Targeting tumor suppressor loss

to unmask vulnerabilities in cancer
for the next generation of precision medicines

Corporate Overview

June 2022

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 and development objectives for Tango's product pipeline. In some cases, you can identify forward-looking statements by terminology such as "may", "should", "expect", "intend", "will", "path", "achievable", "milestones", "goal", "forecast", "estimate", "anticipate", "believe", "predict", "potential" or "continue", or the negatives of these terms or variations of them or similar terminology. For example, statements concerning the following include or constitute forward-looking statements: Tango has a sustainable pipeline of novel drugs and drug programs; the Company's drug candidates planned for 2022; TNG908 is a potentially first in class PRMT5 inhibitor that is synthetic lethal with MTAP deletion; Company has a cash runway through 2H 2024; the expected timing of: (i) development candidate declaration for certain targets, (ii) initiating IND-enabling studies; (iii) filing INDs, (iv) clinical trial initiation and (v) the release of preliminary and final safety and efficacy data from clinical trials; the Company has a sustainable precision oncology pipeline of novel targets; the anticipated benefits of synthetic lethal drugs; expected timing of first patient dosed and timing of initial clinical data for TNG908; there is a clear path to clinical POC in MTAP-null solid tumors with multiple histologies; potential for histology-agnostic registration for PRMT5 inhibitor with broad based activity across tumor types; planned expansion cohort of the TNG908 phase 1/2 clinical trial for glioblastomas; TNG908 may be more effective than non-brain penetrant molecules in patients with brain metastases; TNG908's large therapeutic index expected to allow selection of optimal efficacious dose below MTD; the Company will be pursuing novel combination therapies with inhibitors that have a complementary mechanism of action; projected dose escalations in TNG908 phase 1/2 study; TNG908 expected to be brain penetrant in clinical study; TNG462 is potential best-in-class PRMT5 inhibitor (and has potential for broader and deeper clinical activity); the clinical development plan for PRMT5 franchise therapies; one of the largest genetically defined patient populations may benefit from the PRMT5 franchise; future clinical trial designs; the Company's belief regarding a strong IP position for USP1 pipeline product; synergy of USP1 in both PARP-sensitive and -resistance models suggests potential to meaningfully expand patient benefit from PARP inhibitors; Tango has sufficient cash balance to fund operations into second half of 2024 (and is sufficient to achieve multiple projected key milestones); the potential clinical benefit of KRAS inhibitor and TNG908 in MTAP null lung adenocarcinoma; potential for future TNG908 expansion cohorts to evaluate activity in a range of histologies and optionality for multiple registration strategies; Tango is planning multiple rational combination trials in PRMT5 franchise based on strong pre-clinical synergy data; the TNG908 composition of matter patent applications will provide meaningful patent protection through at least 2041; and the anticipated benefits of future product candidates including those identified in the future through the Tango discovery platform. 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 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 (and may utilize cash resources more quickly than anticipated); Tango has limited experience with conducting clinical trials (and will rely on a third party to operate the clinical trial for TNG908) and may not be able to commence the clinical trial or dose patients when expected and may not generate results in the anticipated timeframe (or at all); the benefits of Tango pipeline products and potential combination therapies that are seen in pre-clinical 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 combination therapies); Tango has incurred significant operating losses and anticipates continued losses for the foreseeable future; we will need to raise capital in the future and if we are unable to raise capital when needed or on attractive terms, we would be forced to delay, scale back or discontinue some of our development programs or future commercialization efforts; we may be unable to advance our 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; 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 limited resources to pursue a particular product candidate or indication 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; our products 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; 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 the COVID-19 pandemic. 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 fiscal year ended December 31, 2021 as filed with the SEC on March 28, 2022. 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.

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COMPANY OVERVIEW

Tango summary

Precision oncology company based on synthetic lethality, combining discovery and clinical development in the same genetic context

Expanding oncology target space into tumor suppressor gene loss with a productive, state-of-the-art discovery platform

Sustainable pipeline of novel drug programs for cancers with specific tumor suppressor gene

Multiple development candidates declared in 2022

A novel synthetic lethal PRMT5 inhibitor for MTAP-deleted cancers in the clinic and a next generation molecule in IND-enabling studies

A novel synthetic lethal inhibitor targeting STK11-induced immune evasion in IND-enabling studies

Broad strategic collaboration with Gilead based on immune evasion effects of tumor suppressor gene loss

Management team with deep expertise in cancer genetics, drug discovery, clinical development

Cash runway through 2H 2024

Leaders in drug discovery, cancer biology, functional genomics and translational medicine

LEADERSHIP

Barbara Weber, MD
CEO

Alan Huang, PhD
CSO

Daniella Beckman
CFO

Charles Davis, PhD
Pharmaceutical Sciences

Doug Barry
General Counsel

John Ross
Human Resources

Heather DiBenedetto
Development Operations

Jannik Andersen, PhD
Biology

Bill Mallender, PhD
Biochemistry

John Maxwell, PhD
Chemistry

BOARD OF DIRECTORS

Alexis Borisy
Chairman

Lesley Calhoun

Aaron Davis

Reid Huber, PhD

Malte Peters, MD

Mace Rothenberg, MD

Barbara Weber, MD

Scientific advisors

In memoriam
1959-2021

José Baselga, MD PhD
Head of Oncology R&D
AstraZeneca

Alan Ashworth, PhD FRS
President
UCSF Cancer Center

Bill Kaelin, MD
Professor, Dana Farber
Cancer Institute

Antoni Ribas, MD PhD
Professor
UCLA

Ulrich Elling, PhD
Investigator
Institute of Molecular
Biotechnology, Vienna

John Doench, PhD
Institute Scientist
Broad Institute

Leaders in cancer genetics, synthetic lethality, CRISPR technology and immuno-oncology

A strong strategic partnership with Gilead

SCOPE	RESEARCH AND DEVLOPMENT	RIGHTS	SHARED ECONOMICS	DEAL TERMS
15 TARGETS IMMUNE EVASION 2 licensed, 2 option-extended to date	**TANGO** TARGET VALIDATION TO CLINICAL POC Funded by milestone payments during option extension	**TANGO** FULL RIGHTS RETAINED TO THREE LEAD PROGRAMS All new cell autonomous targets	**5 PROGRAMS** CO-DEVELOP AND CO-PROMOTE	**$125M** UPFRONT **$20M** EQUITY
$6B MILESTONES $410M/program Up to $110M through clinical POC	**GILEAD** MULTIPLE TIMEPOINTS TO LICENSE A PROGRAM	**GILEAD** LICENSE RIGHTS All immune evasion targets	**50/50** US PROFIT/LOSS ON CO-CO PROGRAMS	LOW DOUBLE DIGIT ROYALTIES

TANGO therapeutics

GILEAD

A sustainable precision oncology pipeline of novel targets

PROGRAM	PATIENT SELECTION	DISCOVERY	IND-ENABLING	CLINICAL TRIALS		ANTICIPATED MILESTONES
				Phase 1/2	Phase 3	
PRMT5 TNG908	MTAP-del cancers					Initial clinical data 1H 2023
PRMT5 TNG462						IND filing 1H 2023
TARGET 3* TNG260	STK11-mut cancers					IND filing 2023
USP1	BRCA1/2-mut cancers					Development candidate 2H 2022
Multiple synthetic lethal targets	Tumor suppressor gene loss					

Gilead options and licensed targets not listed

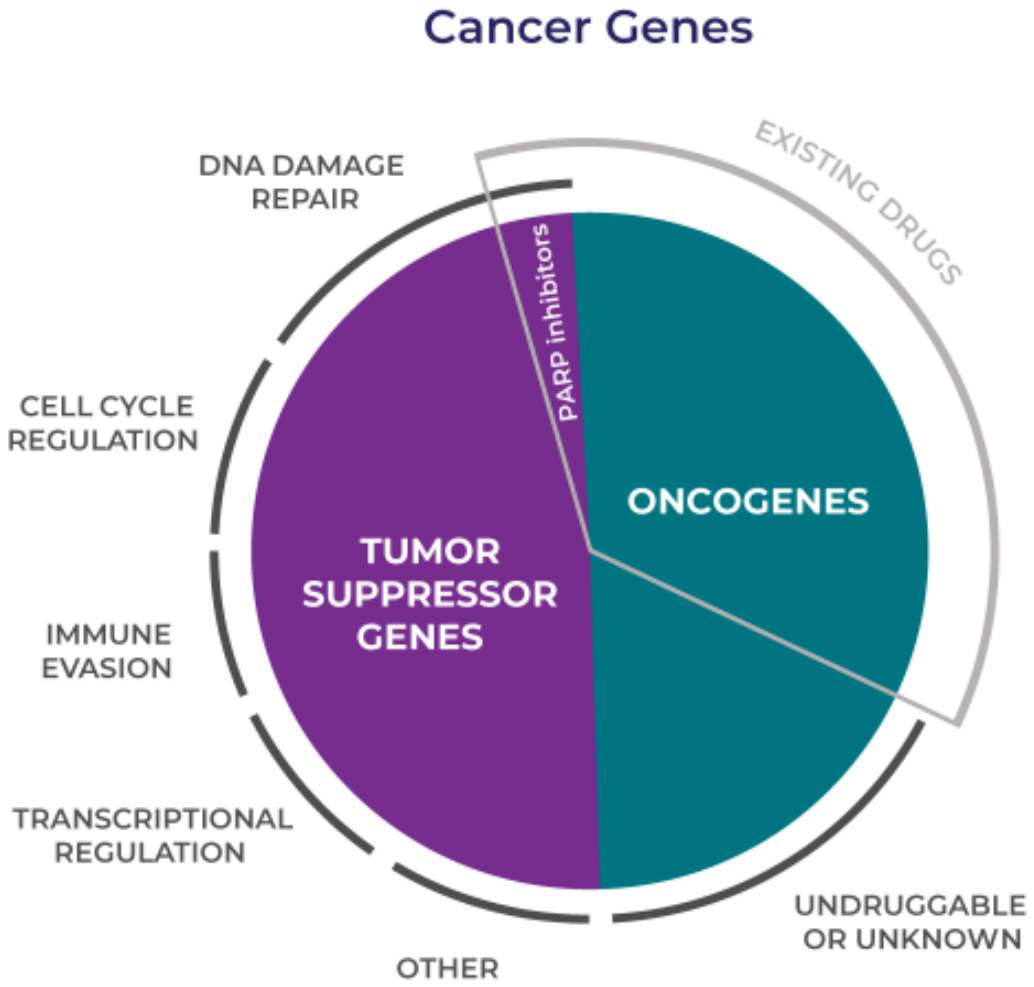
*Wholly-owned immune evasion program

SYNTHETIC LETHALITY FOR CANCER THERAPEUTICS

Most cancer targets are not drugged yet

TUMOR SUPPRESSOR GENES

- Important drivers of cancer inactivated or deleted in almost all human cancers
- Not directly druggable
- Indirectly targeted with synthetic lethality
- PARP inhibitors are the first examples of synthetic lethal targeting



SYNTHETIC LETHALITY

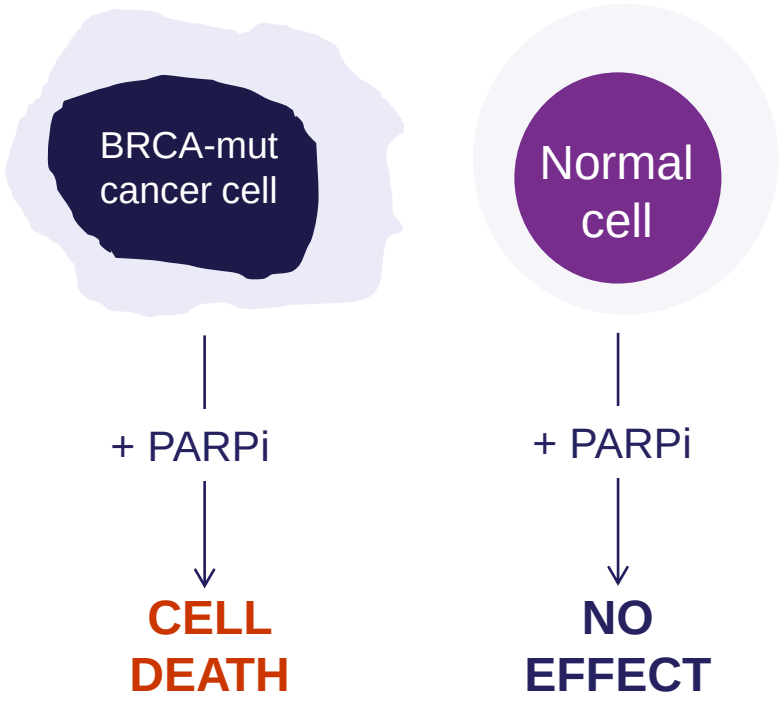
is currently the only way to target tumor suppressor gene loss

