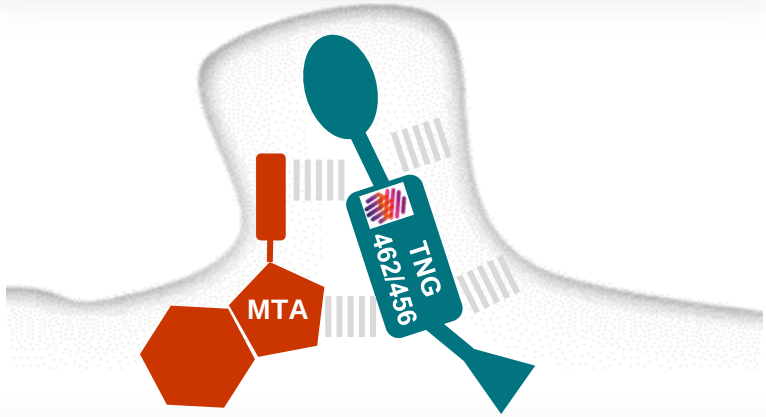
Normal cells



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



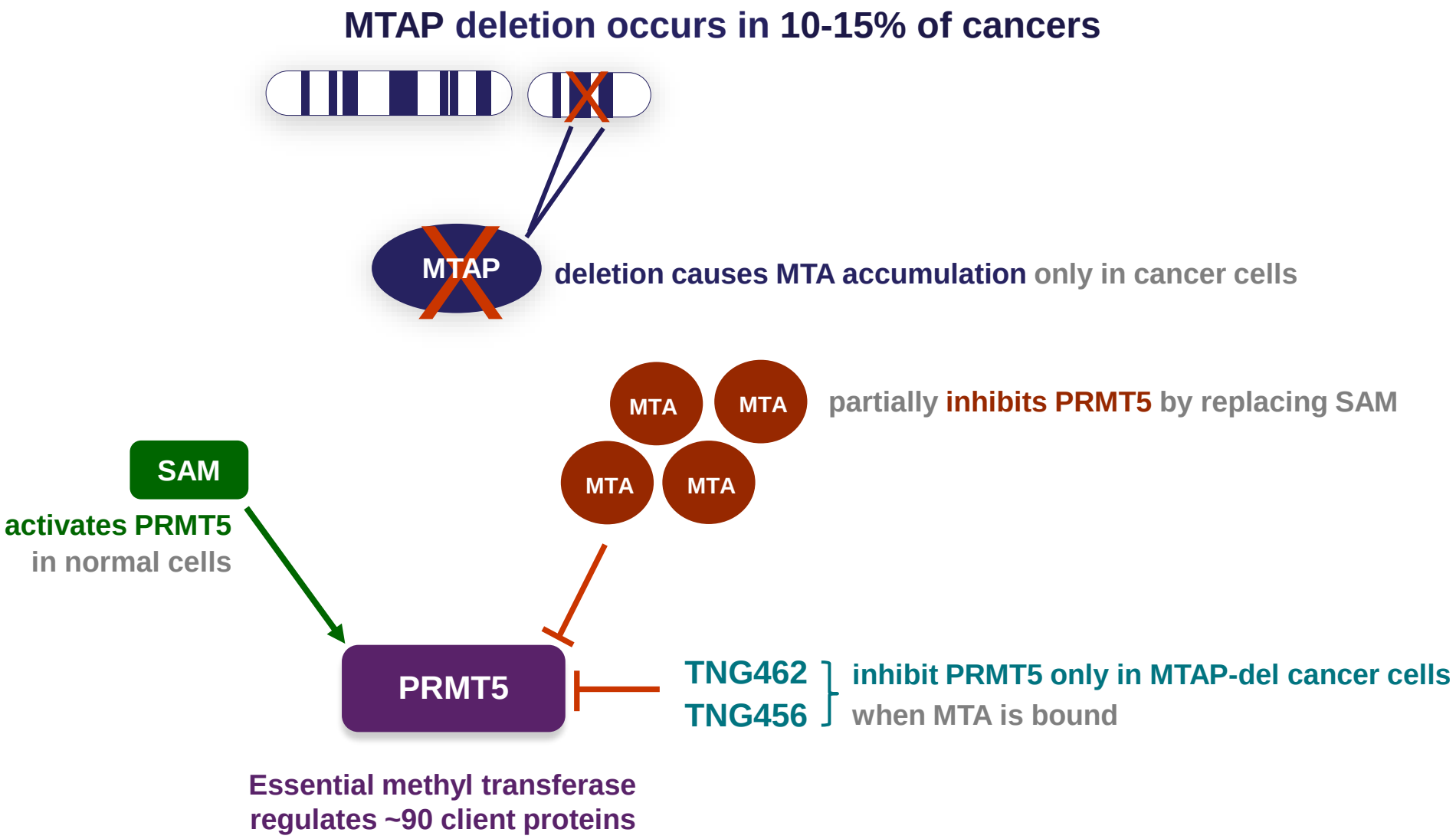
Inactive PRMT5

- 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

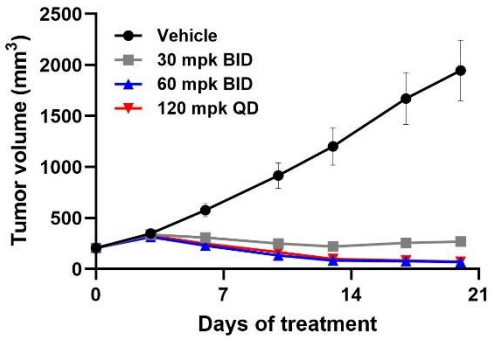


Tango PRMT5 inhibitors have superior preclinical efficacy

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

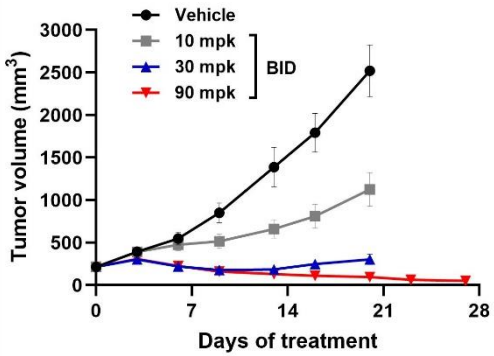
Tango PRMT5 inhibitors

TNG462



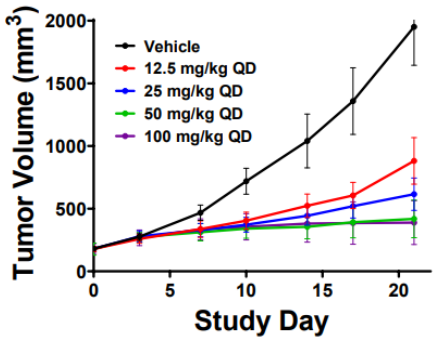
Deep tumor regression

TNG456



