Vopimetostat and RAS(ON) combination data

June 8, 2026

TANGO therapeutics™

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Finally, while Tango believe its internal research is reliable, such research has not been verified by any independent source.

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Agenda for today

Leader in PRMT5 targeted therapy for cancer
Malte Peters, MD | President and Chief Executive Officer

Vopimetostat + RAS(ON) combination data show transformative potential in pancreatic cancer
Brian Wolpin, MD | Dana-Farber Cancer Institute & Harvard Medical School

Strategy to accelerate registration-directed development of vopimetostat
Adam Crystal, MD PhD | President of Research and Development

Capital allocation plan and financial highlights
Matthew Gall | Chief Financial Officer

Closing remarks
Malte Peters, MD | President and Chief Executive Officer

Q&A
All


Malte Peters, MD


Brian Wolpin, MD


Adam Crystal, MD PhD


Matthew Gall

TANGO therapeutics

Leader in PRMT5 targeted therapy for cancer

Malte Peters, MD, President and Chief Executive Officer

At the forefront of transformative shift in pancreatic cancer treatment

Scientific leader
in PRMT5 inhibition

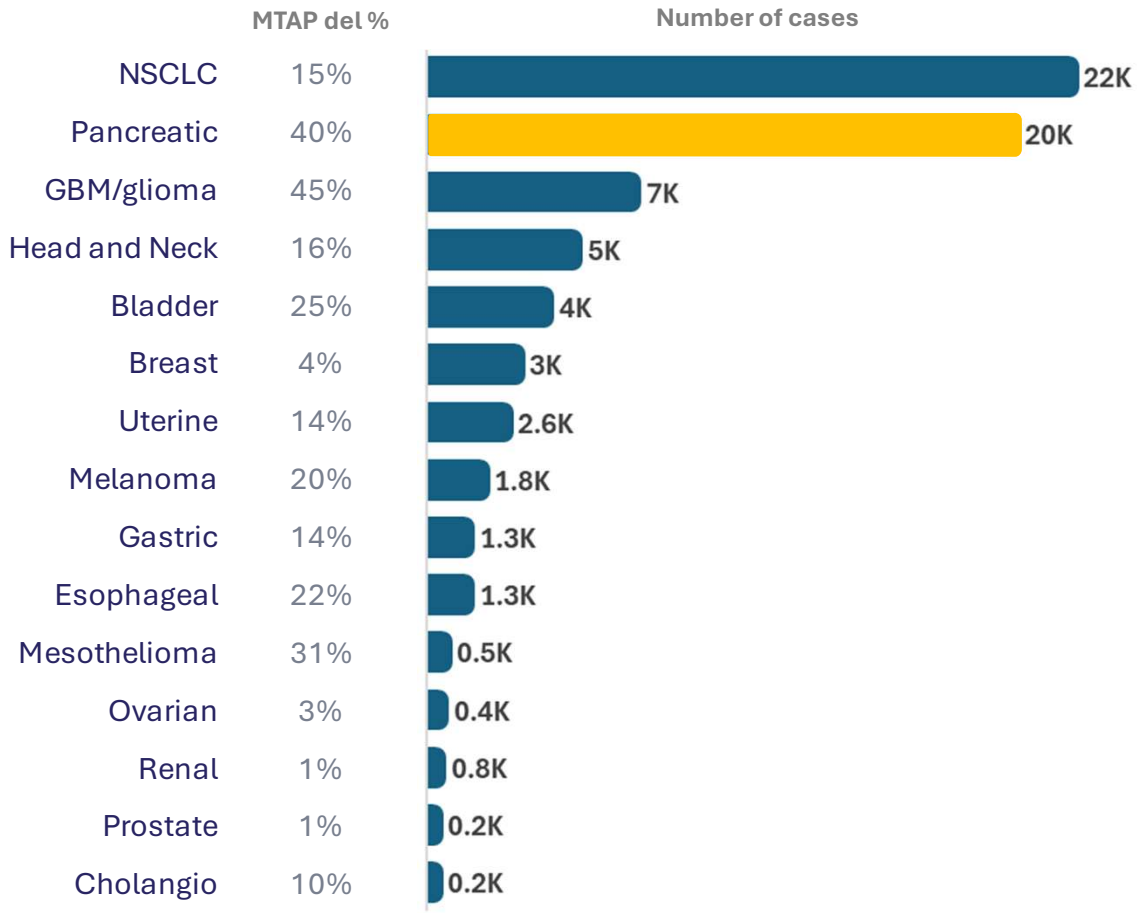
Transformative
92% ORR in 2/3L PDAC
in combination with daraxonrasib

Clear strategy
for front line development with chemotherapy free regimen

Near-term **focus on potential blockbuster PDAC opportunity**
Pipeline supporting data-driven **indication expansion** to drive long-term growth

PDAC, pancreatic ductal adenocarcinoma; 2/3L, second/third line.
Data from ongoing Phase 1/2 clinical trial. Data as of 28 May 2026.

~60,000 patients with MTAP del metastatic cancers annually in the US



Patient population sizes estimated using data from SEER, Kantar, TCGA PanCancer Atlas and other sources. PDAC, pancreatic ductal adenocarcinoma. NSCLC, non-small cell lung cancer.

Plan to initially prioritize PDAC

- Potential blockbuster opportunity for vopimetostat in PDAC alone
  - Nearly all patients with an MTAP deletion have a co-occurring KRAS mutation
  - Significant medical need with potential for meaningful improvement over standard of care
  - Opportunity to lead in rapidly changing landscape
- Multiple indication expansion opportunities (NSCLC, GBM) to drive long-term growth

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Brian Wolpin is a leader in the study and treatment of pancreatic cancer

- Professor of Medicine, Harvard Medical School
- Robert T. & Judith B. Hale Chair in Pancreatic Cancer, Dana-Farber Cancer Institute
- Director, Hale Family Center for Pancreatic Cancer Research and Gastrointestinal Cancer Center, Dana-Farber Cancer Institute
- Director, Dana-Farber – Lustgarten Foundation Dedicated Laboratory for Pancreatic Cancer Research
- Medical oncologist with clinical specialty in pancreatic cancer
- Research laboratory dedicated to the investigation of pancreatic ductal adenocarcinoma (PDAC) biology and treatment

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Vopimetostat + RAS(ON) combination data show transformative potential in pancreatic cancer

Dr. Brian Wolpin, MD, MPH
Dana-Farber Cancer Institute & Harvard Medical School

Evolution of standard of care for pancreatic cancer

CHEMOTHERAPY

Current standard;
Limited efficacy

Today

RAS INHIBITORS[1]

