Vopimetostat clinical update

23 October 2025

TANGO therapeutics™

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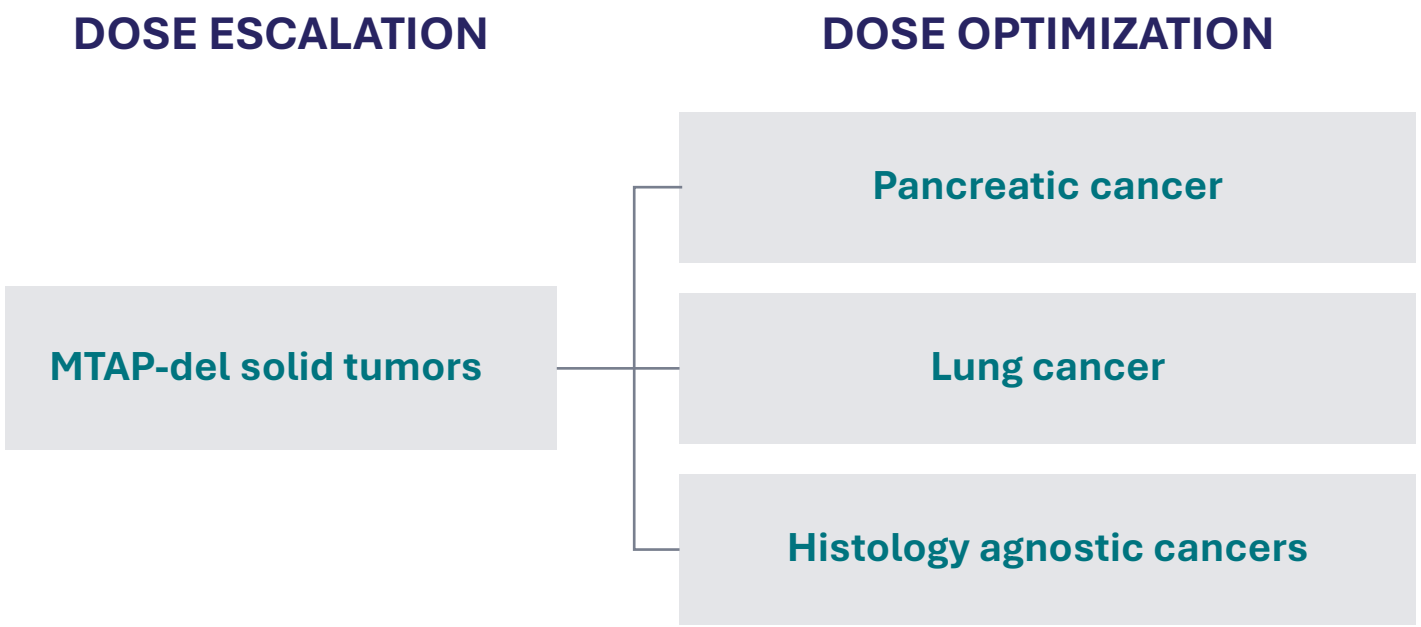
Vopimetostat (TNG462) overview

- Oral, once a day, MTAP-selective PRMT5 inhibitor
- Potential best-in-class molecule with superior target coverage and safety profile
- A potential turning point in multiple hard to treat cancers, with demonstrated durable tumor control and favorable tolerability in the ongoing clinical trial, where current standard of care has neither
- Key indications for development in approximately 60,000 patients/yr (MTAP-del, US)
  - Pancreatic cancer (~20,000 patients/yr)
  - Lung cancer (~22,000 patients/yr)
  - Histology agnostic (~20,000 patients/yr)
- RAS combination studies ongoing in pancreatic and lung cancer
- Pivotal study in second line (2L) pancreatic cancer planned to initiate 2026, potential to be first-to-market in 2L MTAP-del pancreatic cancer

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

Vopimetostat phase 1/2 study



All pancreatic cancers are adenocarcinomas. All lung cancers are non-small cell histology.