Deep tumor regression

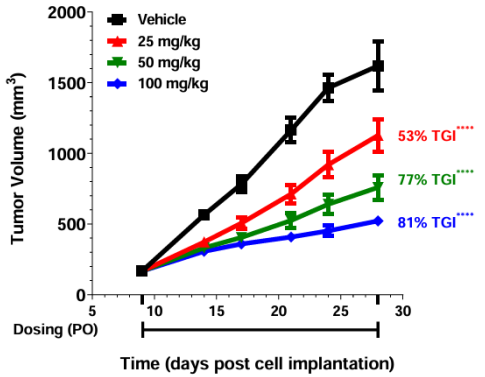
MRTX1719



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

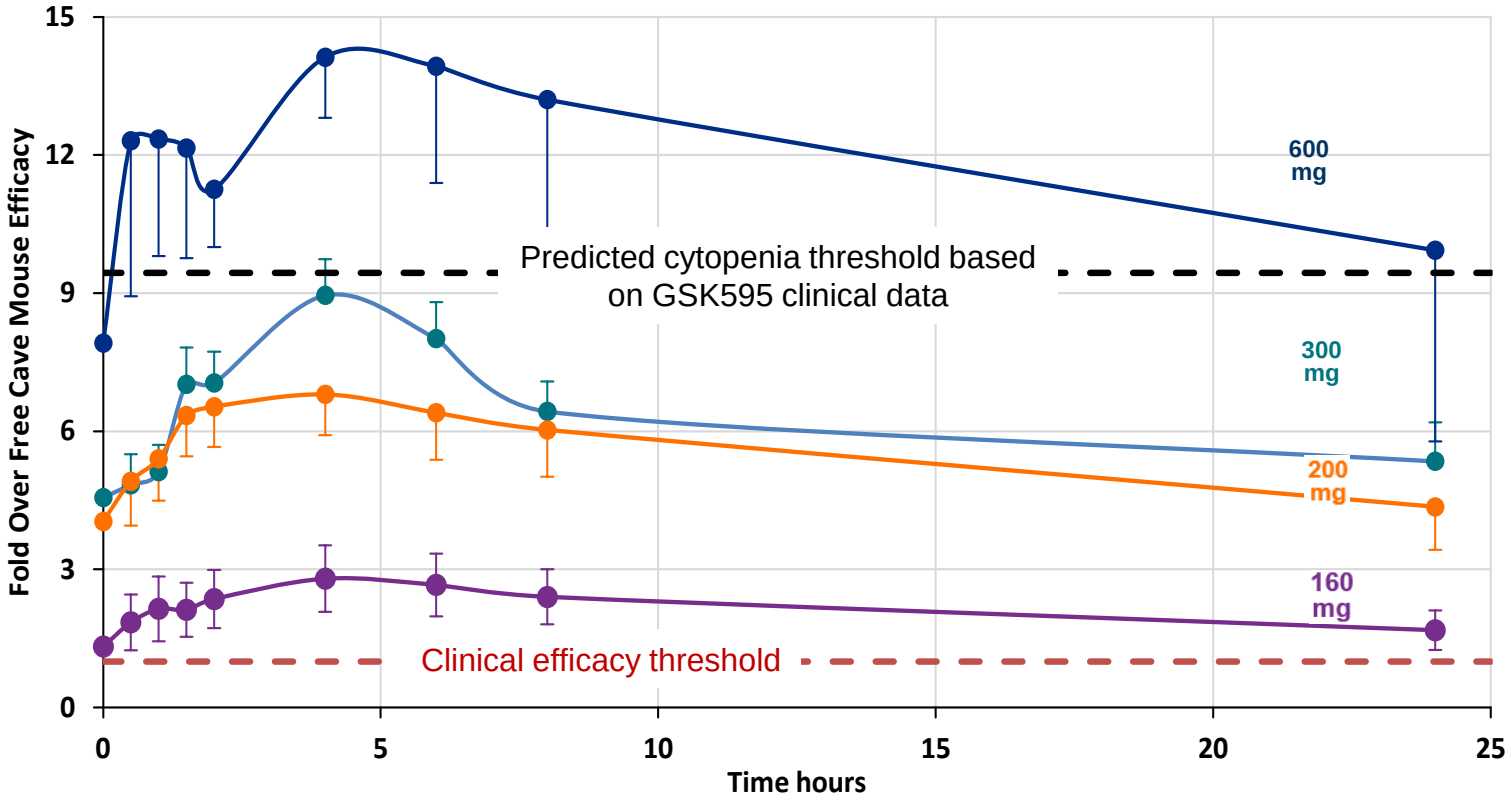
- RECIST partial responses in multiple tumor types, including NSCLC and pancreatic cancer*
- Median time to RECIST response 16 weeks
- 24 weeks mPFS in escalation cohort (AMG193 16 weeks, BMS not disclosed)
- Data continue to mature, with longest follow up in cholangiocarcinoma subset
  - 43% TNG462 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