Improved response
and durability

Emerging

**RAS INHIBITORS +
PRMT5 INHIBITORS**

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Increased response rate and
prolonged durability

Potential Next Generation

1. Wolpin et al. ASCO, 2026.

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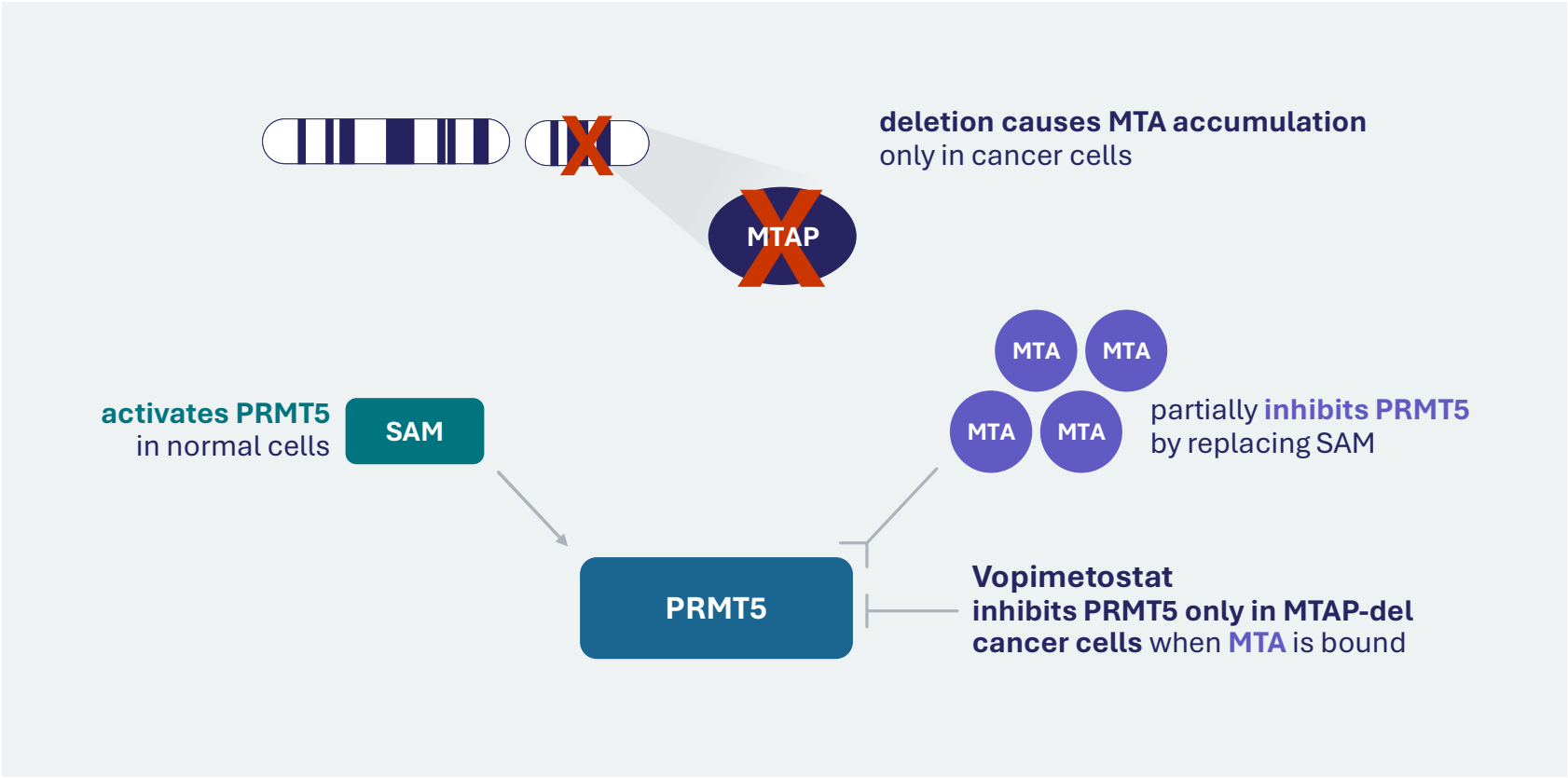
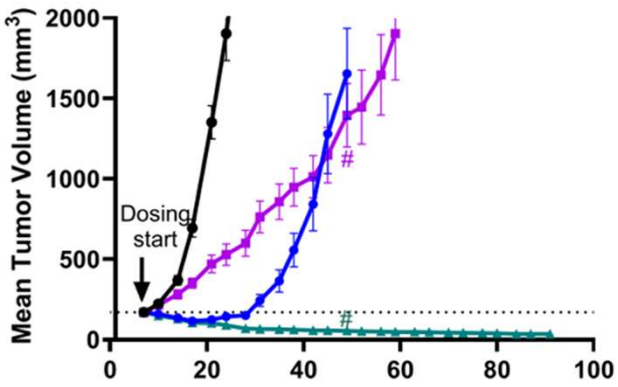
Vopimetostat selectively inhibits the cell essential gene PRMT5 in MTAP deleted cancer cells

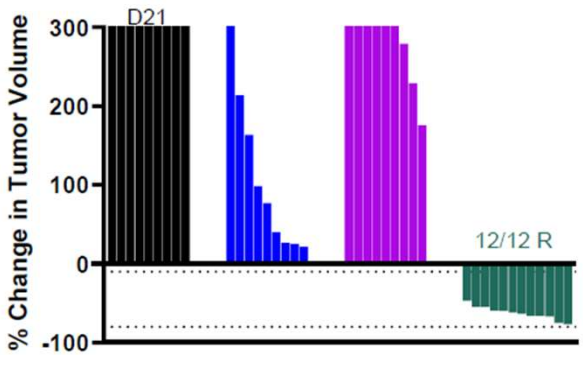


PRMT5 + RAS inhibition demonstrated preclinical synergy

In vivo model demonstrated striking combination efficacy

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





Vehicle

100 mpk QD RMC-9805

20 mpk QD BID TNG462

RMC-9805 + TNG462

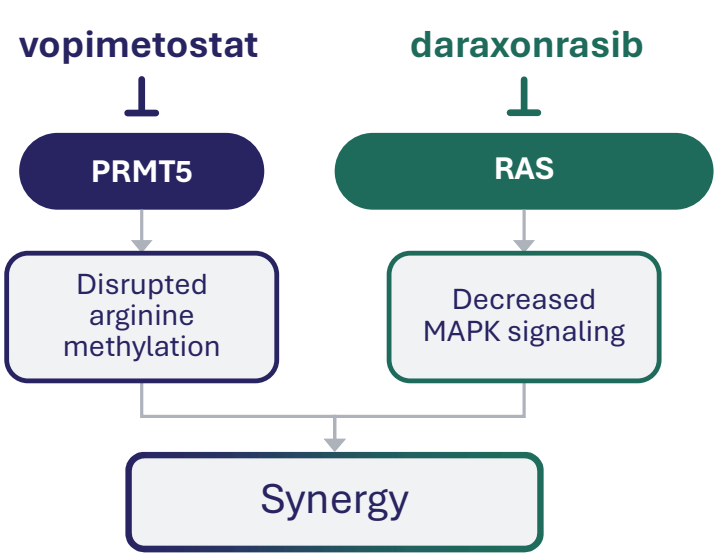
Key points

- KRAS inhibition + PRMT5 inhibition is synergistic in multiple preclinical models[1]
- Clinical data to date support synergy of combination in patients