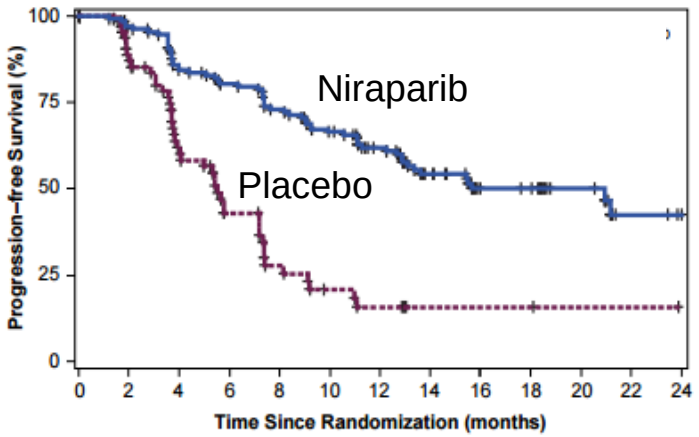
CRISPR TECHNOLOGY

makes large scale synthetic lethal discovery efforts feasible

PARP is the first synthetic lethal drug target

BRCA1/2 mutation and PARP inhibition are a synthetic lethal pair





PARP inhibitors are approved in BRCA mutant breast, ovarian, pancreatic and prostate cancer

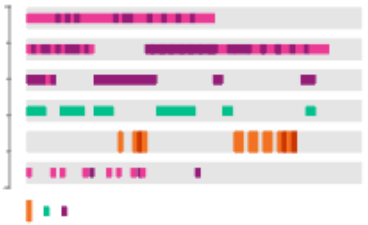
- PARP inhibitors are clinical validation for synthetic lethal drug targeting
- Synthetic lethal drugs inherently have a wide therapeutic index
- Multiple analyses suggest hundreds of synthetic lethal pairs exist in human cancer

A unique approach to target discovery and clinical development in the same genetic context

DISCOVERY AND DEVELOPMENT IN THE SAME GENETIC CONTEXT

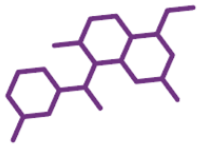
1 SELECT
cancer subtypes with high unmet need

2 DEFINE
genetic alterations in cancer subtype "genetic context"



3 IDENTIFY
drug targets dependent on genetic context for activity "context-specific"

4 DISCOVER
drugs against context-specific target



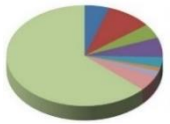
5 DEVELOP
drugs in same genetic context used for target discovery

A robust discovery platform linked to a precision medicine approach

NOVEL TARGET DISCOVERY

Multiple, highly optimized CRISPR systems

Combinatorial, T cell co-culture and *in vivo* genetic screens



Druggable genome, paralog and genome-wide CRISPR libraries

Efficient screening, actionable hits

Cancer genetics

Leveraging massive public data sets from Broad, NIH and Sanger Institute

Functional data

Proprietary genetic perturbation data from hundreds of CRISPR screens

COMPUTATIONAL ANALYSIS

TANDEM

Tango cancer dependency map

Sophisticated and proprietary

Linking large Tango and public datasets

Integrating target, genetic context & functional data

PRECISION MEDICINE

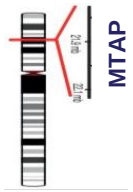
Cancer types with high unmet medical need

Genetic selection from the first patient dosed

Increased probability of meaningful clinical results

PRMT5 inhibition in MTAP-deleted cancers

Lead program is a potentially first-in-class synthetic lethal PRMT5 inhibitor



TNG908

MTA-cooperative PRMT5 inhibitor that is synthetic lethal with MTAP deletion that is blood-brain barrier penetrant

TNG462

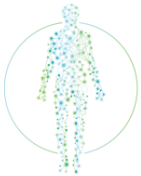
Next-generation MTA-cooperative PRMT5 inhibitor with enhanced potency and MTAP-selectivity

DIFFERENTIATED MECHANISM

Novel MTA-cooperative mechanism targeting tumor cells with MTAP deletion enables stronger target inhibition than non-selective PRMT5 inhibitors

LARGE PATIENT OPPORTUNITY

10-15% of all human cancers have MTAP deletion

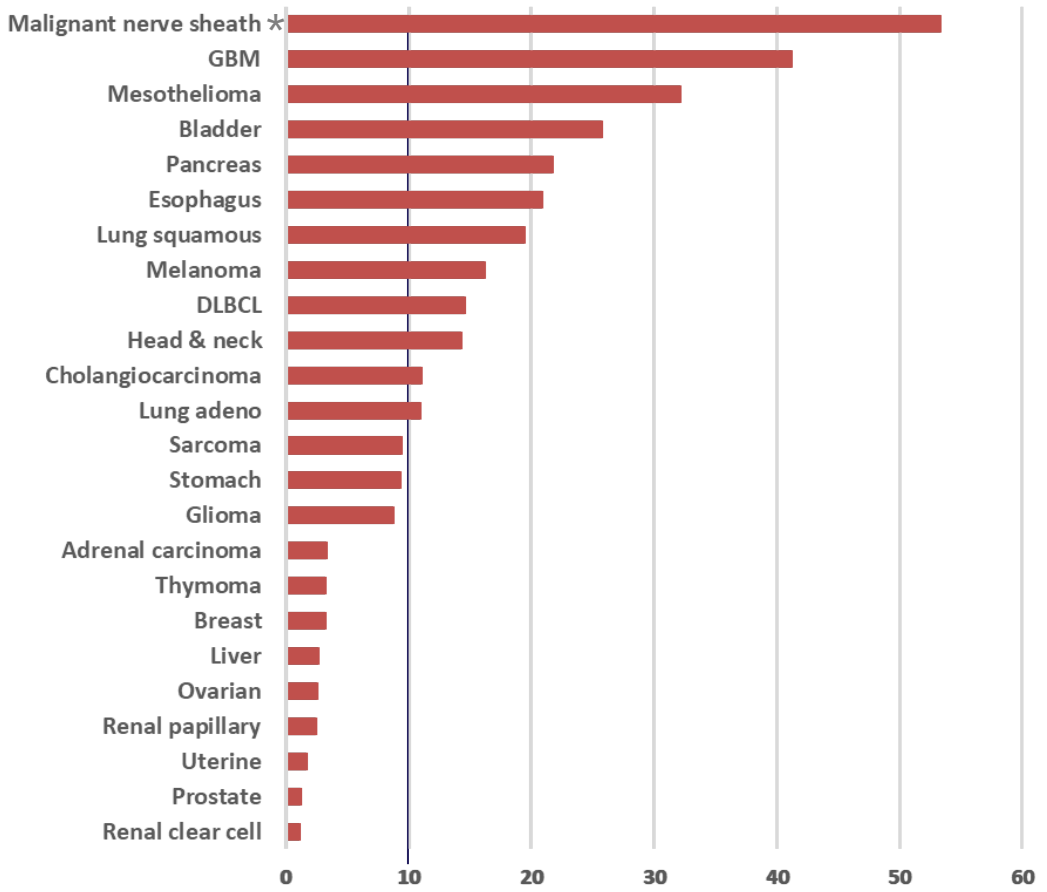


NEAR TERM MILESTONES

Phase 1/2 is open for enrollment, first patient dosed planned 2Q 2022, initial clinical data 1H 2023

10-15% of all human cancers are MTAP-null

MTAP DELETION FREQUENCY

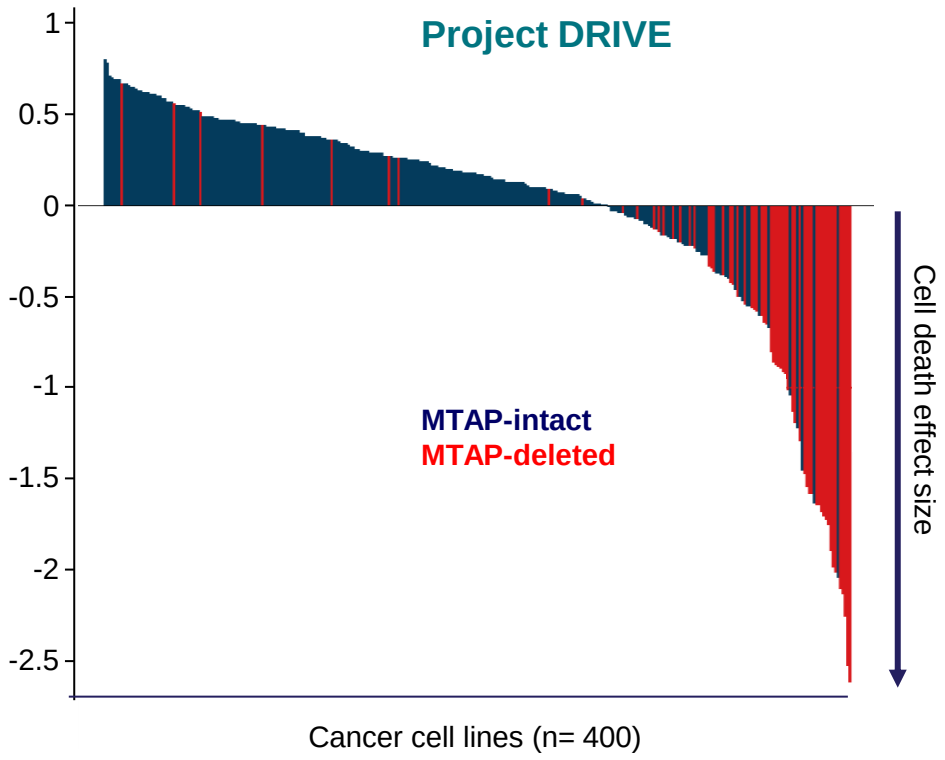


- MTAP co-deleted with tumor suppressor gene CDKN2A
- Clear path to clinical POC in MTAP-null solid tumors with multiple histologies
- Potential for histology-agnostic registration with broad-based activity across tumor types

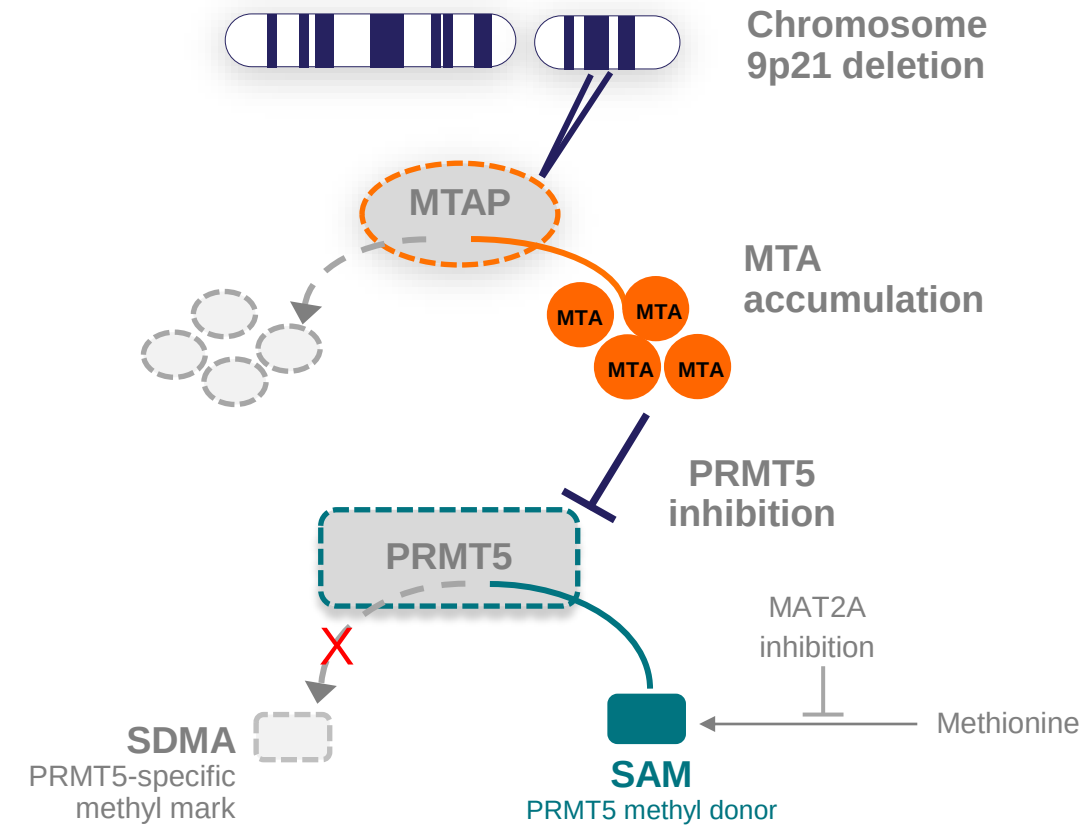
TCGA PanCancer Atlas
*Lee et al, Nature Genetics 2014