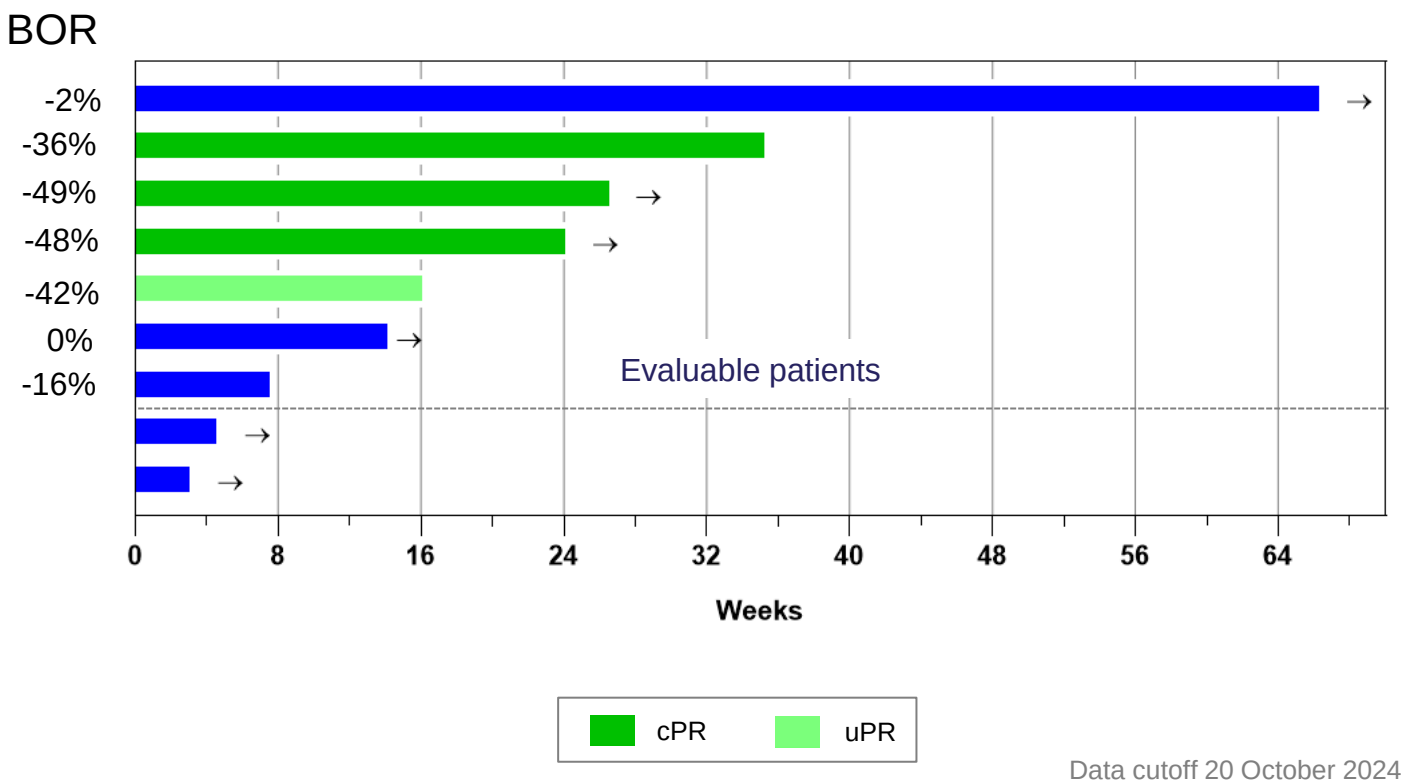
Dose limiting cytopenias observed

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

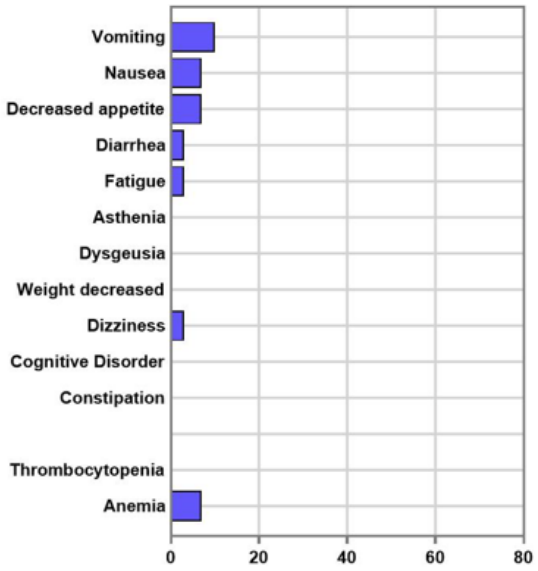
Key points

- 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

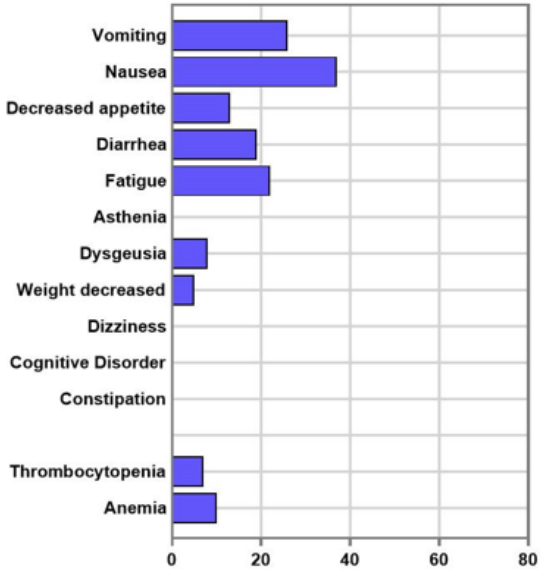
TNG462 200 mg*



0/30 dose reductions (0%)

No thrombocytopenia
Minimal nausea and fatigue
No dysgeusia

BMS-504 200-600 mg

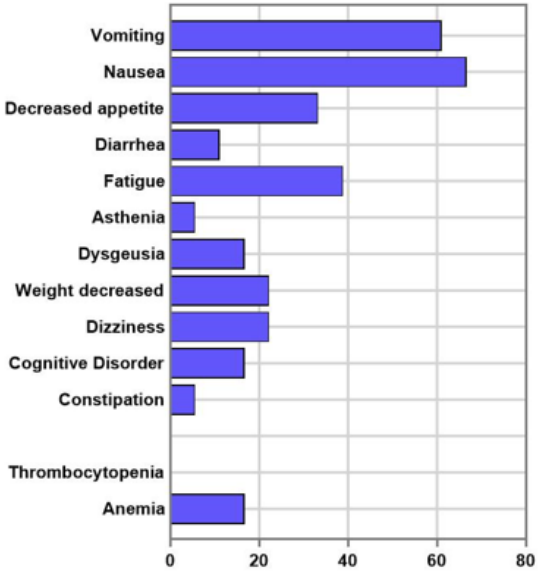


Dose reductions unknown

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)

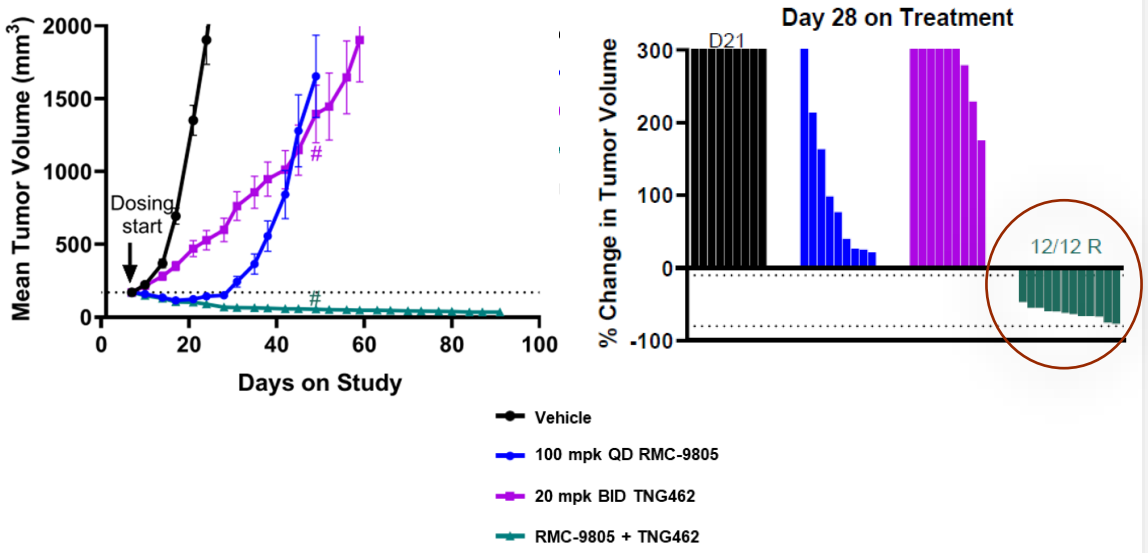
Targeting RAS-mut/MTAP-del cancers in collaboration with Revolution Medicines