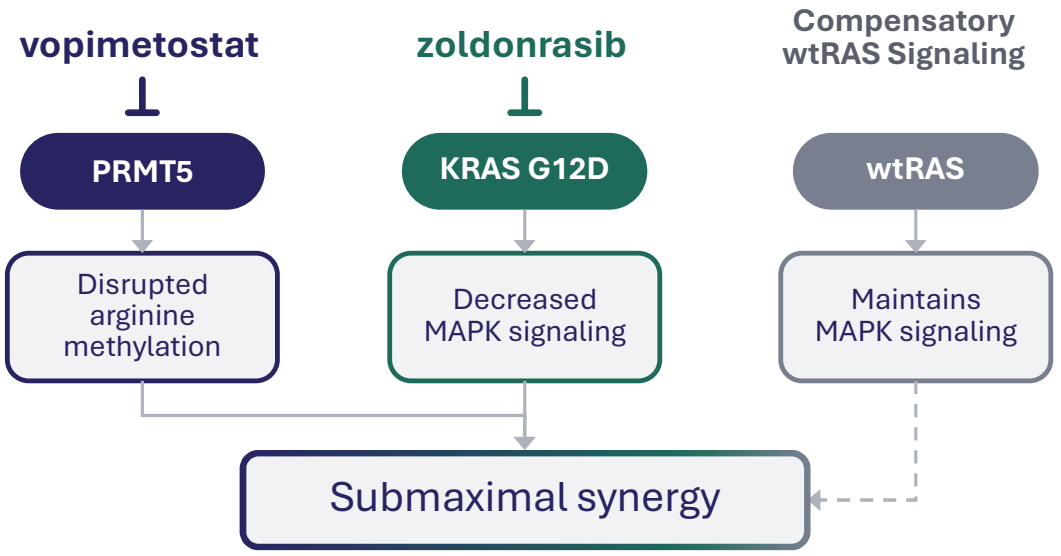
1. Knoll, Cancer Research 2025; Drizyte-Miller, Cancer Research 2025
PDAC, pancreatic ductal adenocarcinoma; QD, once daily; BID, twice daily.

Vopimetostat + panRAS inhibition may yield maximal synergy

panRAS inhibition may result in maximal synergy



G12D specific inhibition may allow partial rescue by wtRAS



Cancer Discovery. 2020;10(4): 556–569. Ryan MB, Fece de la Cruz F, Phat S, et al. Cell Reports. 2022;39(2):110993. Feng H, et al. Oncogene. 2023;42: 1–13. Wang X, et al. Pathology & Oncology Research. 2024;30:1611948.

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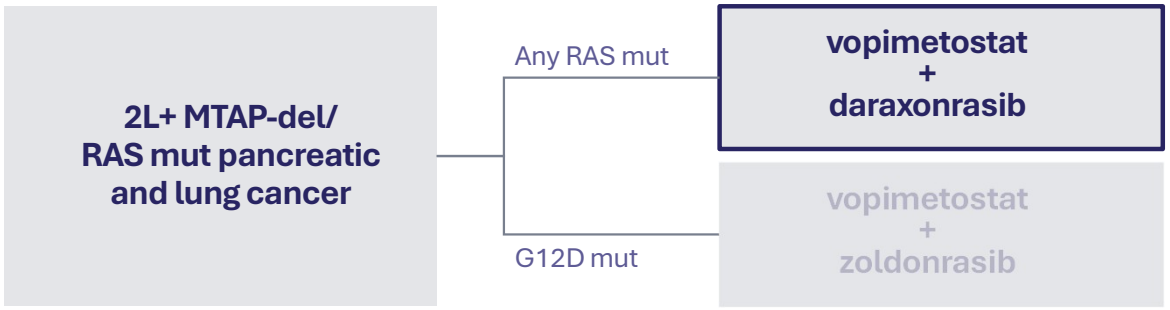
First PRMT5 inhibitor combined with RAS inhibitors in the clinic

Phase 1 dose escalation trial



Key inclusion criteria:

- MTAP loss by NGS or IHC
- 1-2 lines prior systemic therapy in metastatic setting
- ECOG PS 0 or 1
- No prior PRMT5i or RASi

Vopimetostat + daraxonrasib:

- **Dose escalation range:**

  200 mg – 250 mg vopimetostat QD
  + 100 mg daraxonrasib QD

- **Evaluable patients**

  Safety n=25

  Efficacy n=15

MTAP status for enrollment:

85% by NGS / 15% by IHC

~95% concordance (NGS and IHC)

Data extract 28 May 2026. Patients who received first dose at least 14 weeks prior to data cutoff were efficacy evaluable. All treated patients were safety evaluable. 2L, second line; NGS, next-generation sequencing; IHC, immunohistochemistry.

Patient baseline characteristics

	vopimetostat + daraxonrasib (PDAC)	**Vopimetostat + daraxonrasib** (NSCLC)	**vopimetostat + zoldonrasib** (PDAC)
N	**20**	**5**	**34**
Sex, male, n (%)	9 (45)	3 (60)	18 (53)
Age, years, median (range)	66 (46-74)	55 (38-71)	66 (37-81)
Number of prior lines of systemic therapy in metastatic setting, n (%)			
0	1 (5)*	-	-
1	6 (30)	1 (20)	15 (44)
2	13 (65)	3 (60)	19 (56)
3	-	1 (20)	-
Median number of prior lines of systemic therapy in metastatic setting	2	2	2
Patients with liver metastatic disease, n (%)	14 (70)	1 (20)	26 (77)
ECOG, n (%)			
0	12 (60)	2 (40)	9 (26)
1	8 (40)	3 (60)	25 (74)

Data extract 28 May 2026. One patient treated with vopimetostat + daraxonrasib (PDAC) withdrew consent in cycle 1. *Patient was not candidate for chemotherapy and enrolled according to protocol. PDAC, pancreatic ductal adenocarcinoma; NSCLC, non-small cell lung cancer.