Current and planned vopimetostat disclosures

October 2025

- Phase 1/2 trial safety, tolerability and efficacy data
  - 179 patients, 154 at active doses, 84 at go-forward dose (250 mg QD)
- Pancreatic cancer cohort
  - 64 patients at active doses, 39 pts with >6 mo FU
  - 29 2L patients, 10 pts with >6 mo FU
  - 2L pancreatic cancer pivotal study design
- Histology agnostic cohort
  - 47 patients, 41 patients with >6 mo FU

2026

- Vopimetostat + daraxonrasib or zoldonrasib initial 2L+ safety and efficacy data
- Initial 1L pancreatic combination data and durability update on 2L+ cohort
- Lung cancer cohort safety and efficacy data, development plans
- TNG456 phase 1 single agent safety and efficacy data

Data extract 1 Sept 2025
FU, follow-up. Active doses are defined as 200 mg QD and above.

Vopimetostat has robust, durable clinical activity in multiple MTAP-del cancer types

- Overall response rate (ORR) 27% across cancer types currently best-in-class*, FDA agreement on 250 mg QD go-forward dose
- Median progression-free survival (mPFS) 7.2 months and ORR 25% in 2L MTAP-del pancreatic cancer supports planned pivotal study start 2026
- Robust enrollment in ongoing combination study of vopimetostat + RAS(ON) inhibitors in 2L+ MTAP-del pancreatic and lung cancer patients, expansion to first line (1L) cohort planned
- Lung cancer cohort fully enrolled (n=41), emerging data consistent with expectations, update planned 2026
- 49% ORR and mPFS 9.1 months in histology agnostic cohort of multiple late line cancer types (excluding sarcoma) provides further evidence of strong vopimetostat activity and additional optionality for development
- Potential best-in-class safety and tolerability profile with no drug-related dose discontinuations and ~8% dose reduction suggests good combinability with other agents

Data extract 1 Sept 2025
*Based on previously reported data, BMS504 ORR 23% (ASCO 2025), AMG193 ORR 21% (ESMO 2024). No head-to-head studies have been conducted.
The histology agnostic cohort includes all patients excepting lung cancer, pancreatic cancer and sarcoma patients.

Vopimetostat efficacy matures over time

Vopimetostat phase 1/2 trial

Follow-up	N	ORR	Median follow-up
Any	127	20%	7.4 mo
> 4 mo	114	22%	7.6 mo
> 6 mo	85	27%	9.3 mo

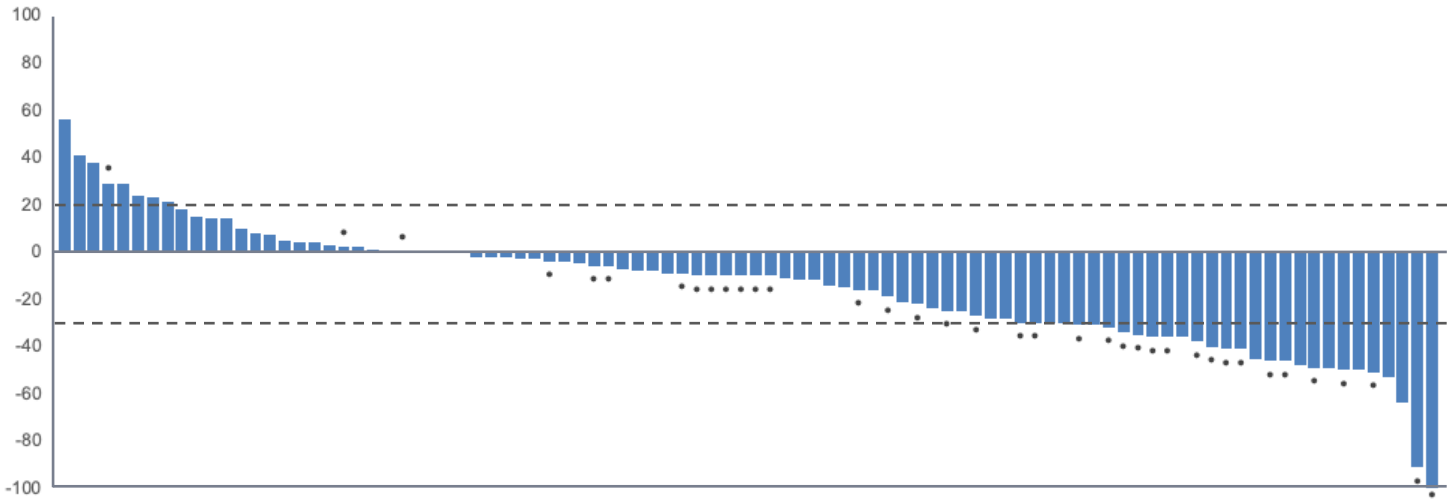
All patients dosed more than 6 months before data cutoff at 200 mg QD and above