PRMT5 and MTAP are a synthetic lethal pair

MTAP-deleted cancer cell lines are sensitive to PRMT5 knockdown



MTAP deletion leads to PRMT5 inhibition

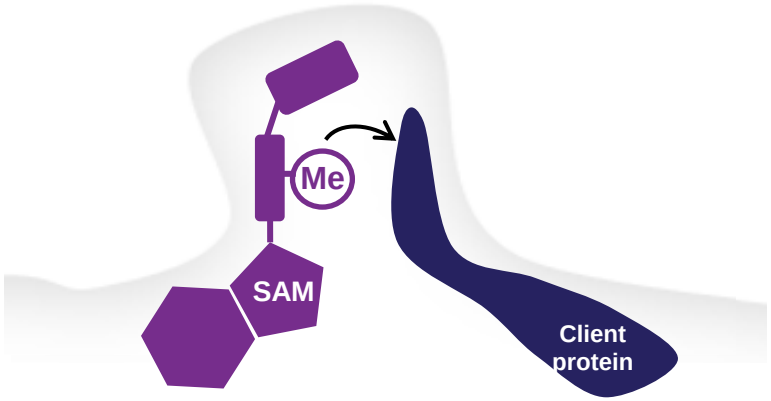


Mavrakis et al., Science 2016; Kryukov et al., Science 2016

TANGO therapeutics

TNG908 is an MTA-cooperative PRMT5 inhibitor that is synthetic lethal with MTAP deletion

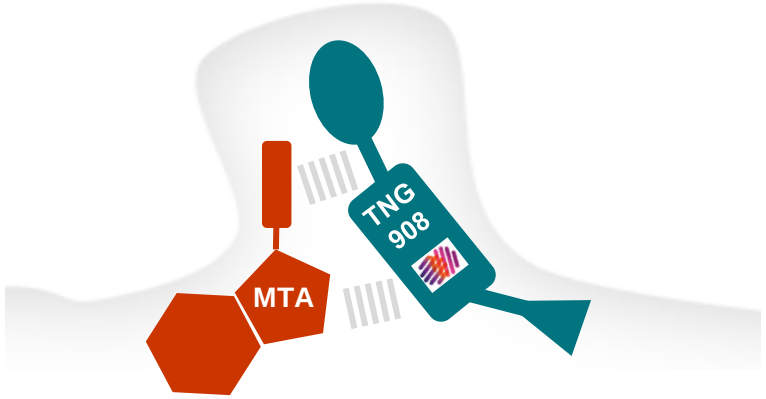
Normal cells



Active PRMT5

- Most PRMT5 in normal cells is bound to SAM
- PRMT5 requires SAM for activity
- Non-synthetic lethal PRMT5 inhibitors suppress PRMT5 equally in normal and MTAP-del cells

MTAP-deleted cancer cells



Inactive PRMT5

- Most PRMT5 in MTAP-deleted cells is bound to MTA
- MTA-bound PRMT5 is inactive
- Synthetic lethal PRMT5 inhibitors bind to the PRMT5-MTA complex

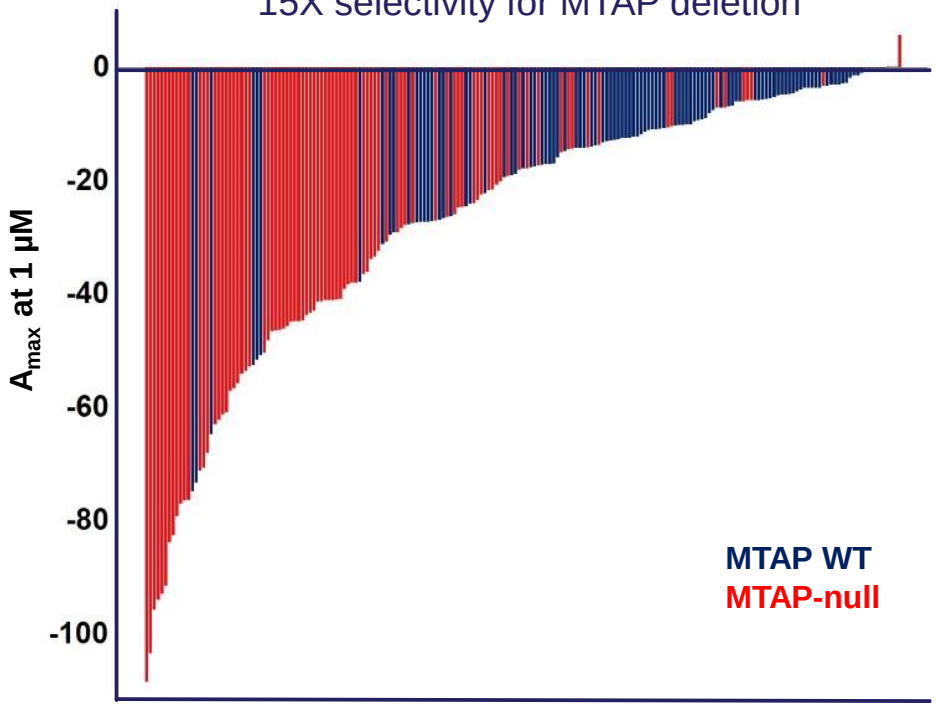
MTA-cooperative PRMT5 inhibitors

- Work by locking PRMT5 into the MTA-bound inactive state
- Induce cytotoxicity in MTAP-deleted cells at much lower concentrations than in normal cells

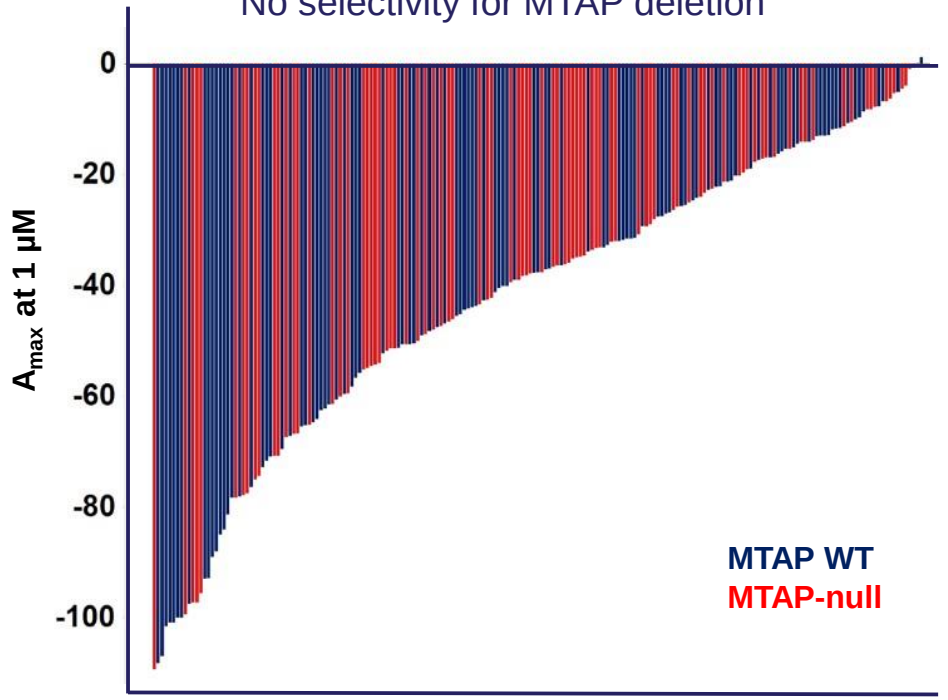
MTA-cooperative PRMT5 inhibitors are highly selective for MTAP-null cancer cell lines

200 cancer cell lines representing multiple lineages

TNG908
IC_{50} = 110 nM
15X selectivity for MTAP deletion



GSK3326595
IC_{50} = 120 nM
No selectivity for MTAP deletion

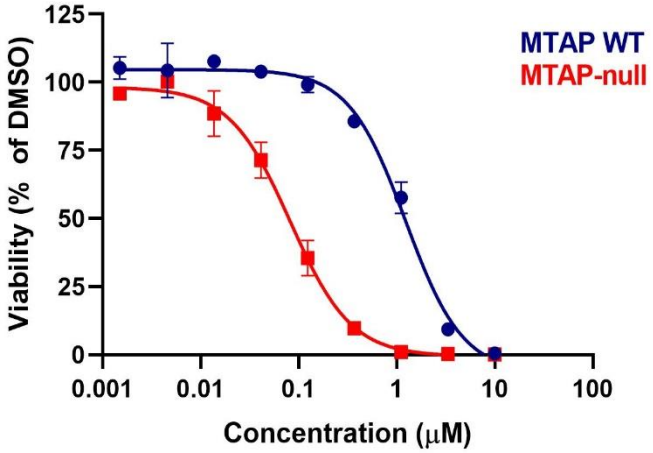


7-day viability assay
All cell lines represented in both panels

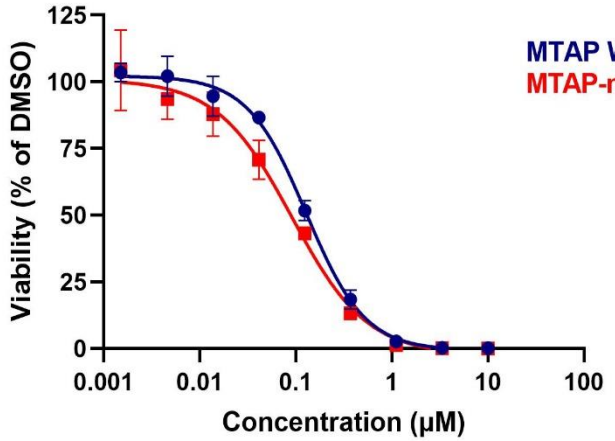
TNG908 is 15X selective for MTAP-null cells

MTAP selectivity of TNG908 makes MTAP-deleted tumors 15X more sensitive than normal cells

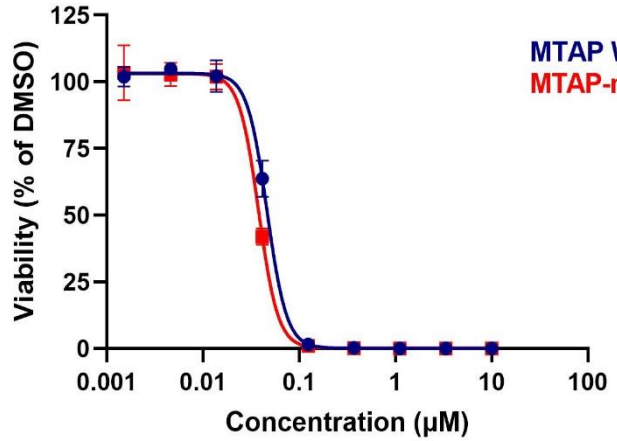
TNG908
IC_{50} = 110 nM
15X MTAP selectivity