- 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

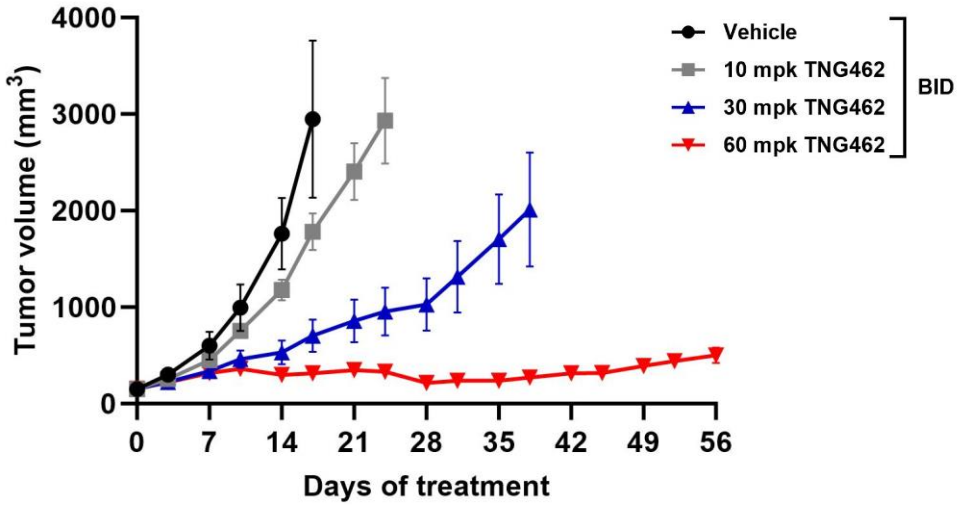
KP4
MTAP-null, KRAS^{G12D} PDAC CDX



*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

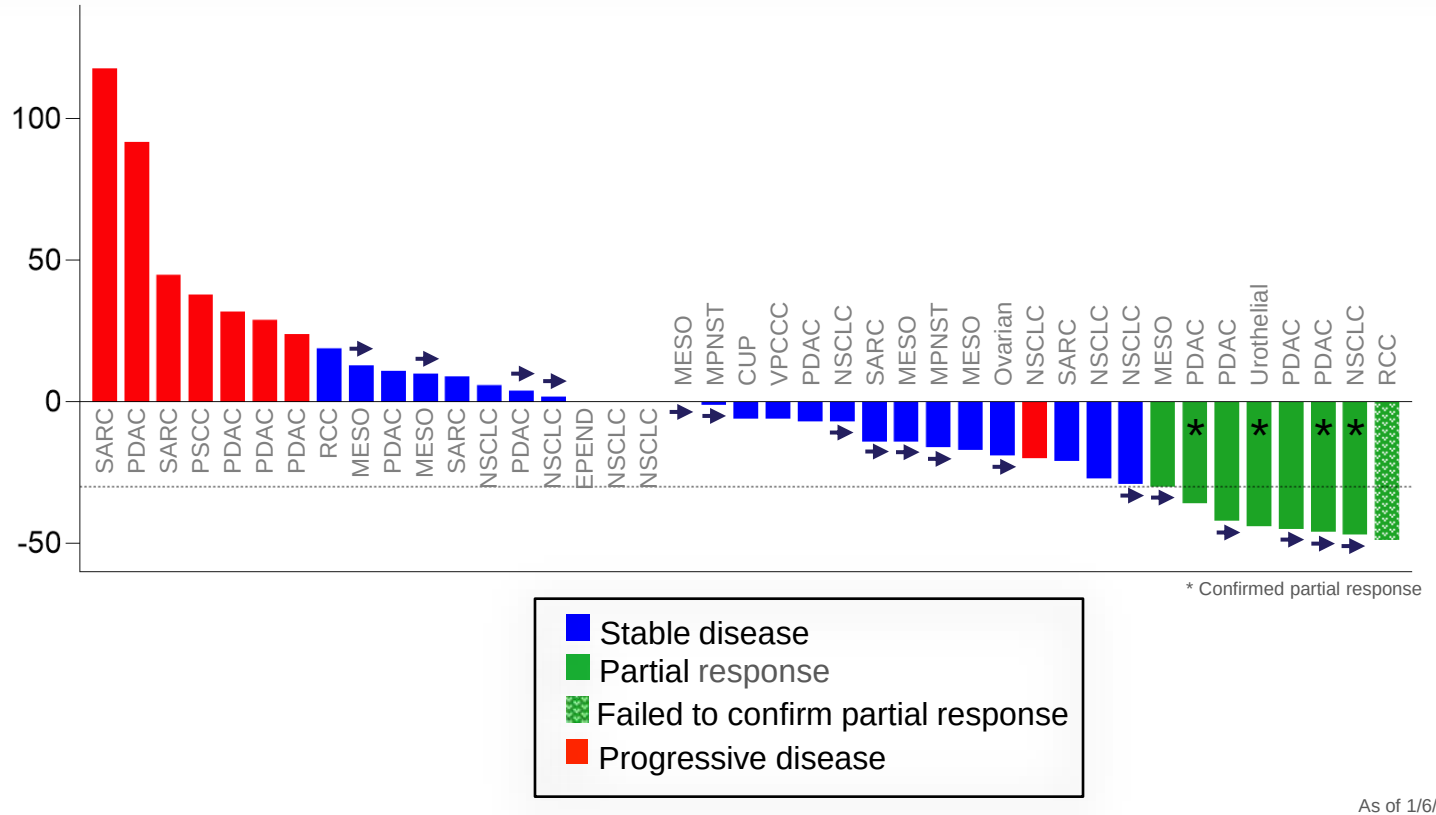
- 33 patients enrolled, 23 evaluable at active doses
- Median time on study less than 8 weeks
- CSF exposure ~30% of plasma exposure is below efficacy threshold

* 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

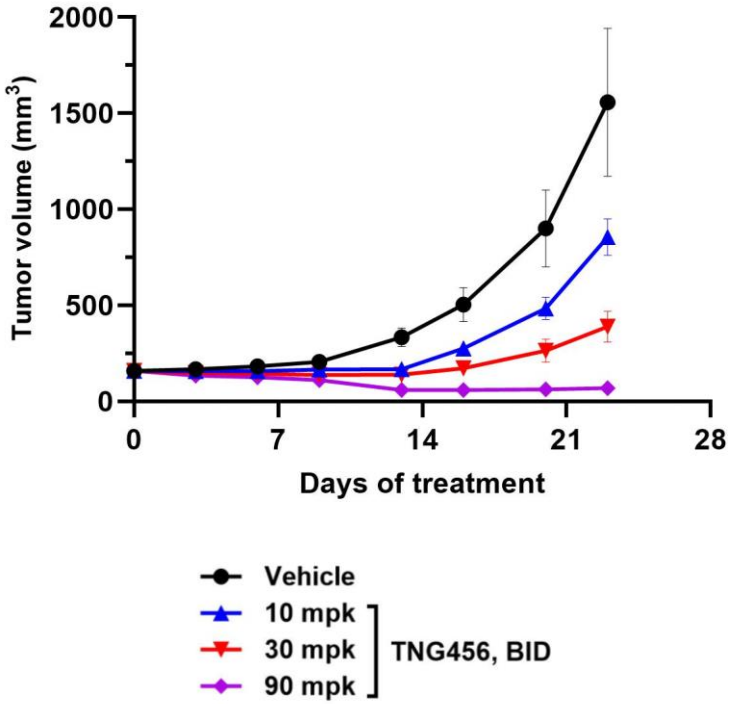
- Enhanced potency and MTAP selectivity
- Predicted CNS exposure well above efficacy threshold
- Key indication for development - MTAP-deleted glioblastoma (7,000 patients/yr US)
- First patient dose planned 1H2025

	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

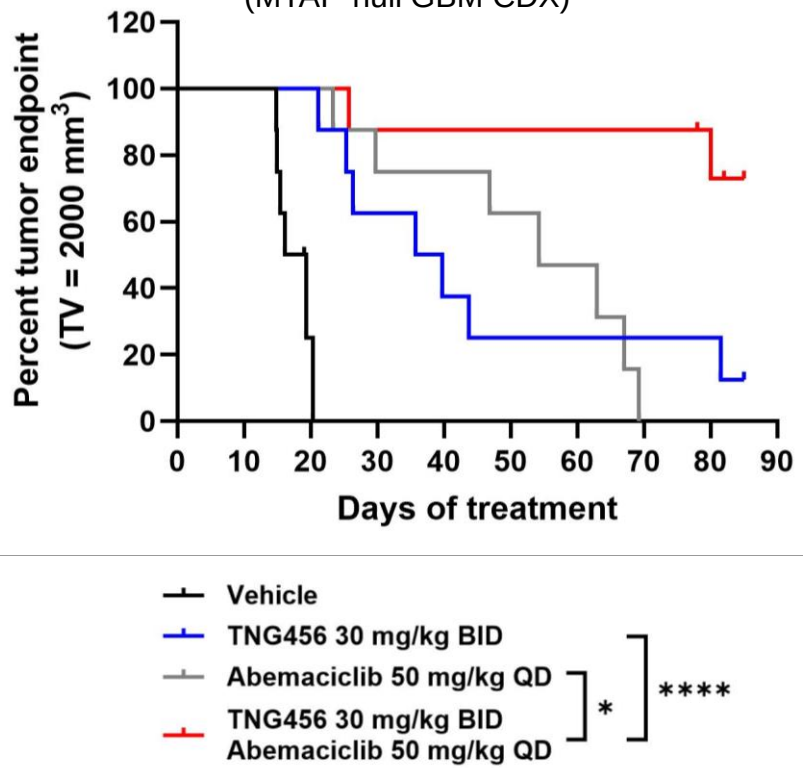
TNG456 monotherapy

U87MG
(MTAP-null GBM CDX)