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Vopimetostat + daraxonrasib in MTAPdel 2/3L PDAC: ORR 92% - 11 PRs in 12 patients

N=12	
ORR	92%
DCR	100%

- 9 cPR
- 2 uPR pending confirmation

Dose levels:
DL1: 200 mg vopimetostat + 100 mg daraxonrasib
DL2: 250 mg vopimetostat + 100 mg daraxonrasib

Data extract 28 May 2026. Dashed line indicates threshold for PR (-30%). Objective response rate per RECIST v1.1 includes patients who received first dose of the study drug at least 14 weeks prior to the data extract to allow for 2 post-baseline scans. Median duration of follow-up 6.8 months (3.3 - 9.7). *Patient discontinued due to non-compliance. Disease control rate (DCR) defined as fraction of patients with overall response of SD, PR, or CR at the time of the first scheduled scan. PDAC, pancreatic ductal adenocarcinoma; ORR, objective response rate; DCR, disease control rate; 2/3L, second/third line.

Vopimetostat + daraxonrasib in MTAPdel NSCLC and PDAC: ORR 93% - 14 PRs in 15 patients

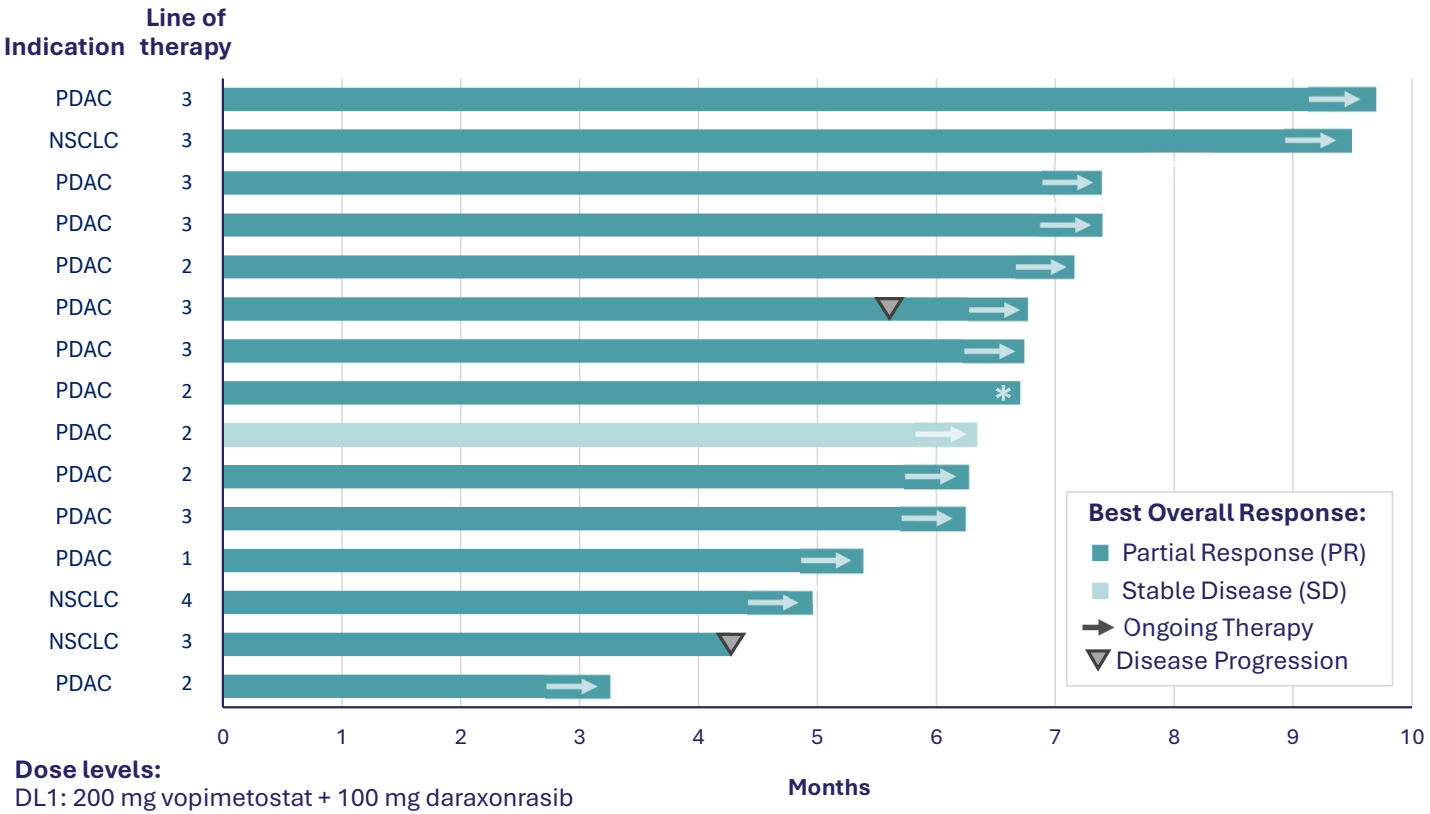
N=15	
ORR	93%
DCR	100%

- 12 cPR
- 2 uPR pending confirmation

Dose levels:
DL1: 200 mg vopimetostat + 100 mg daraxonrasib
DL2: 250 mg vopimetostat + 100 mg daraxonrasib

Data extract 28 May 2026. Dashed line indicates threshold for PR (-30%). Objective response rate (ORR per RECIST v1.1) and all efficacy data is reported in patients who received their first dose of the study drug combination at least 14 weeks prior to the data extract to allow for 2 potential post-baseline scans. Median duration of follow-up 6.7 months (3.3 - 9.7). *Patient discontinued due to non-compliance. Disease control rate (DCR) defined as fraction of patients with overall response of SD, or PR at the time of the first evaluation. PDAC, pancreatic ductal adenocarcinoma; NSCLC, non-small cell lung cancer. ORR, objective response rate; DCR, disease control rate; 2/3L, second/third line.