GSK3326595
IC_{50} = 120 nM
1X MTAP selectivity



Prelude*
IC_{50} = 90 nM
1X MTAP selectivity

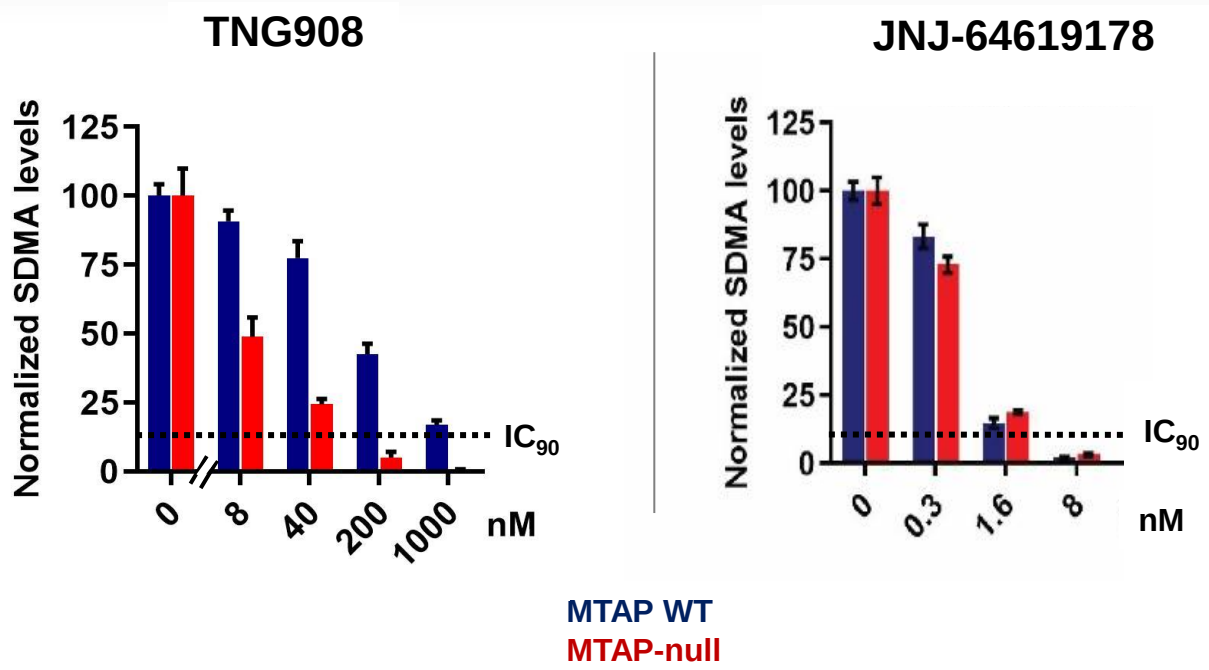


Isogenic HAP1 cells (parental WT line)

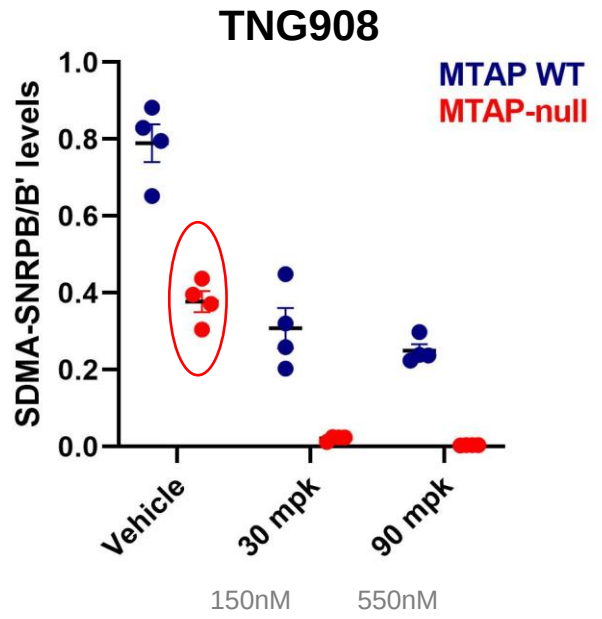
* Compound I from Patent WO2020168125, chemical structure of Prelude clinical molecules not disclosed

TNG908 PRMT5 inhibition is dose-dependent and MTAP-null selective

HAP1 MTAP isogenic cell lines



HCT116 colon cancer xenografts



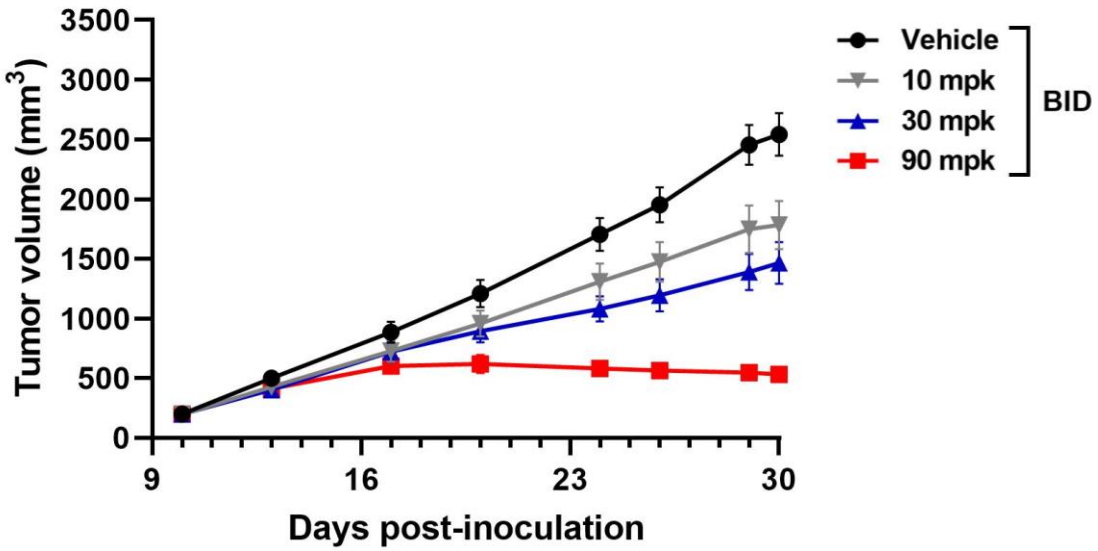
- SDMA measures PRMT5-specific methylation
- SDMA suppression in MTAP-null and WT cells cannot be uncoupled by non-selective PRMT5 inhibitors

TNG908 anti-tumor activity is dose and MTAP-deletion dependent

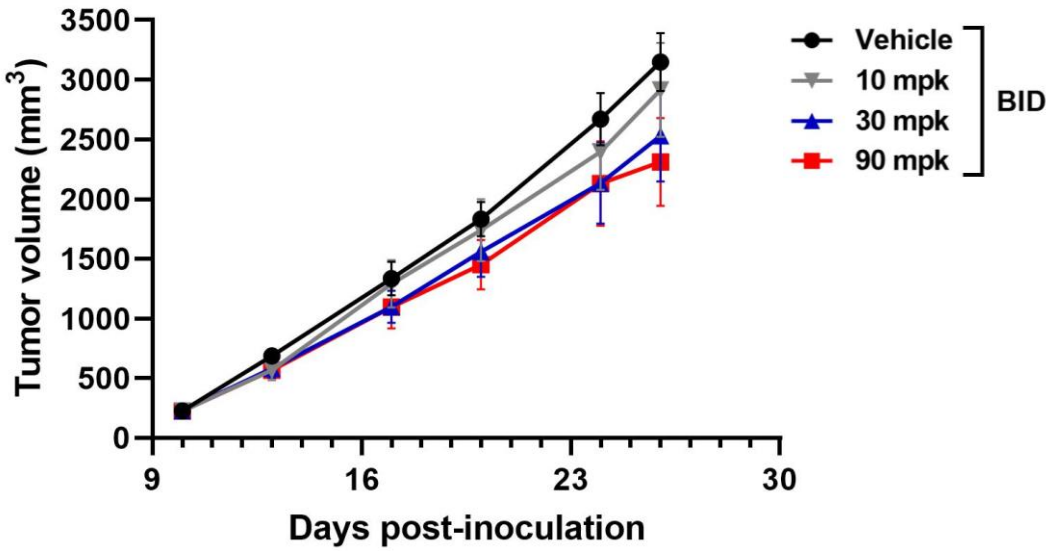
TNG908 IC50 110 nM, 15X selectivity for MTAP deletion

HCT116 (colon)

MTAP-null



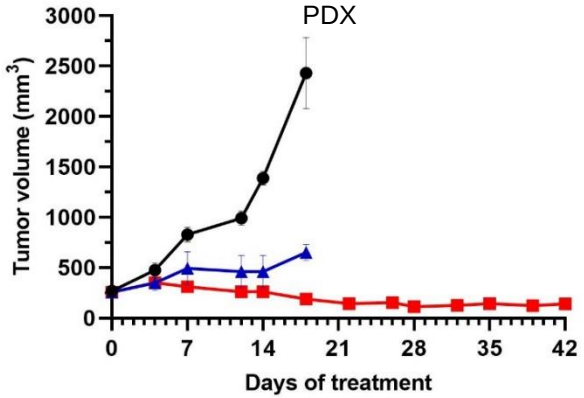
MTAP-WT



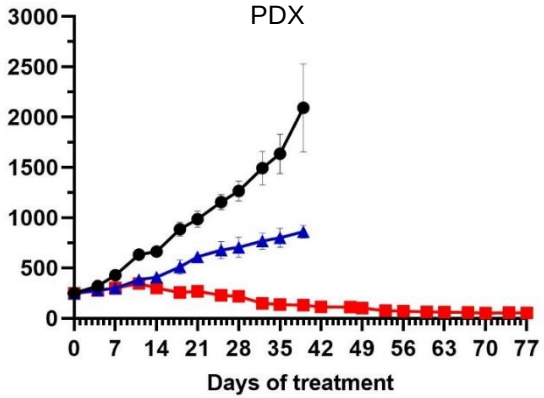
TNG908 drives tumor regression in MTAP-null xenograft models across lineages