TNG456 + abemaciclib drives additional survival benefit

U87MG
(MTAP-null GBM CDX)

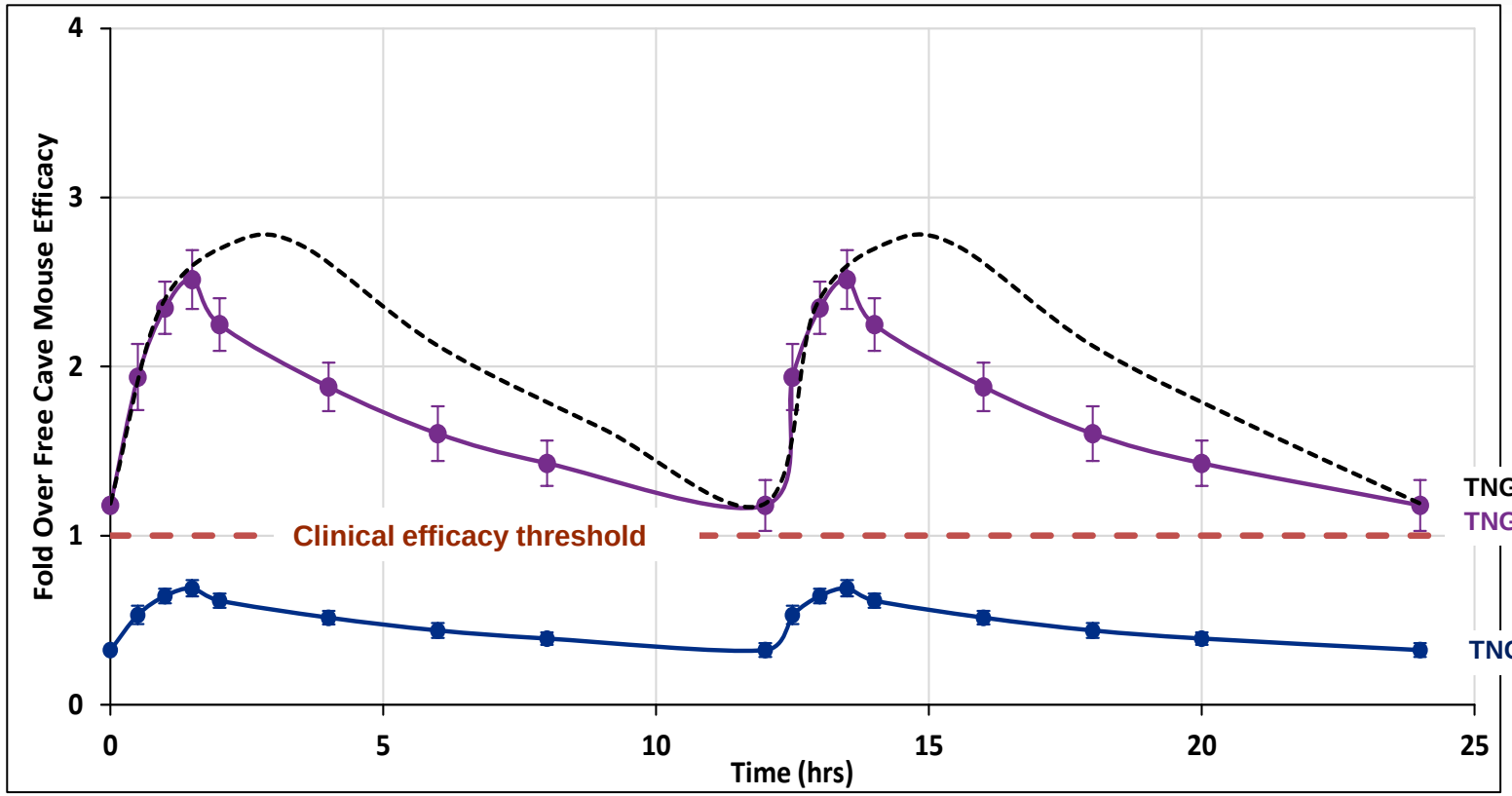


Summary

- 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

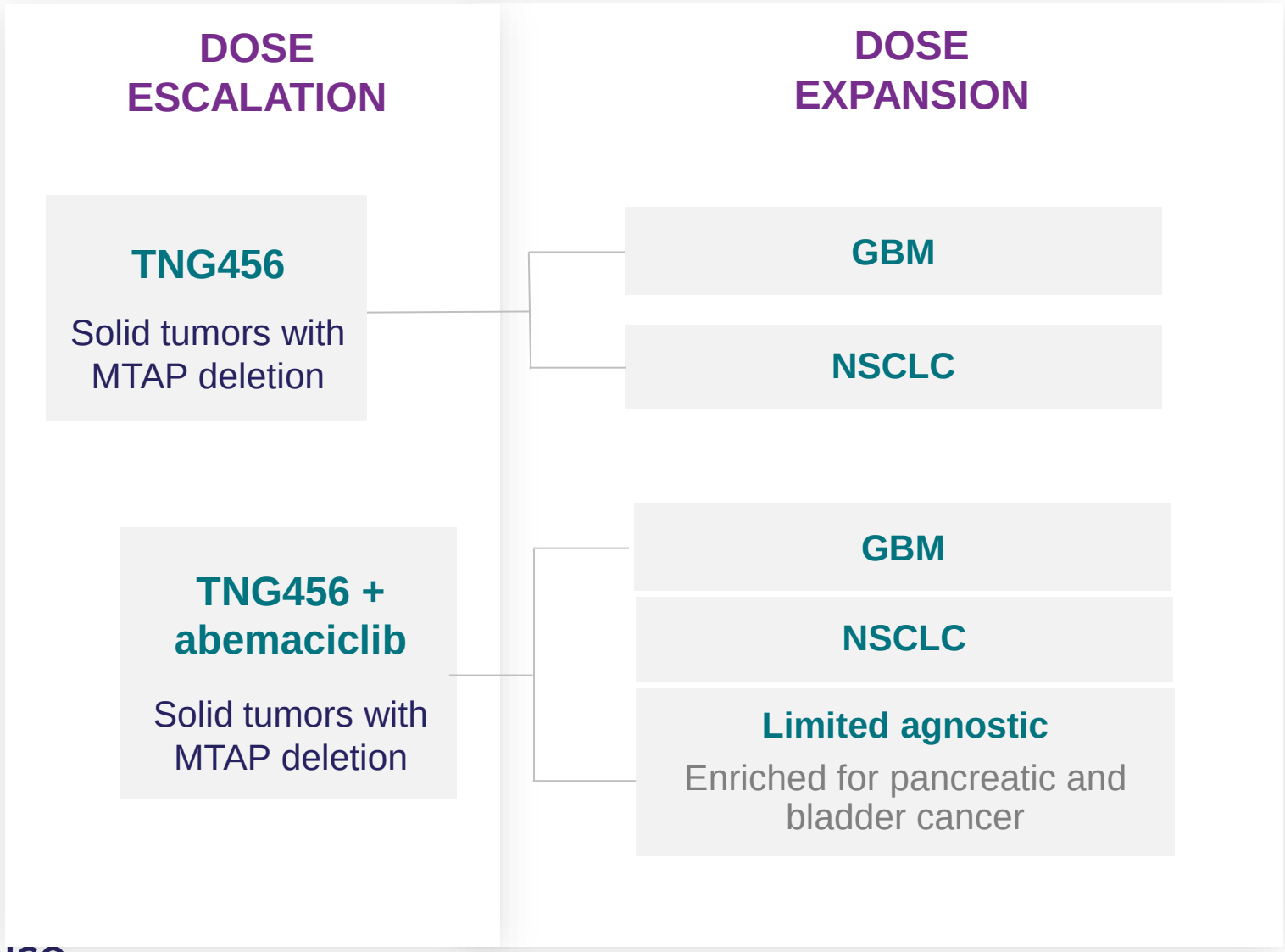
Steady-state clinical exposure in plasma and CSF