Encouraging durability with vopimetostat + daraxonrasib



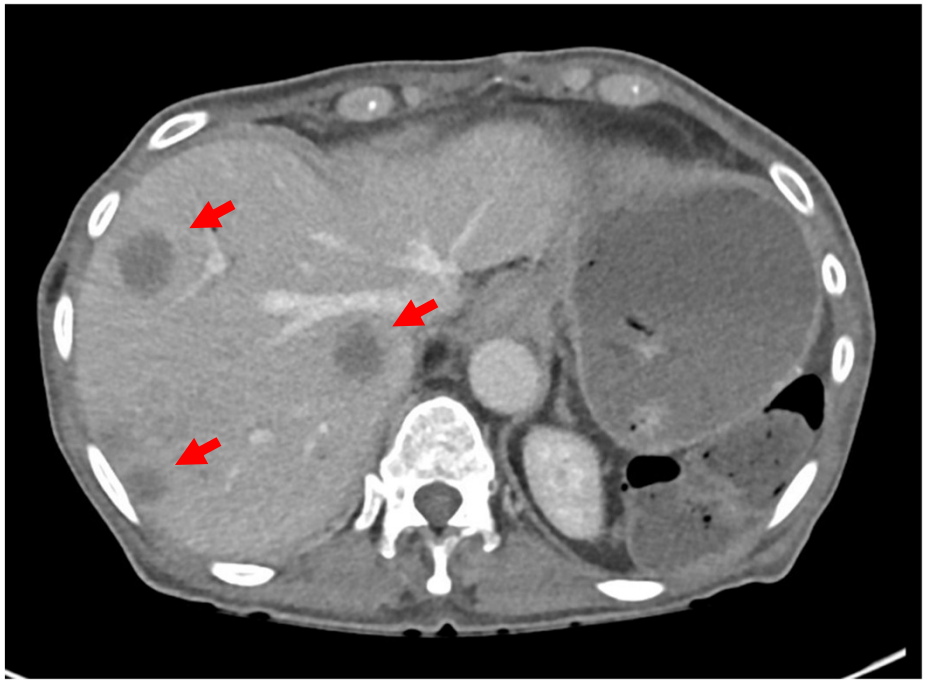
Dose levels:
DL1: 200 mg vopimetostat + 100 mg daraxonrasib
DL2: 250 mg vopimetostat + 100 mg daraxonrasib

Key Metrics

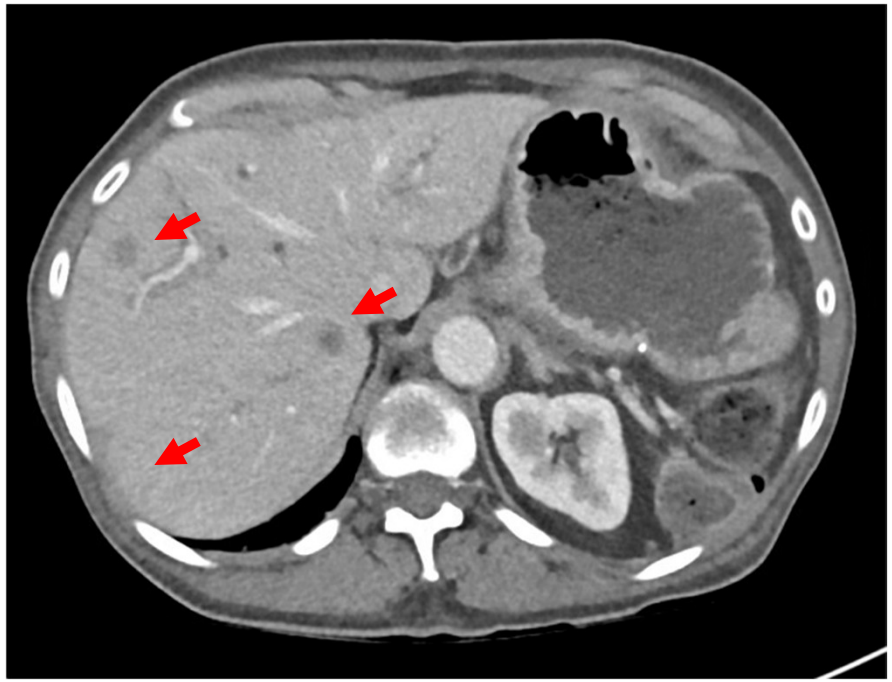
- Two disease progressions observed
- Longest treatment ~10 months, ongoing
- Median PFS NR (NE-NE)
- 90% 6-month PFS rate in PDAC (95% CI: 47-99)
- 50% of PDAC patients are 3L
- Patients not yet efficacy evaluable (n=9) are all ongoing with no disease progression

Data extract 28 May 2026. The swimmer plot displays all patients who received their first dose of the study drug combination at least 14 weeks prior to the data extract to allow for 2 potential post-baseline scans. *Patient discontinued due to non-compliance. PDAC, pancreatic ductal adenocarcinoma. NSCLC, non-small cell ling cancer. CI, confidence interval.

72 year old woman with MTAPdel, KRAS-G12R metastatic pancreatic cancer who received vopimetostat + daraxonrasib in the 3L setting



Baseline



Cycle 7, day 1:
cPR (-52%)
Response ongoing

Data extract 28 May 2026. 3L, third line; cPR, confirmed partial response.

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Vopimetostat + daraxonrasib was generally well tolerated

	Dose level 1 200 mg vopimetostat + 100 mg daraxonrasib PDAC, N=16		Dose level 1 200 mg vopimetostat + 100 mg daraxonrasib NSCLC, N=5		Dose level 2 250 mg vopimetostat + 100 mg daraxonrasib PDAC, N=4	
	All grades	**Grade 3**	**All grades**	**Grade 3**	**All grades**	**Grade 3**
TRAEs ≥15%						
Patients with any event	12 (75)	4 (25)	5 (100)	-	4 (100)	3 (75)
Rash*	7 (44)	-	5 (100)	-	4 (100)	1 (25)
Diarrhea	5 (31)	-	4 (80)	-	3 (75)	-
Stomatitis/mucositis	9 (56)	-	1 (20)	-	1 (25)	1 (25)
Fatigue	2 (13)	-	1 (20)	-	3 (75)	1 (25)
Thrombocytopenia	4 (25)	2 (13)	1 (20)	-	1 (25)	-
Nausea	2 (13)	-	2 (40)	-	1 (25)	-
Peripheral edema	2 (13)	-	-	-	2 (50)	-

Safety Summary

- No new safety signals observed
- No discontinuations due to AEs
- Two dose reductions – dose level 1
- One dose reduction – dose level 2
- Most AEs were Grade 1 or 2
- No related Grade 4 or 5 AEs
- No related SAEs
- At dose level 1: No DLTs
- At dose level 2:
  - DLTs in 2 patients:
    - Grade 3 acneiform rash (dose reduced, continued on study)
    - Grade 3 stomatitis and fatigue (withdrew consent)

Plan to advance dose level 1 into further clinical development

Data extract 28 May 2026. The safety population includes all patients with PDAC who received at least one dose of the study drug combination prior to the data extract. Median duration of follow-up 5.8 (1.0-9.7). *Rash includes TRAEs of rash, rash maculo-papular and dermatitis acneiform. DLT, dose-limiting toxicity. SAE, serious adverse event. TRAE, treatment-related adverse event.