TNG908 IC50 110 nM, 15X selectivity for MTAP deletion

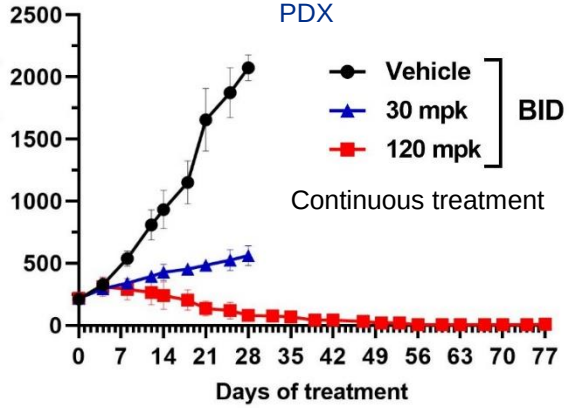
Cholangiocarcinoma
PDX



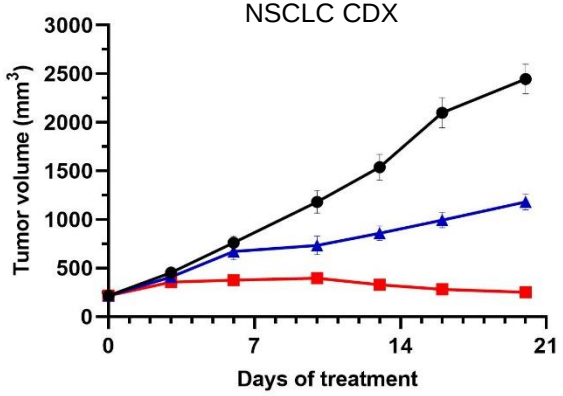
NSCLC (adeno)
PDX



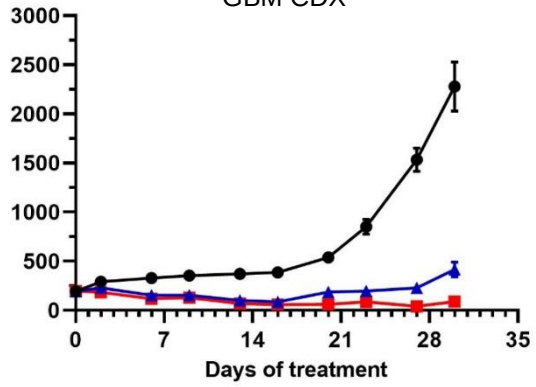
Bladder (TCC)
PDX



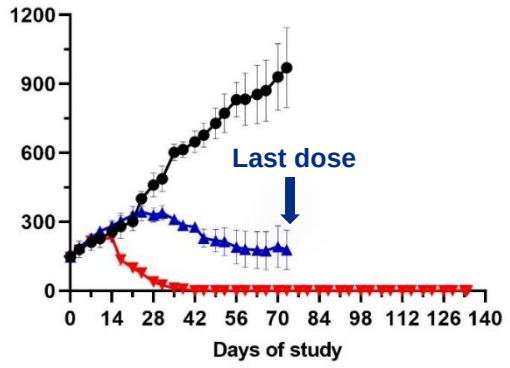
LU-99
NSCLC CDX



U87MG
GBM CDX



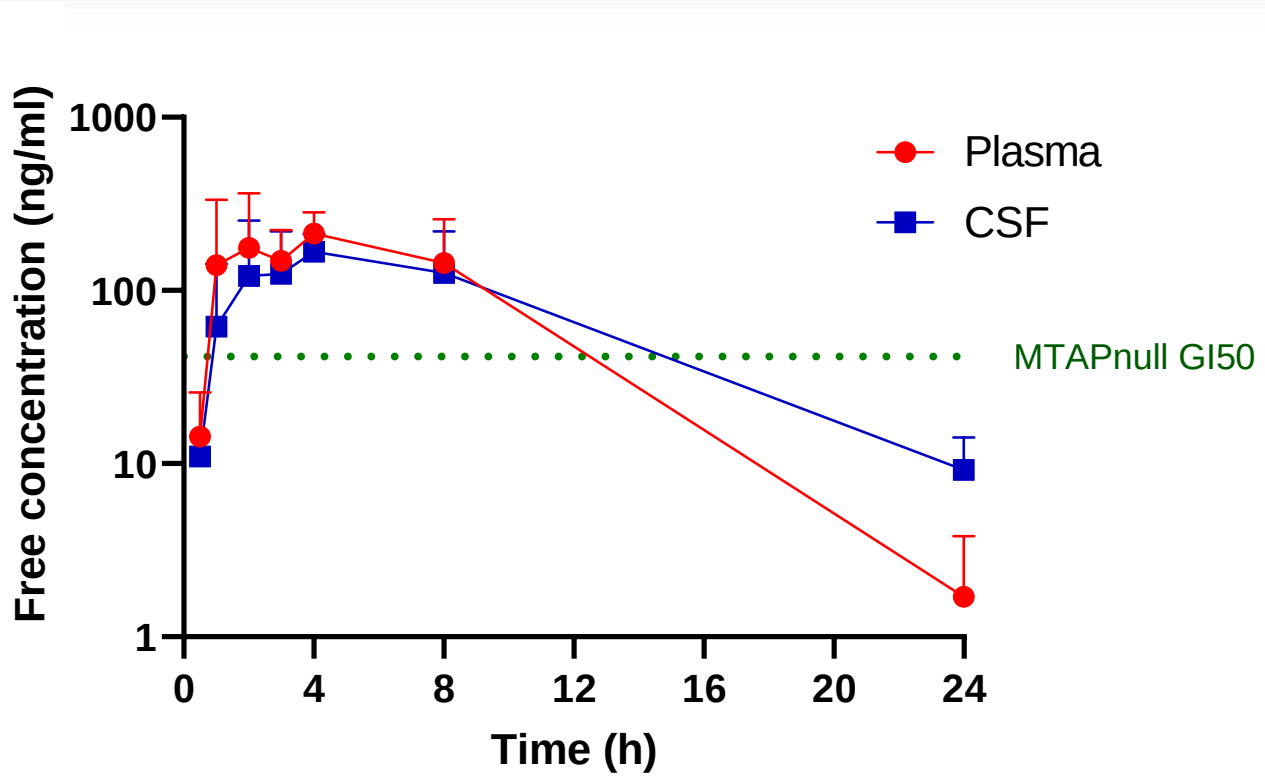
NSCLC (squamous)
PDX



- Tumor growth inhibition, stasis or regression in all models (n=52)
- Deep regressions in multiple histologies
- All models dosed continuously except NSCLC (squamous) PDX

TNG908 is brain penetrant in non-human primates

TNG908 exposure is equivalent in plasma and cerebrospinal fluid

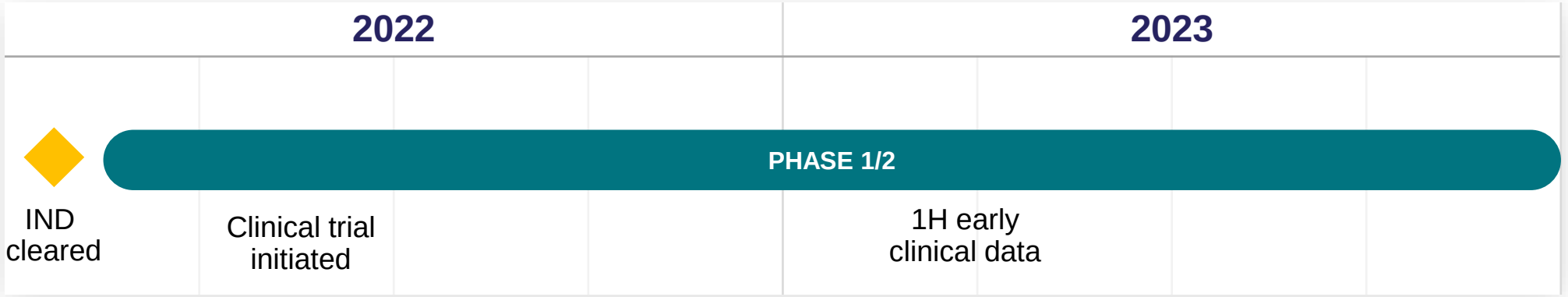


10 mg/kg PO

Summary

- CSF (cerebrospinal fluid) concentration after oral administration is a well-established surrogate for free brain concentration
- MTAP deletions occur in ~40% of glioblastomas, which we plan to evaluate in an expansion cohort of the Phase 1/2 trial
- TNG908 may be more effective than non-brain penetrant molecules in patients with brain metastases

TNG908 is a potentially first-in-class PRMT5 inhibitor that is synthetic lethal with MTAP deletion



CLINICAL STAGE PROGRAM

- Deep and durable regressions in cell-based and patient-derived xenograft models across histologies
- First patient dosed planned in Q2 2022, multiple clinical sites open for enrollment
- FDA Fast Track designation granted February 2022
- Large therapeutic index expected to allow selection of optimal efficacious dose below MTD
- Pursuing novel combinations with inhibitors that have complementary mechanism of action
- Filed composition of matter patent applications provide meaningful protection through at least 2041

Efficient trial design to evaluate efficacy in multiple indications

DOSE ESCALATION

- Solid tumors with MTAP deletion
- Projecting 4-5 dose escalations into therapeutic range

Malignant peripheral nerve sheath tumors
n ~ 20

30-50%
MTAP-null

Non-small cell lung
Mesothelioma
Cholangiocarcinoma
Glioblastoma
n ~ 20 each

15-40%
MTAP-null

Histology-agnostic cohort
n ~ 20

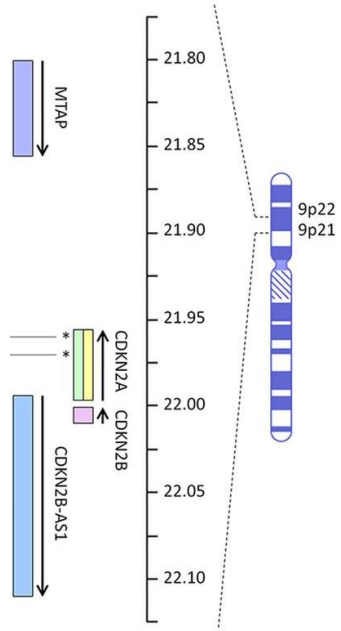
20-35%
MTAP-null

PHASE 1/2 STUDY

- Safety, PK/PD and efficacy as primary endpoints
- Multiple clinical sites open for enrollment
- Evaluating optimally efficacious dose vs. MTD
- Expansion cohorts provide optionality for multiple registration strategies
- Expected to be brain penetrant

Investing in our PRMT5 franchise with a nextGen molecule

MTAP deletions occur in ~10-15% of all human cancers



The most common homozygous deletion in human cancer

- One of the largest precision oncology patient populations
- TNG908 is a novel synthetic lethal PRMT5 inhibitor 15X more potent in MTAP-null cells than normal cells with good blood-brain barrier penetrance in non-human primates
- TNG462 is a potential best-in-class PRMT5 with enhanced potency, greater selectivity for MTAP deletion and extended target coverage

A COMPREHENSIVE DEVELOPMENT PLAN

- Multiple combination trials based on strong preclinical data and rationale
- Extensive effort to define and address resistance mechanisms in a range of genetic backgrounds
- Both TNG908 and TNG462 to be evaluated in clinical studies

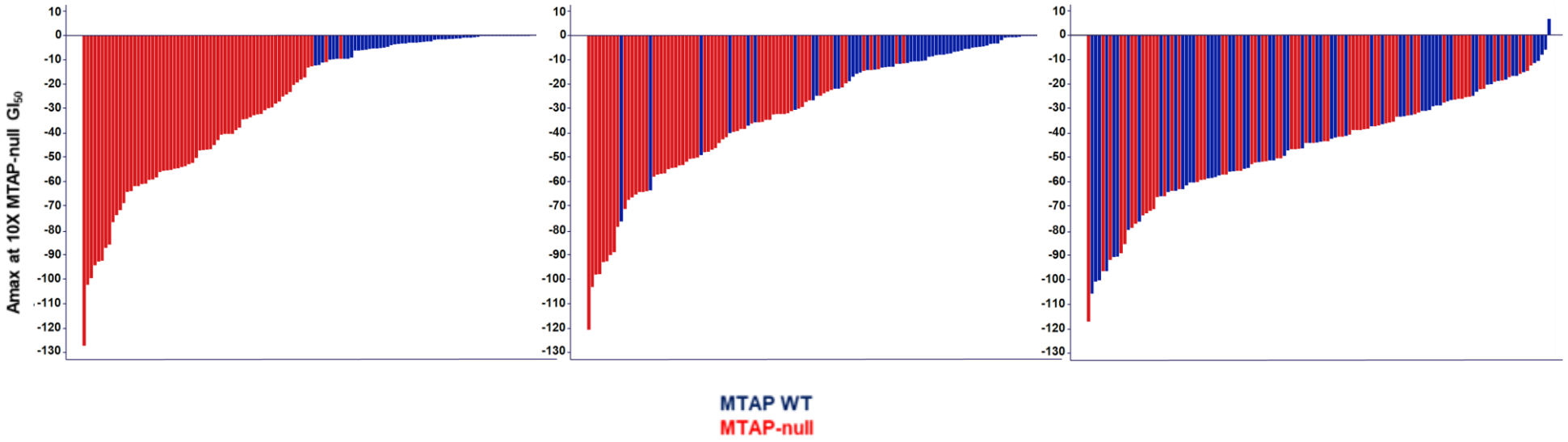
TNG462 is highly potent and 45X selective for MTAP deletion

179 cancer cell lines from multiple lineages

TNG462
IC_{50} = 4 nM
45X selectivity for MTAP deletion

TNG908
IC_{50} = 110 nM
15X selectivity for MTAP deletion

GSK3326595
IC_{50} = 120 nM
No selectivity for MTAP deletion



7-day viability assay
Same cell lines represented in all panels

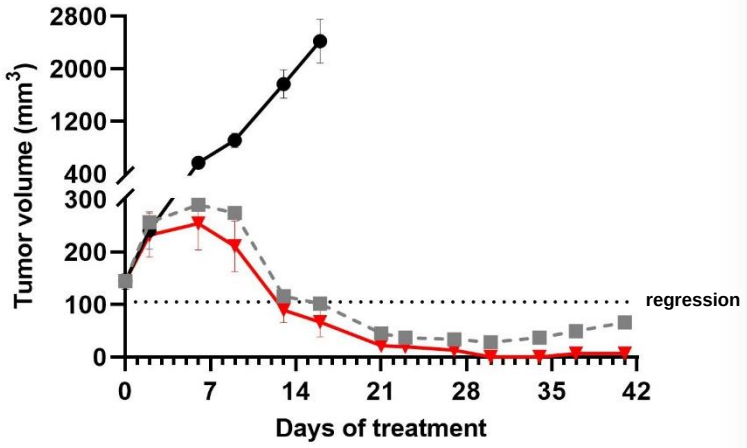
Next-generation PRMT5 inhibitor development candidate

- TNG462 has an optimized PK profile for enhanced target coverage
- Enhanced potency and MTAP selectivity has the potential for broader and deeper clinical activity