Median time to RECIST response 3.5 months

Data extract 18 Aug 2025.

Vopimetostat 27% ORR across cancer types

Active doses >6 mo follow-up n=94



Key points

- ORR 27%
- mPFS 6.4 months
- DCR 78%
- 37/94 patients ongoing
- Active in all tumor types enrolled except sarcoma (ORR 0%, n=9)
- Median follow-up 9.4 months

Data extract 1 Sept 2025.

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

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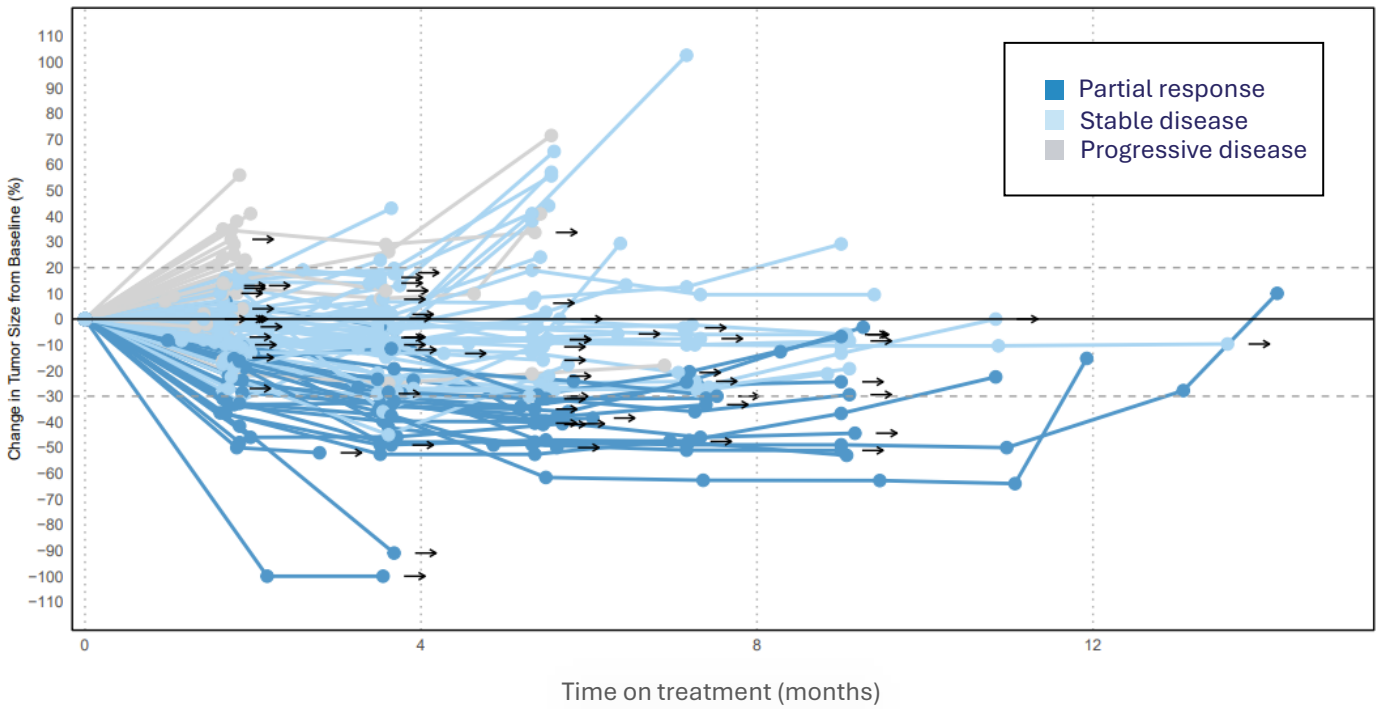
Durable disease control with vopimetostat across cancer types