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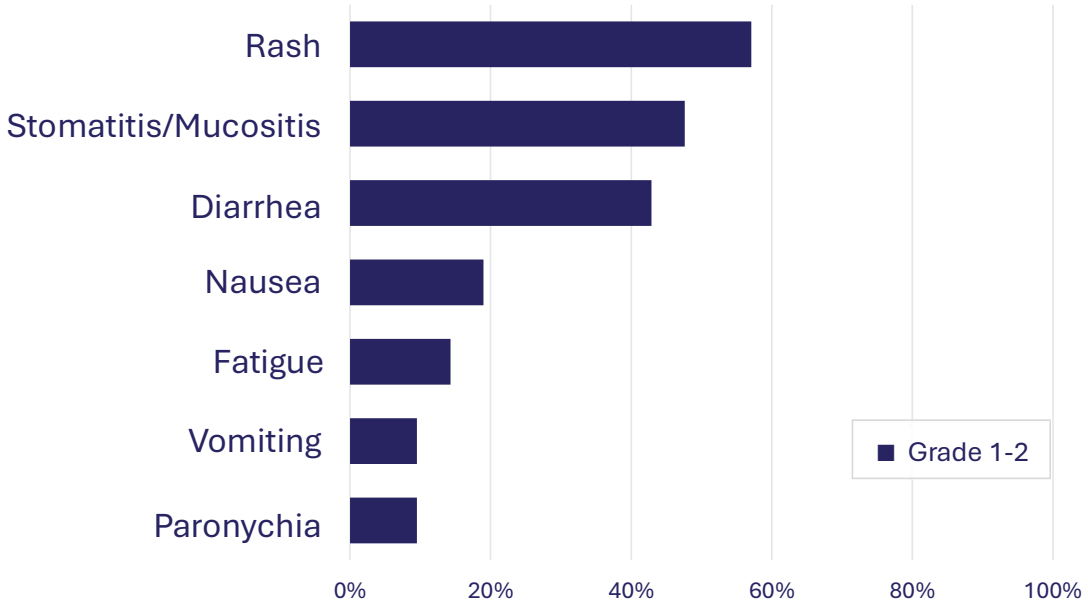
Vopimetostat + daraxonrasib has favorable RAS associated safety profile

vopimetostat 200 mg + daraxonrasib 100 mg (PDAC and lung)
n=21 (TRAEs, % patients)



Median follow-up: 5.0 months

Pharmacokinetics and safety
dose level 1

- Daraxonrasib AUC: 4106 hr*ng/ml (n=13, CV 40.5%)
  - Similar to daraxonrasib 300 mg single agent[1]
- PRMT5 inhibition may improve RAS inhibitor-mediated on target toxicity due to upregulation of MAPK activation / pERK[2]
- No grade ≥ 3 RAS associated TRAEs

Data extract 28 May 2026. Data displayed are AEs most frequently associated with RAS inhibitors. There were no Grade 3+ related AEs.
1. Wolpin et al, NEJM, N Engl J Med 2026;394:1790-1802. 2. Knoll, Cancer Research 2025; Drizyte-Miller, Cancer Research 2025

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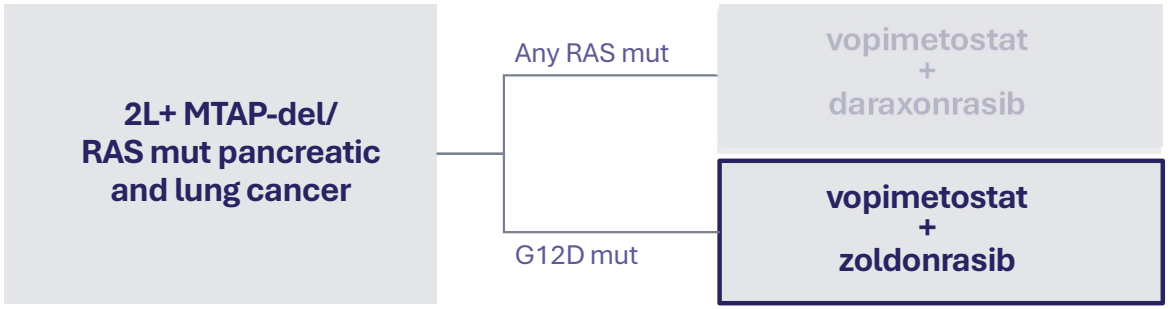
First PRMT5 inhibitor combined with RAS inhibitors in the clinic

Phase 1 dose escalation trial



Key inclusion criteria:

- MTAP loss by NGS or IHC
- Prior lines:
  - PDAC: 1-2 lines prior systemic therapy in metastatic setting
- ECOG PS 0 or 1
- No prior PRMT5i or RASi

Vopimetostat + zoldonrasib:

- **Dose escalation range:**
  - 200 – 250 mg vopimetostat QD +
  - 600 – 1200 mg zoldonrasib QD
- **Evaluable patients:**
  - Safety n=34
  - Efficacy n=27

MTAP status for enrollment:

85% by NGS / 15% by IHC

~95% concordance (NGS and IHC)

Data extract 28 May 2026. Patients who received first dose at least 14 weeks prior to data cutoff were efficacy evaluable, all treated patients safety evaluable. 2L, second line; NGS, next-generation sequencing; IHC, immunohistochemistry; PDAC, pancreatic ductal adenocarcinoma; NSCLC, non-small cell lung cancer.