TNG462 is a potentially best-in-class PRMT5 inhibitor

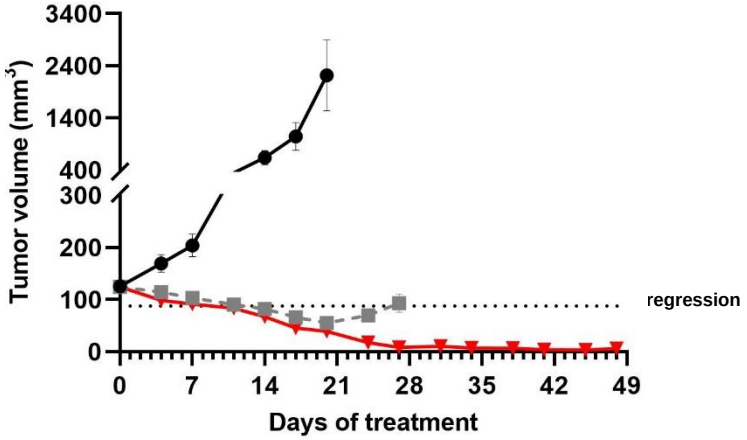
TNG908 IC50 110 nM, 15X selectivity for MTAP deletion
TNG462 IC50 4 nM, 45X selectivity for MTAP deletion

Cholangiocarcinoma
PDX



Mean % $TV_{initial}$			
Maximum	Final		
-	-	Vehicle	BID
-77	-54	120 mpk TNG908	
-100	-95	60 mpk TNG462	

DLBCL
OCI-LY19 CDX



Mean % $TV_{initial}$			
Maximum	Final		
-	-	Vehicle	BID
-55	-25	120 mpk TNG908	
-97	-95	60 mpk TNG462	

TNG462 induces deep and durable regressions across histologies

	TNG908	TNG462
LN18 (GBM)	16%	**73%**
LU99 (lung)	48%	**66%**
OCI-Ly19 (DLBCL)	55%	**97%**
Bladder PDX	80%	**82%**
Cholangio PDX	77%	**100%**

% tumor regression

5/6 mice with cholangiocarcinoma and 5/6 mice with DLBCL had complete regressions when treated with TNG462

TNG462 IND filing planned 1H 2023

PROGRAM	PATIENT SELECTION	DISCOVERY	IND-ENABLING	CLINICAL TRIALS		ANTICIPATED MILESTONES
				Phase 1/2	Phase 3	
TNG462	MTAP-deleted cancers					IND filing 1H 2023

ADVANCED DRUG DISCOVERY

- Same mechanism of action as TNG908 with enhanced pharmacological properties
- Potential to be a best-in-class inhibitor with increased therapeutic index and efficacy
- Currently in IND-enabling studies

CLINICAL TRIAL

- Clinical trial design similar to TNG908
- Glioblastoma excluded as TNG462 not expected to cross the blood-brain barrier
- Both TNG908 and TNG462 to be evaluated in clinical trials

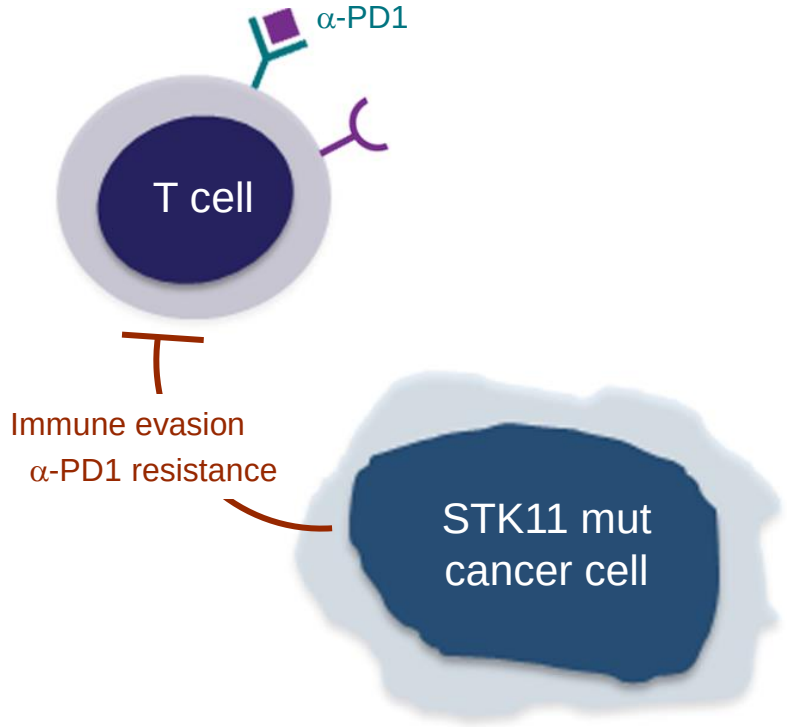
SIGNIFICANT PATIENT OPPORTUNITY

- MTAP-deletions occur in approximately 10-15% of all human cancers

Target 3 inhibition reverses immune evasion in STK11 mutant cancers

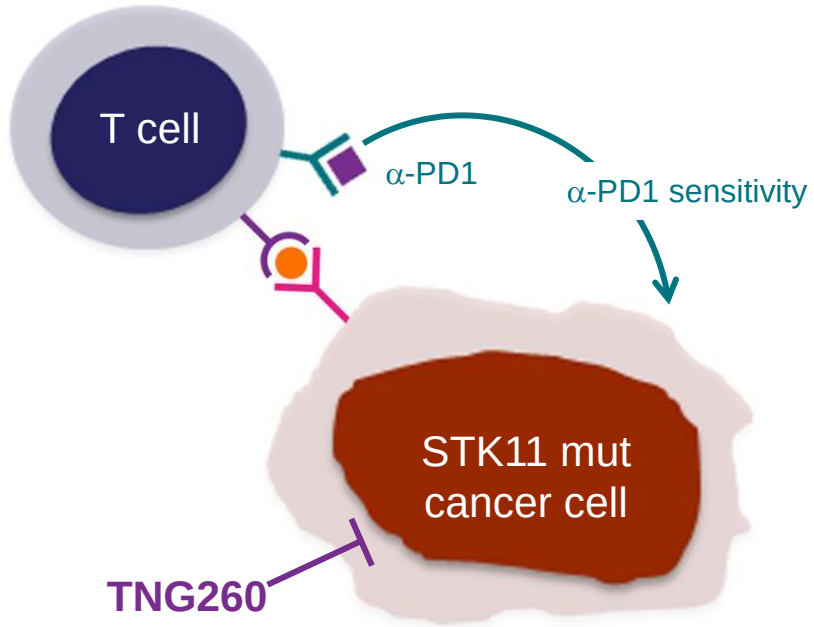
TNG260 reverses immune evasion caused by STK11 loss-of-function mutations

Immune evasion driven by tumor suppressor gene loss



STK11 re-activation is not feasible

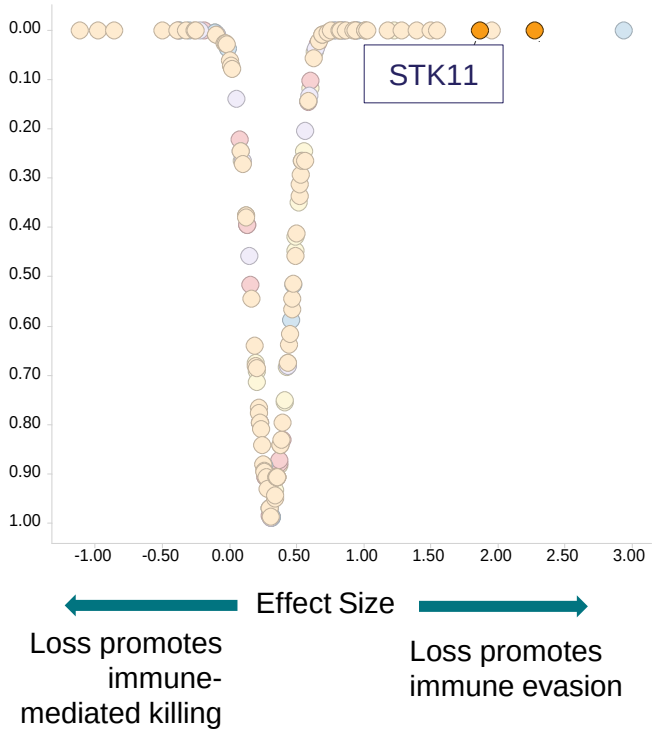
TNG260 reverses immune evasion driven by STK11 mutations



TNG260 target inhibition in cancer cells enables immune-medicated cytotoxicity

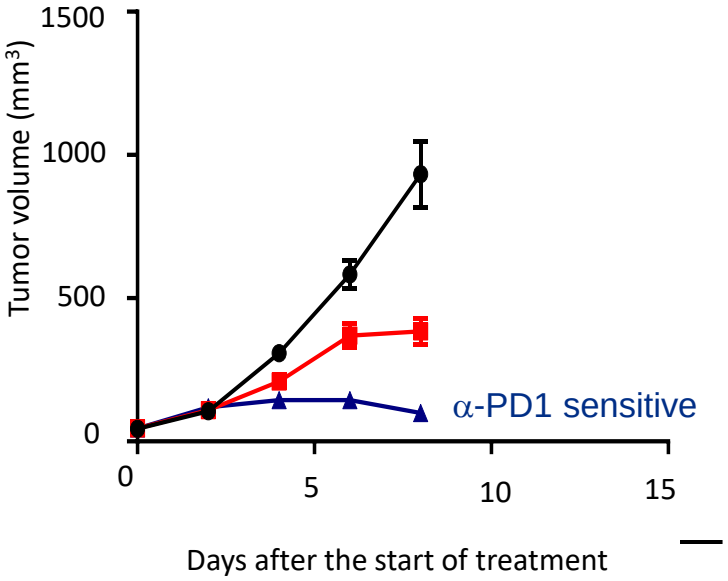
STK11 loss-of-function mutations drive immune evasion

STK11 knock-out drives immune evasion

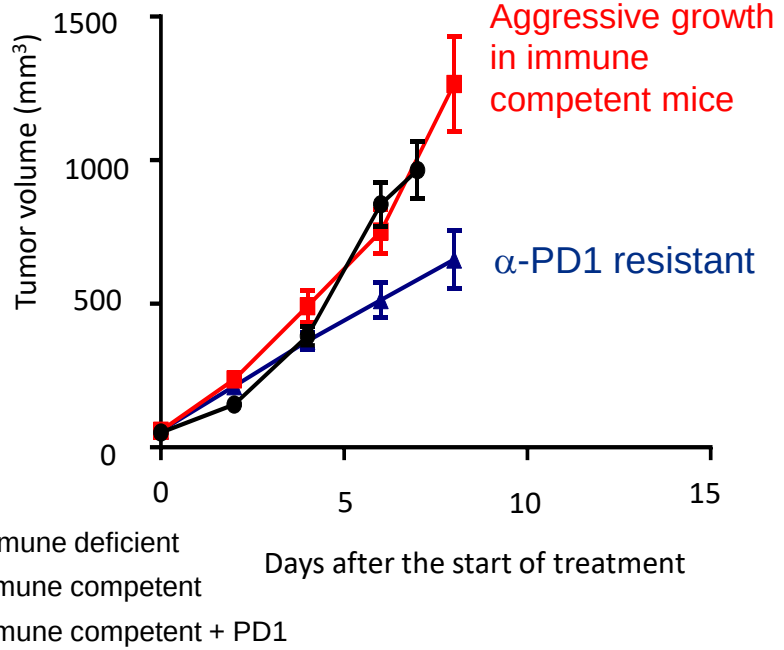


STK11 knock-out causes α-PD1 resistance

Control
(MC38)