All tumor evaluable patients at active doses (n=131)



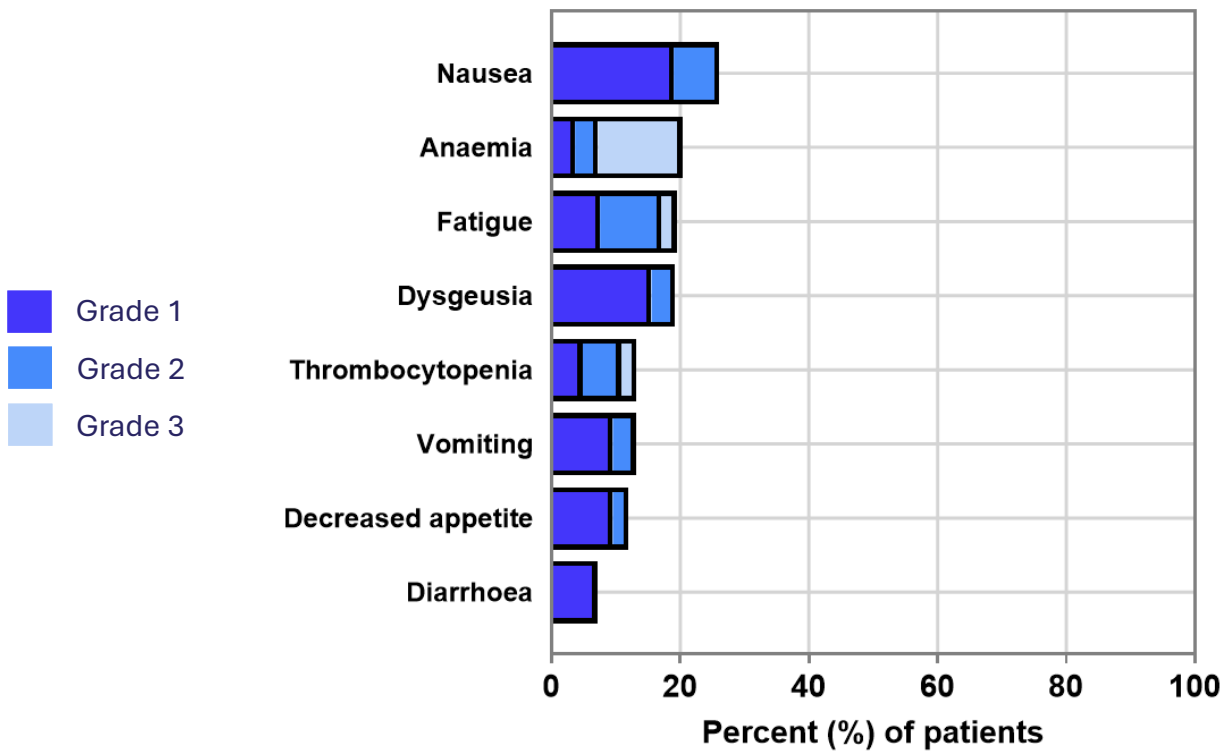
Key points

- Overall mPFS 6.4 months
  - PR pts 11.1 months
  - SD pts 7.3 months
  - PD pts <2 months
- Median time to response 3.5 months

Data extract 1 Sept 2025.
mPFS calculation includes all patients (n=143); spider plot represents only tumor-evaluable subset of patients (n=131).