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Vopimetostat + zoldonrasib was generally well tolerated

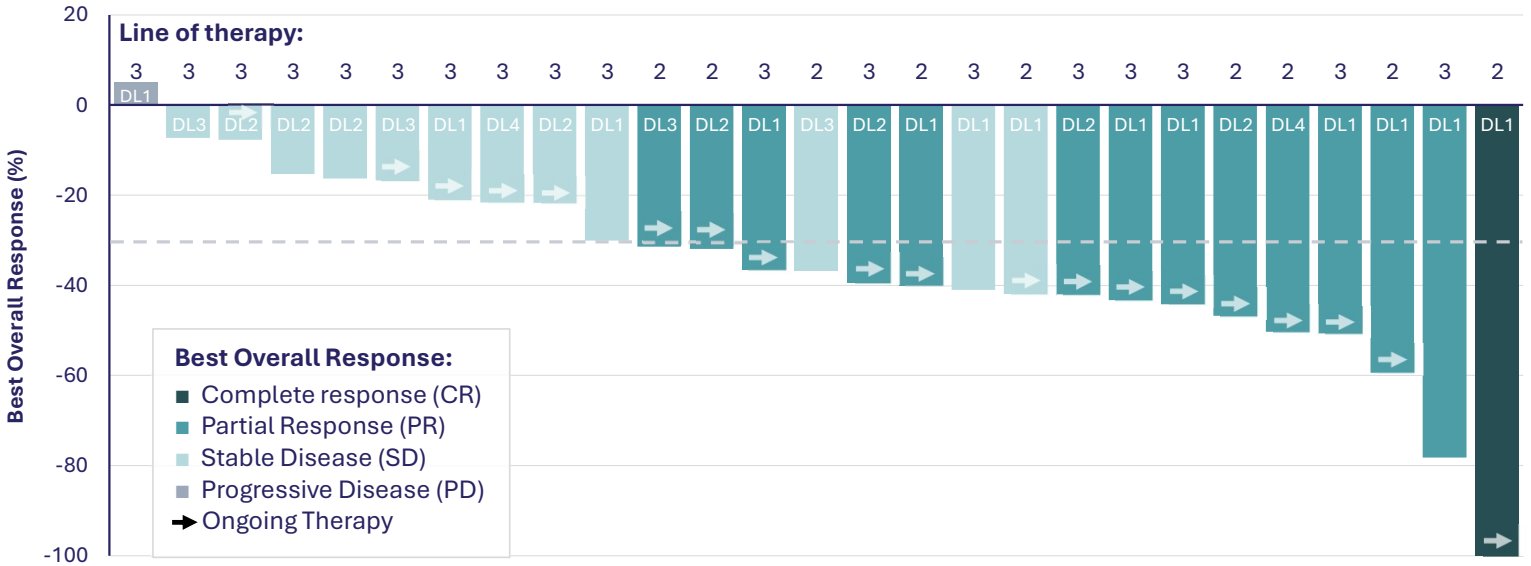
	All dose levels vopimetostat + zoldonrasib N=34	
	All grades	**Grade 3**
TRAEs ≥15%		
Patients with any event	28 (82)	9 (26)
Anemia	8 (24)	6 (18)
Nausea	12 (35)	-
Vomiting	12 (35)	-
Rash (all grade 1)	8 (24)	-
Diarrhea	7 (21)	1 (3)
Fatigue	7 (21)	-
Dysgeusia	6 (18)	-

Safety Summary

- No new safety signals observed
- No discontinuations due to AEs
- One dose reduction
- Most AEs were Grade 1 or 2
- No related Grade 4 or 5 AEs
- 3 treatment related SAEs
  - Anemia
  - Thrombocytopenia
  - Vision blurred
- No DLTs

Data extract 28 May 2026. Safety-evaluable population includes patients who received at least 1 dose of the study drug combination. There were no related Grade 4 or 5 events. Median duration of follow-up 4.9 months (0.6-11.1). TRAE, treatment-related adverse event; SAE, serious adverse event; DLT, dose-limiting toxicity.

Vopimetostat + zoldonrasib in MTAPdel KRAS G12D 2/3L PDAC: ORR 52% - 14 PRs in 27 patients



N=27	
ORR	52%
DCR	96%

- 10 cPR
- 4 uPR pending confirmation
- 74% 6-month PFS rate (95% CI: 49-88)

Dose levels:
DL1: 200 mg vopimetostat + 600 mg zoldonrasib
DL2: 250 mg vopimetostat + 600 mg zoldonrasib
DL3: 250 mg vopimetostat + 1200 mg zoldonrasib
DL4: 200 mg vopimetostat + 1200 mg zoldonrasib

Data extract 28 May 2026. Dashed line indicates threshold for PR (-30%). Objective response rate (ORR) is reported in patients who received their first dose at least 14 weeks prior to the data extract to allow for 2 potential post-baseline scans. ORR includes patients with PR or CR that has been confirmed (n=10) or is pending confirmation (n=4). Median follow-up 5.6 months (3.3-11.1). DCR, disease control rate, defined as fraction of patients with overall response of stable disease or better at the time of the first scheduled on-treatment evaluation (6 weeks). TRAE, treatment-related adverse event. DLT, dose-limiting toxicity. SAE, serious adverse event, CI, confidence interval.

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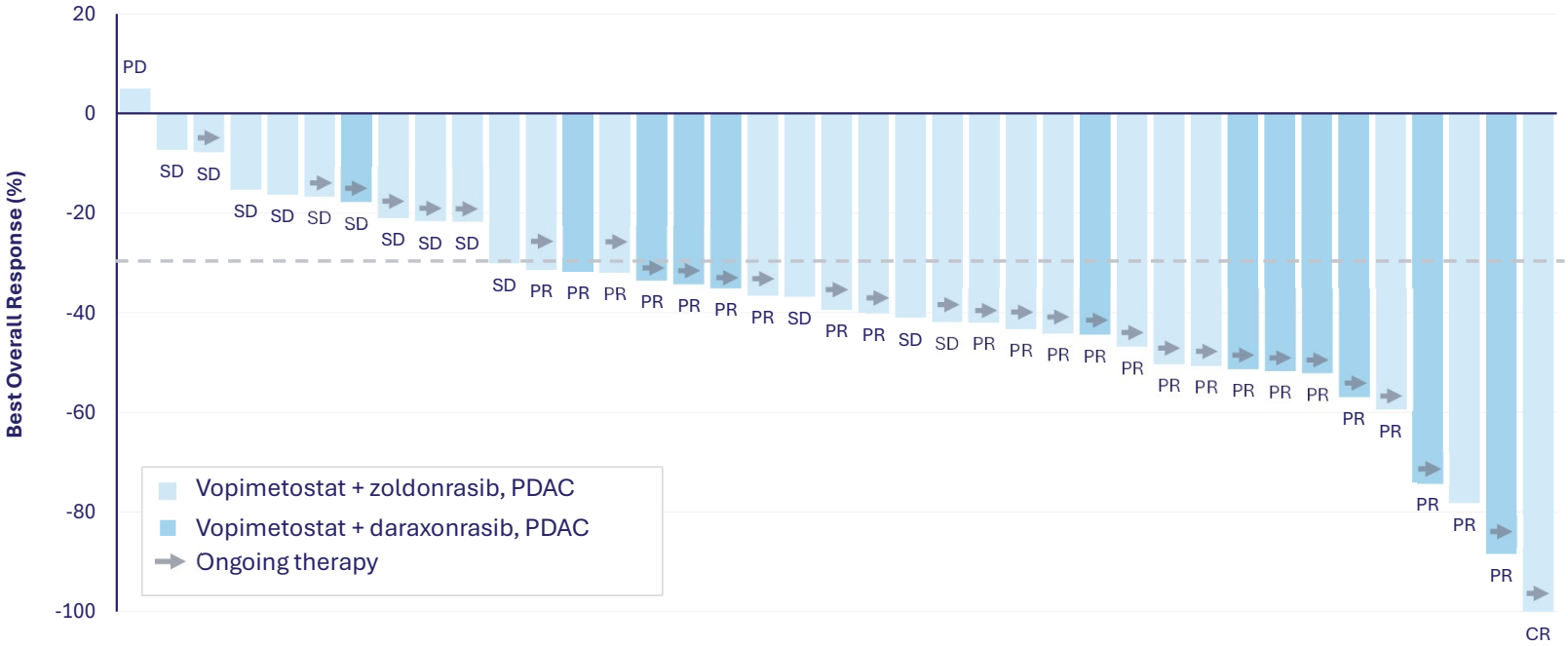
Combined ORR 64% in 2/3L PDAC demonstrates clinical synergy of vopimetostat + RAS(ON) inhibition