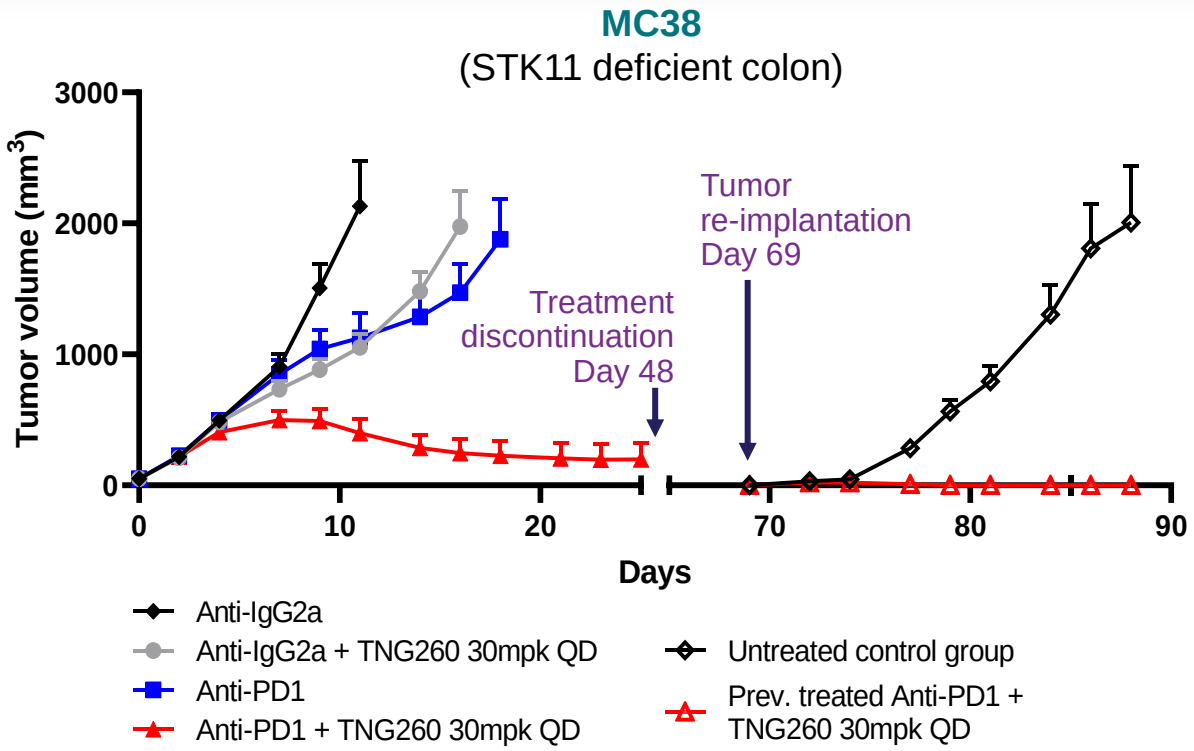
STK11 knockout
(MC38)



Multiple peer-reviewed data sets support STK11 loss-of-function mutations are associated with clinical immune checkpoint inhibitor resistance

TNG260 inhibition induces complete regression and establishes immune memory in an STK11 mutant tumors

TNG260 IC50 5nM, 10X isoform selectivity



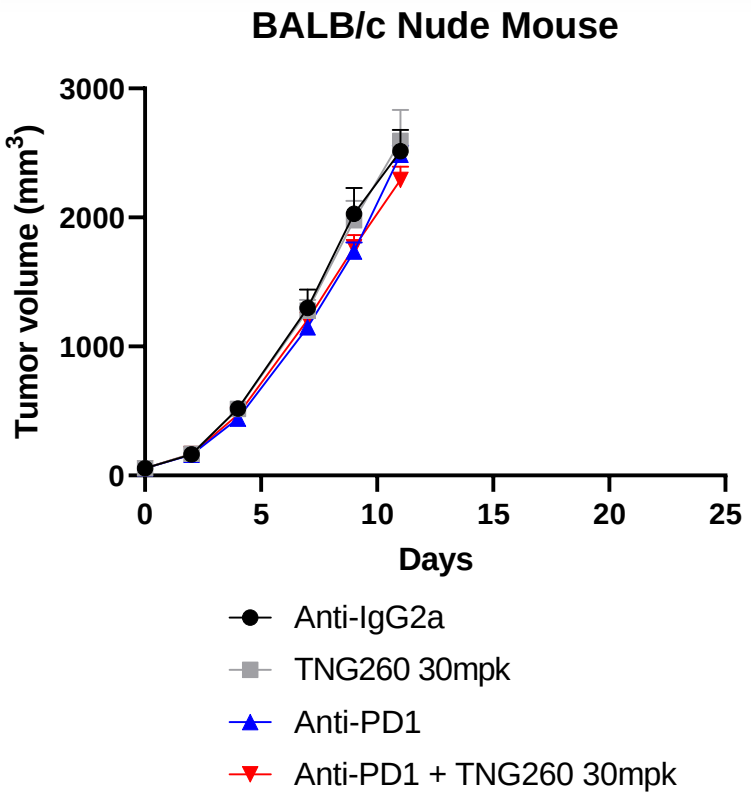
- 5/8 mice had complete tumor regression at day 34, treatment discontinued at day 48
- All mice with complete regression remained tumor free off treatment for 21 days
- 5/5 with complete regression rejected tumor reimplantation

TNG260

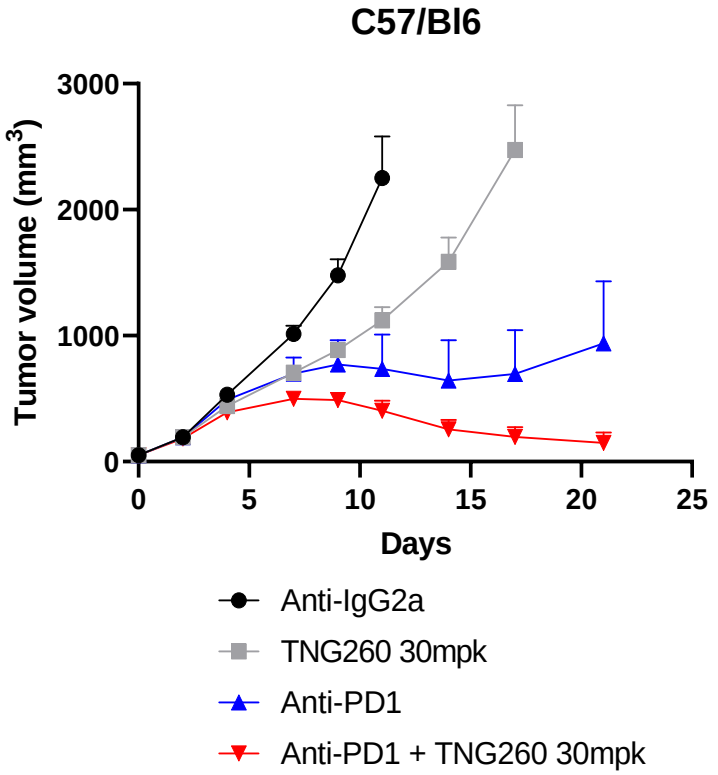
- TNG260 reverses immune evasion in STK11 mutant tumors
- TNG260 has strong *in vivo* efficacy in combination with anti-PD1 antibody
- TNG260 induces immune memory and renders treated mice resistant to tumor re-implantation
- Potent, highly selective molecule with good pharmacologic properties
- Currently in IND-enabling studies

Anti-tumor efficacy of TNG260 requires an intact immune system

Immunocompromised mice



Immunocompetent mice

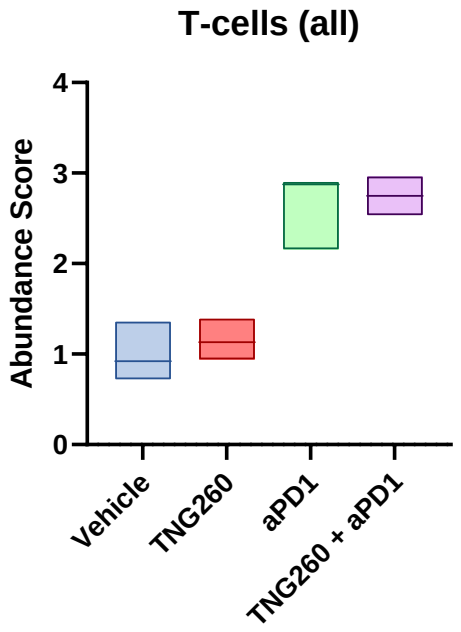


TNG260

- Development candidate selected 2Q 2022
- Anti-tumor effect of TNG260 not observed in mice lacking T cells

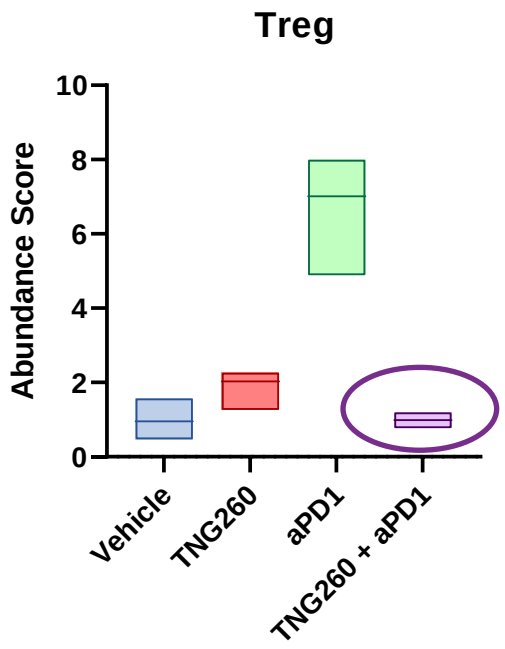
TNG260 eliminates Treg infiltration caused by α-PD1 without reducing T effector influx

α-PD1 induces tumor cell cytokine secretion that recruits T effectors



- CXCL9, 10 and 11 recruit T effector cells that mediate tumor cell killing and is increased by the combination

TNG260 eliminates immune suppressive Treg infiltration caused by α-PD1



- α-PD1 markedly increases Treg infiltration
- CCL1 and CCL22 recruit Tregs that drive immune evasion and are reduced to baseline by the combination

MECHANISM OF ACTION

- TNG260 results in specific transcriptional changes in STK11 mutant cells
- TNG260 mediated transcriptional changes alter tumor secretion of specific cytokines
- Changes in cytokines secretion caused by TNG260 + α-PD1 change the T cell ratio in the tumor to strongly favor immune-mediated tumor cell killing

Trial design to assess TNG260 inhibitor plus α-PD1 in multiple tumors types to evaluate safety, efficacy and the effect of KRAS mutation on outcome

DOSE ESCALATION

- Any solid tumor with STK11 mutation
- Combination with α-PD1

DOSE EXPANSION

SKT11 mut
KRAS WT lung cancer
n ~ 20

~60% STK11mut lung cancer

SKT11 mut
KRAS mut lung cancer
n ~ 20

~40% STK11mut lung cancer

STK11 mut
Histology-agnostic cohort
(enriched for cervical, unknown primary, pancreatic, breast)
n ~ 20

PHASE 1/2 STUDY

- Combination with α-PD1 to assess safety, PK/PD and efficacy as primary endpoints
- Separate cohorts for KRAS mutant and WT lung cancer to evaluate impact of KRAS mutations on checkpoint inhibitor resistance
- IND filing planned 2023

TNG260 IND filing planned 2023

PROGRAM	PATIENT SELECTION	DISCOVERY	IND-ENABLING	CLINICAL TRIALS		ANTICIPATED MILESTONES
				Phase 1/2	Phase 3	
TARGET 3* TNG260	STK11-mut cancers					IND filing 2023

*Wholly-owned immune evasion program

NOVEL TARGET

- STK11 mutations are key drivers of immune evasion in lung cancers and occur in multiple other tumor types
- TNG260 inhibition reverses checkpoint inhibitor resistance in preclinical STK11-mutant models
- Evidence of immune memory induction after complete regression immunizes mice against tumor regrowth

CLINICAL PLAN

- Novel mechanism with strong *in vivo* efficacy
- Induction of immune memory that prevents tumor regrowth in responders
- In IND-enabling studies with planned filing 2023
- Phase 1/2 clinical study to evaluate efficacy in combination with α-PD1 in STK11 mutant cancers