- 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

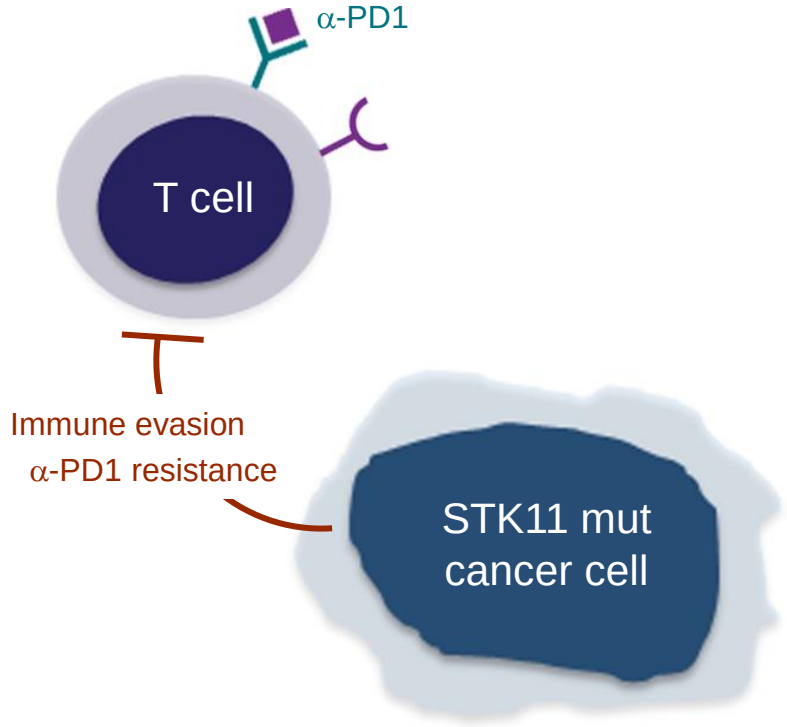
- Monotherapy dose escalation to begin 1H2025
- Combination with abemaciclib planned 2H2025 (pending monotherapy data)

TNG260

CoREST inhibition in STK11-mutant cancers

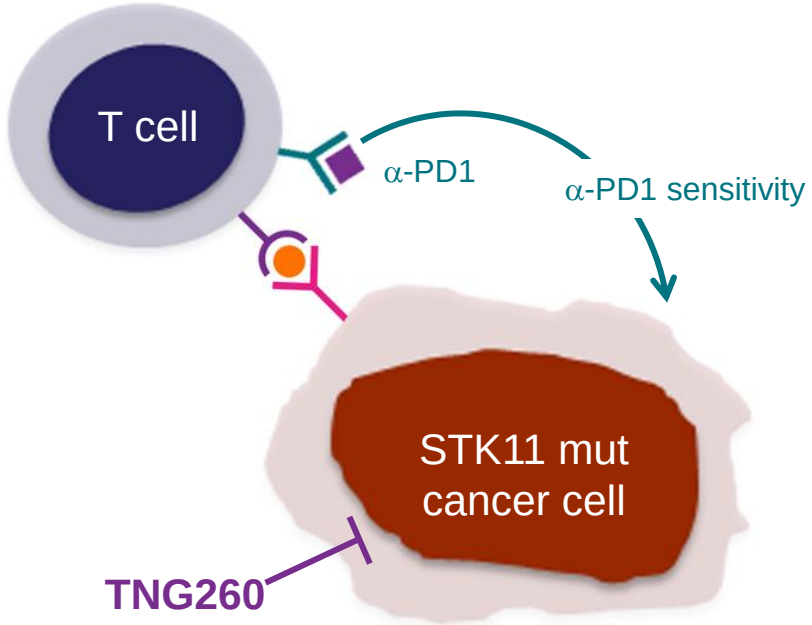
TNG260 reverses immune evasion caused by STK11 mutations

Immune evasion driven by tumor suppressor gene loss



STK11 re-activation is not feasible

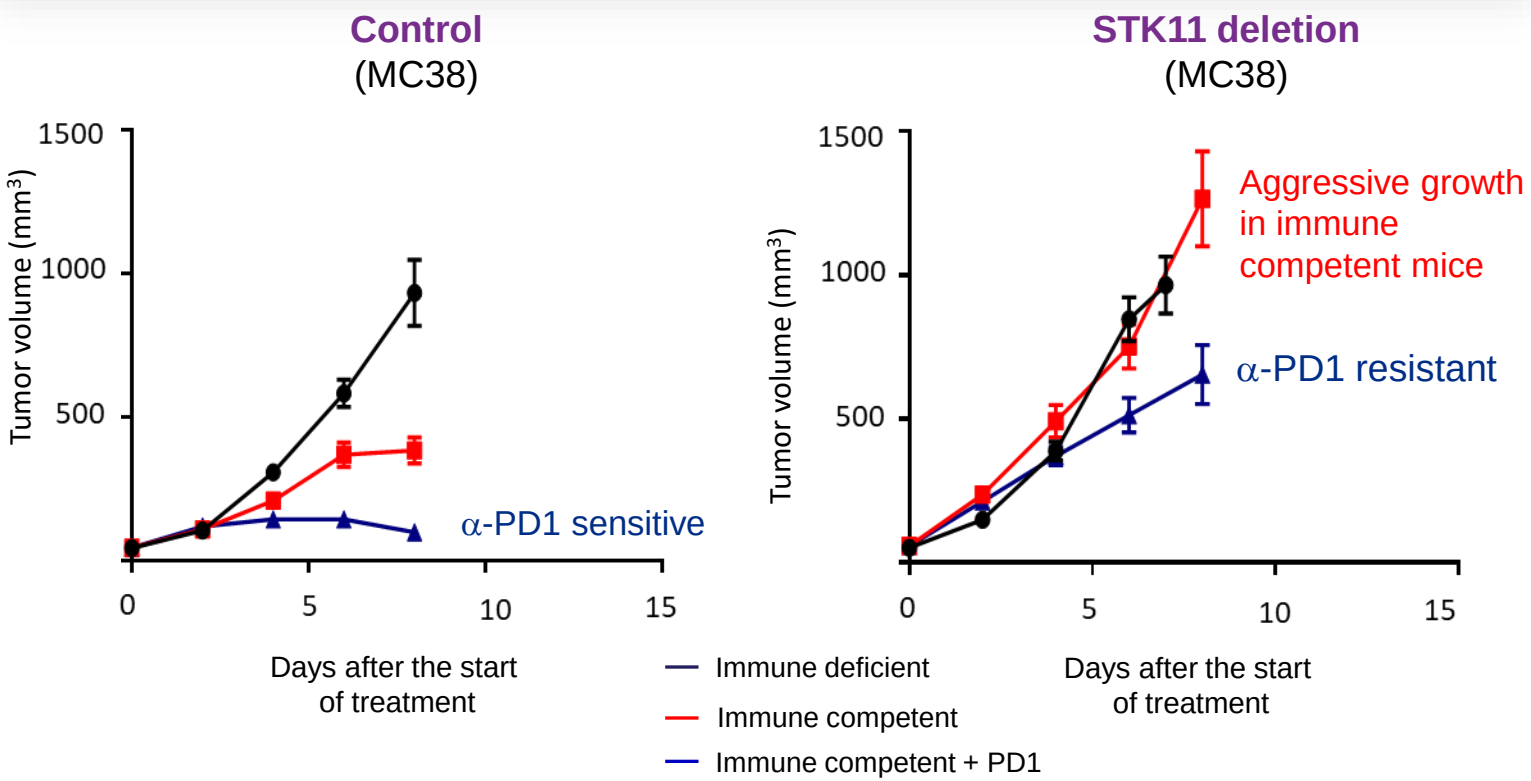
TNG260 reverses tumor-intrinsic immune evasion