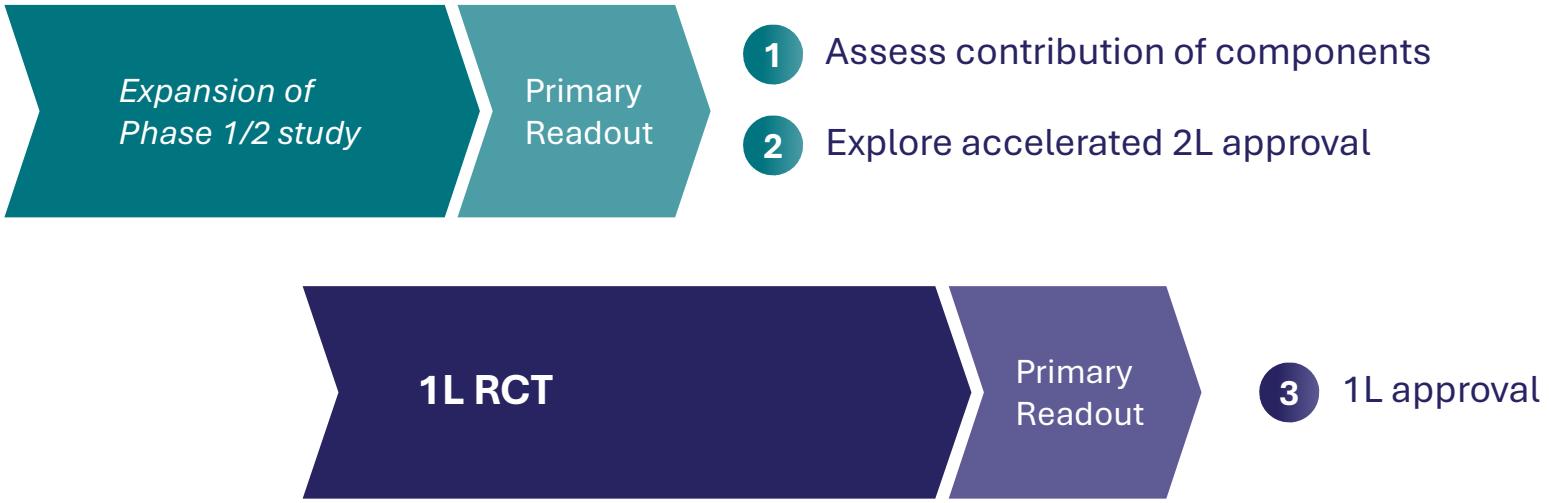
N=39	
ORR	64%
DCR	97%

Data extract 28 May 2026. Dashed line indicates threshold for PR. Objective response rate (ORR) is reported in PDAC patients who received their first dose of the study drug combination at least 14 weeks prior to the data extract to allow for 2 potential post-baseline scans. Median follow-up 6.3 months (3.3 - 11.1). DCR, disease control rate, defined as fraction of patients with overall response of stable disease or better at the time of the first scheduled on-treatment evaluation (6 weeks). PDAC, pancreatic ductal adenocarcinoma.

Strategy to accelerate registration-directed development of vopimetostat

Adam Crystal, MD PhD, President of Research and Development

Tango's strategy to potentially develop vopimetostat + daraxonrasib combination for patients with pancreatic cancer



Plan to engage global regulatory authorities to share Phase 1/2 data and discuss registration strategy

Subject to regulatory feedback. 1L, first line; 2L, second line; RCT, randomized controlled trial.

Capital allocation plan and financial highlights

Matthew Gall, Chief Financial Officer

Disciplined capital allocation focused on most promising, value-creating opportunities

Clear path forward

Rapidly advance 1L PDAC vopimetostat + daraxonrasib chemo-free combination

Accelerate PRMT5 assets to near-term value-inflecting milestones with capital efficiency

Optimize robust monotherapy and combination PRMT5 franchise across multiple indications

Multiple inflection points anticipated by end of 2026

- ❑ Finalize design of Phase 3 randomized-controlled trial of the combination approach in front-line pancreatic cancer in 2H 2026
- ❑ Disclose vopimetostat lung cancer monotx data 2H
- ❑ Release initial TNG456 glioblastoma data 2H
- ❑ Present 2/3L PDAC vopimetostat + RAS(ON) inhibitors combination data to a scientific conference 2H
- ❑ Initiate Phase 1/2 vopimetostat + ERAS-0015 combination study 2H

$380M cash and investments as of March 31, 2026
Cash runway into 2028

PDAC, pancreatic ductal adenocarcinoma.

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Closing remarks

Malte Peters, MD, Chief Executive Officer

At the forefront of transformative shift in pancreatic cancer treatment

Scientific leader
in PRMT5 inhibition

Transformative
92% ORR in 2/3L PDAC
in combination with daraxonrasib

Clear strategy
for front line development with chemotherapy free regimen

Near-term **focus on potential blockbuster PDAC opportunity**
Pipeline supporting data-driven **indication expansion** to drive long-term growth

TANGO therapeutics

PDAC, pancreatic ductal adenocarcinoma; 2/3L, second/third line.
Data from ongoing Phase 1/2 clinical trial. Data as of 28 May 2026.