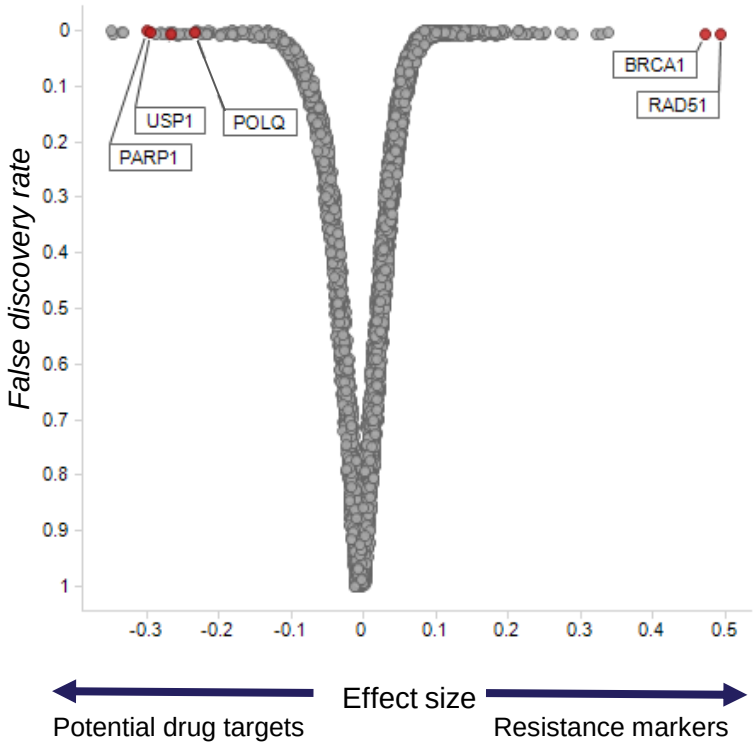
SIGNIFICANT PATIENT OPPORTUNITY

- STK11 mutations occur in ~15% NSCLC, 15% cervical, 10% carcinoma of unknown primary, 5% breast and 3% pancreatic cancers
- STK11 mutations are associated with clinical checkpoint inhibitor resistance
- STK11 mutations among the first genetic patient selection for an immuno-oncology clinical trial

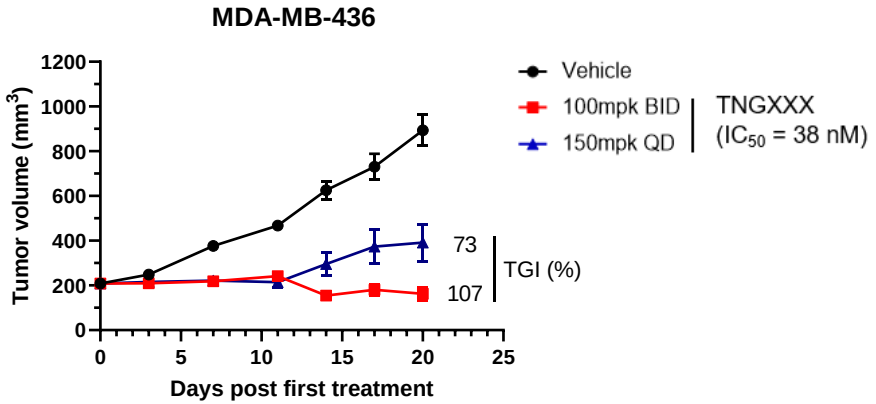
USP1 inhibition in BRCA1/2 mutant cancers

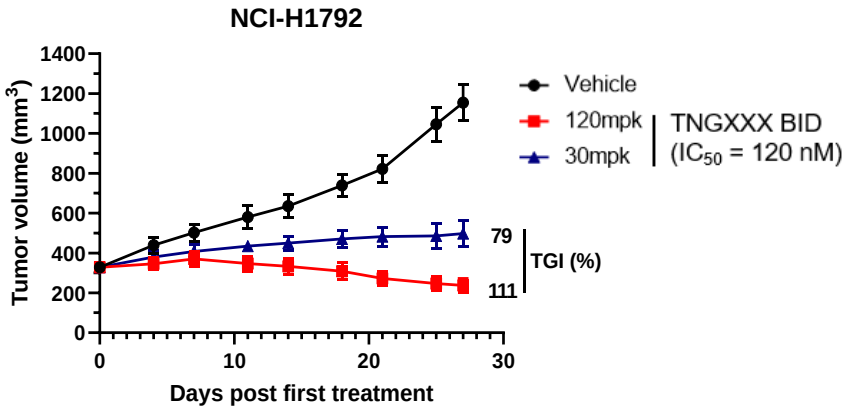
USP1 and BRCA1/2 are a synthetic lethal pair

Tango druggable genome CRISPR screen cell line panel



In vivo efficacy of USP1i



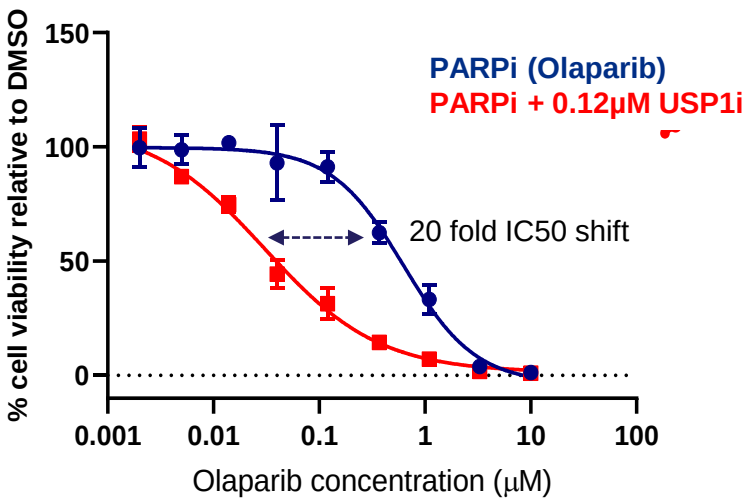


USP1

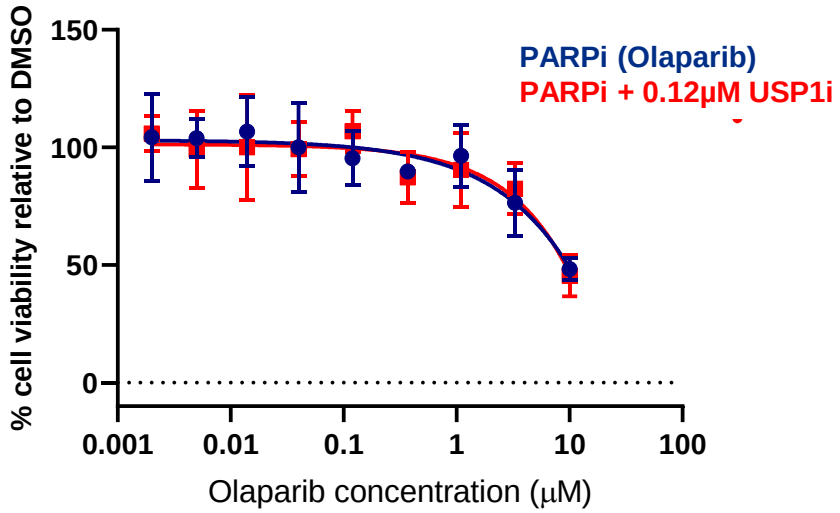
- USP1 is a de-ubiquitinating enzyme (DUB) that is synthetic lethal with BRCA1/2
- Loss of USP1 results in deficient DNA replication in BRCA1/2 mutant cells
- *In vivo* efficacy in BRCA1/2-mut breast and ovarian tumor models
- Some BRCA WT lung cancer cell lines are sensitive to USP1 inhibition, patient selection marker being evaluated

USP1 + PARP inhibition is synergistic in BRCA1/2 mutant cells

SUM149PT
BRCA1 mutant



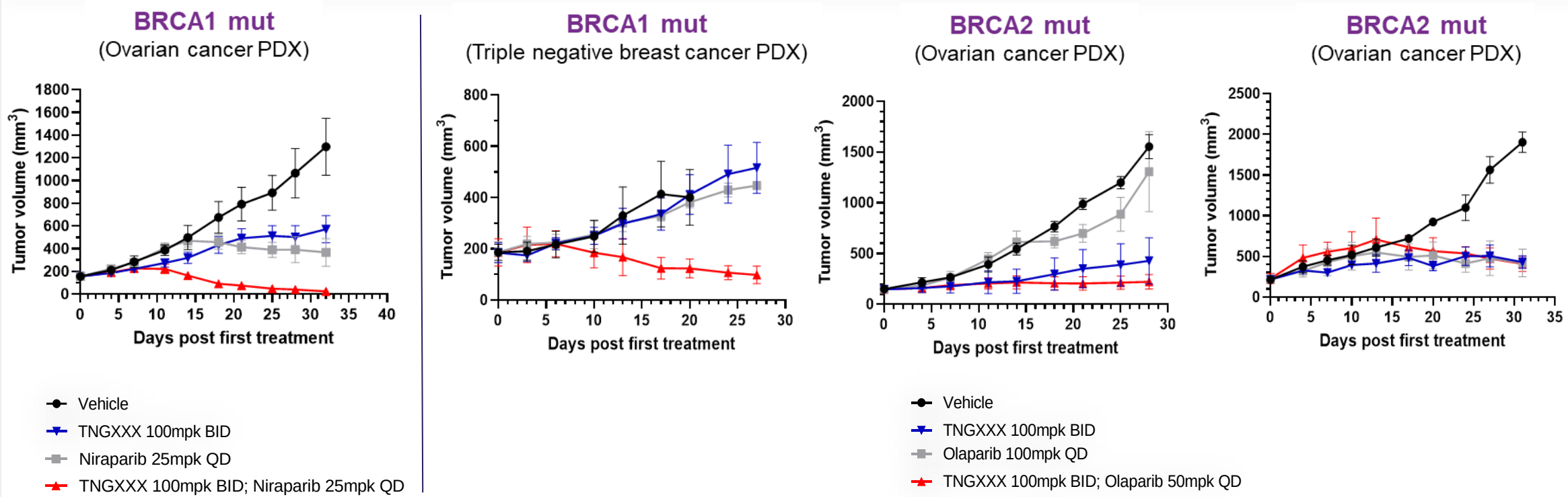
SUM149PT
BRCA1 WT (revertant)



- USP1 + PARP inhibition is synergistic in BRCA1/2-mutant but not WT cells
- BRCA1/2 mutant selective PARPi synergy confirmed in cell line panel

Advanced lead has single agent and PARPi combination activity

TNGXXX IC50 38nM, >200 fold selectivity for BRCA1/2mut vs WT



Single agent and combination activity in PARPi sensitive and resistant models

USP1 development candidate in 2H 2022

PROGRAM	PATIENT SELECTION	DISCOVERY	IND-ENABLING	CLINICAL TRIALS		ANTICIPATED MILESTONES
				Phase 1/2	Phase 3	
USP1	BRCA1/2-mut cancers					Development candidate 2H 2022 IND filing 2023

NOVEL TARGET

- Strong synthetic lethality with BRCA1/2 mutation
- MOA distinct from PARPi with efficacy mediated through ub-PCNA and replication stress
- Single agent activity and strong PARP1 synergy in breast and ovarian preclinical models
- Synergy with PARPi in both sensitive and resistant xenografts

ADVANCED DRUG DISCOVERY

- Believe we have a strong IP position, multiple pending patent families
- Proprietary inhibitor-bound crystal structure enables structure-guided drug design
- Advanced allosteric inhibitors with strong *in vivo* activity, dose range-finding studies ongoing

SIGNIFICANT PATIENT OPPORTUNITY

- BRCA1/2 mutations are present in approximately 15% of ovarian cancers, 10% of breast cancers, 10% of prostate cancers, 5% of endometrial cancers and 5% of pancreatic cancers
- Selective dependency identified in a subset of lung cancer cell lines, patient selection markers being evaluated
- Synergy in both PARPi-sensitive and -resistance models suggests potential to meaningfully expand patient benefit from PARP inhibitors

FINANCIAL HIGHLIGHTS AND MILESTONES

Q1 2022 financial highlights (Nasdaq: TNGX)

Cash balance

- $450M cash, cash equivalents and marketable securities (3/31)
- Includes net proceeds of $327M from SPAC/PIPE closed August 2021

Cash runway

- Sufficient cash to fund operations into 2H 2024

Shares outstanding

- 88M common shares outstanding

Sufficient cash to achieve multiple projected key milestones

2022 FY

- ✓ Initiate TNG908 first-in-human clinical trial in 2Q
- ✓ Development candidate for nextGen PRMT5 TNG462 in 2Q
- ✓ Development candidate for Target 3 in 2Q
- ☐ Development candidate for USP1 in 2H

2023 FY

- ☐ Preliminary safety and efficacy data on TNG908 in 1H
- ☐ IND filing for nextGen PRMT5 TNG462 in 1H
- ☐ IND filing for Target 3
- ☐ IND filing for USP1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