Selective CoREST inhibition in cancer cells enables immune-mediated cytotoxicity

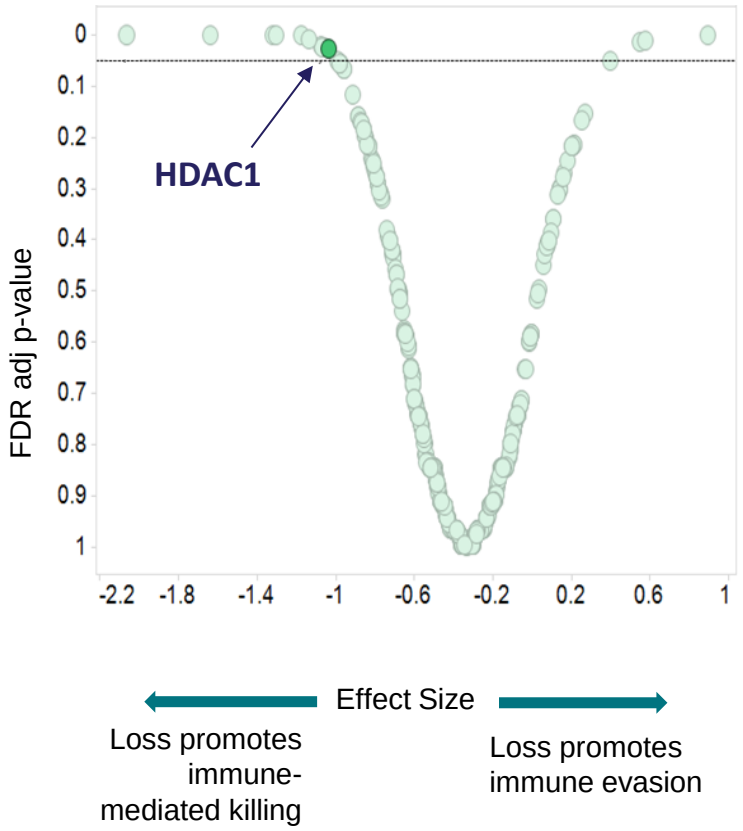
STK11 loss-of-function mutations drive immune evasion

STK11 deletion causes α-PD1 resistance

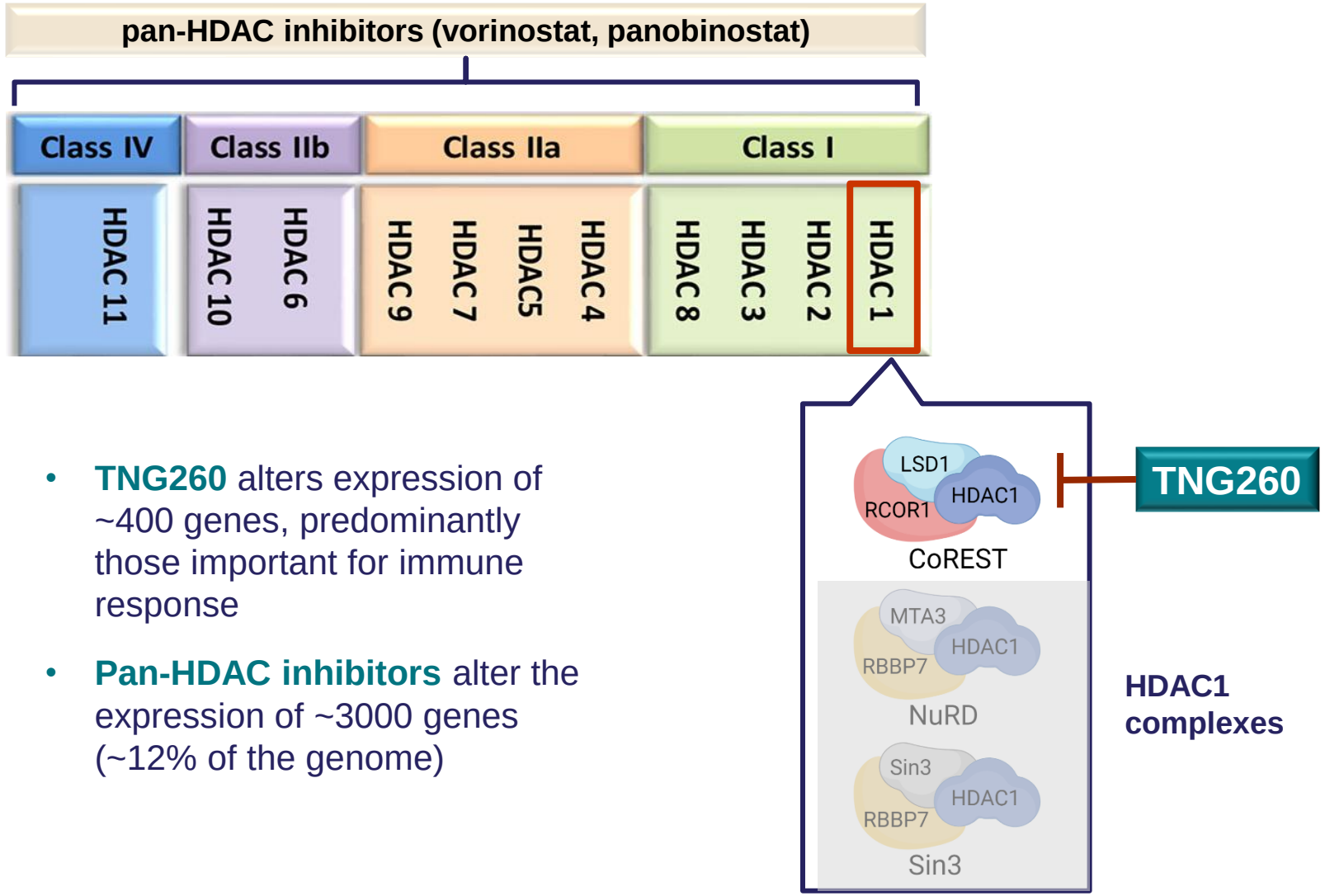


STK11 loss-of-function mutations are associated with clinical immune checkpoint inhibitor resistance

In vivo CRISPR screening identifies mediators of immune evasion reversion



TNG260 is a highly selective CoREST complex inhibitor



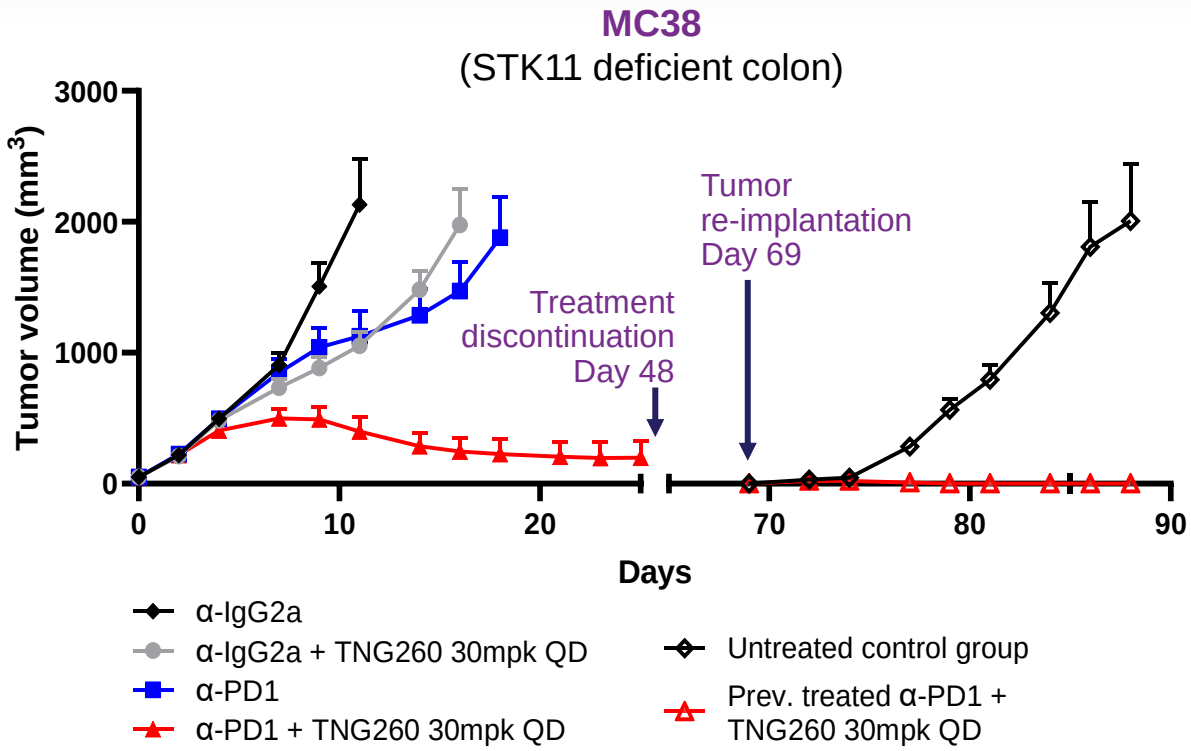
- **TNG260** alters expression of ~400 genes, predominantly those important for immune response
- **Pan-HDAC inhibitors** alter the expression of ~3000 genes (~12% of the genome)

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

DOSE ESCALATION

- Any solid tumor with STK11 mutation

DOSE EXPANSION (ongoing)

STK11 mut NSCLC cancer

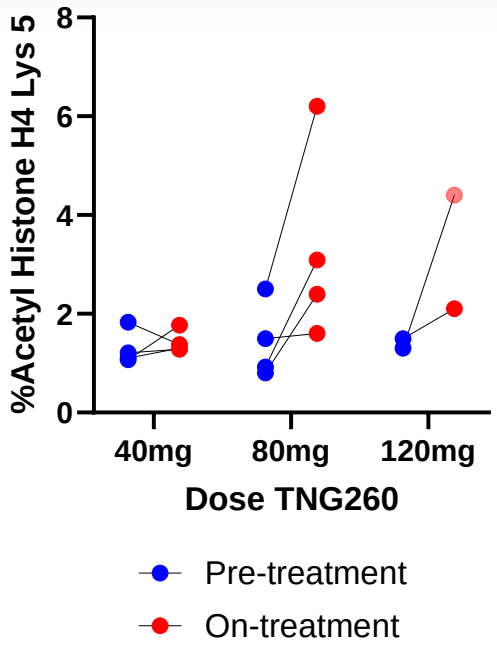
STK11 mut histology-agnostic cohort

PHASE 1/2 STUDY

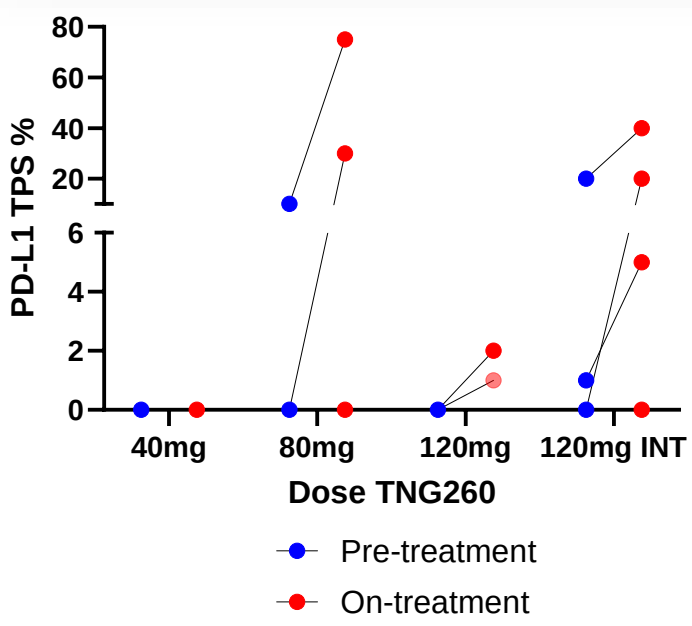
- STK11 mutations occur in ~15% NSCLC, 15% cervical, 10% carcinoma of unknown primary, 5% breast and 3% pancreatic cancers
- Combination with pembrolizumab to assess safety, PK/PD and efficacy as primary endpoints
- FDA Fast Track designation

TNG260 proof-of-mechanism in phase 1 study

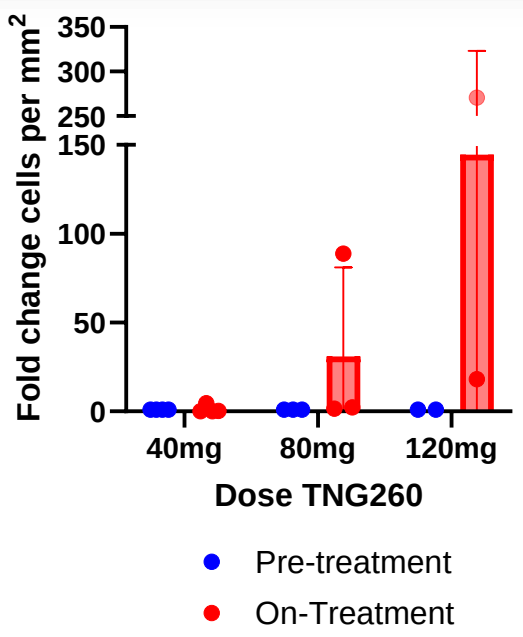
Increased histone acetylation



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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