Vopimetostat 250 mg QD has a potential best-in-class safety profile

Related AEs in ≥5% pts (n=84)



Key points

- Median follow-up 6.1 months
- 8% dose reduction
- 0% discontinuation for related events
- No grade 4-5 related events
- Low grade GI side effects

Vopimetostat AE profile suggests good tolerability in combination with chemo- and targeted therapies

Data extract 1 Sept 2025.

Vopimetostat pancreatic cancer cohort

64 pancreatic cancer patients at active doses*

One prior therapy for advanced disease

- n=29 pts
- 10/29 pts more than 6 months since enrollment (8 pts tumor evaluable)

Two or more therapies for advanced disease

- n=34 pts
- 29/34 pts more than 6 months since enrollment

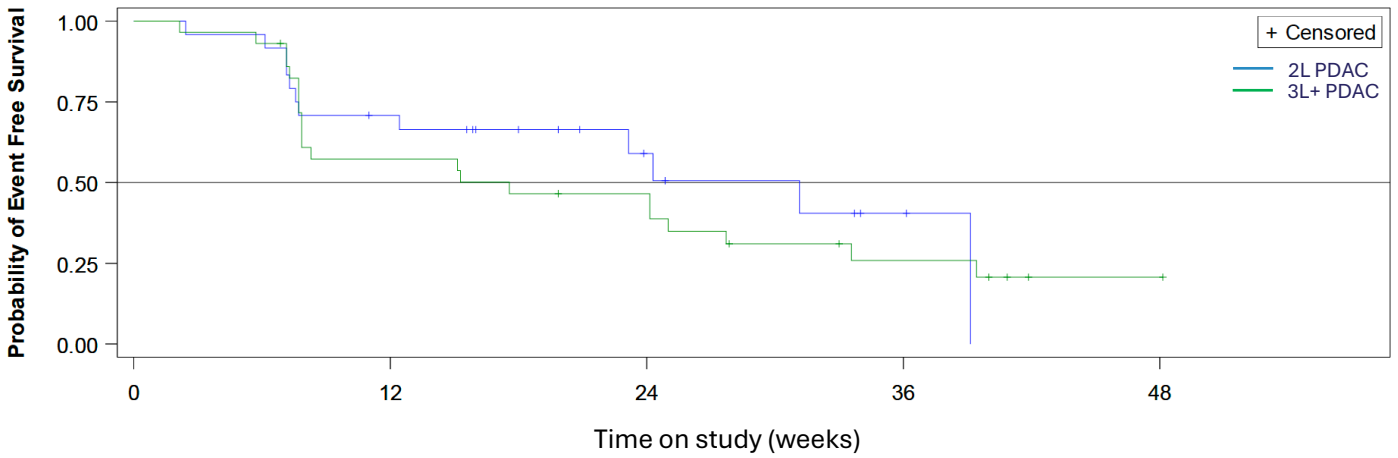
Enrollment by starting dose (QD)

- 200 mg n=22
- 250 mg n=35
- 300 mg n=6
- 600 mg n=1

Data extract 1 Sept 2025
*Includes all patients enrolled in the study more than 6 months prior to the data cutoff, including those remaining on study, progressed or withdrew. Includes one 1L patient.

Vopimetostat mPFS is 7.2 months in 2L pancreatic cancer

Vopimetostat in 2L and 3L+ pancreatic cancer



Line of therapy	N	Events	Censored	mPFS (mo)	95% CI (mo)
2L	24	12	12	7.2	1.7 - NR
3L+	29	20	9	4.1	1.8 – 7.7

Summary

Vopimetistat

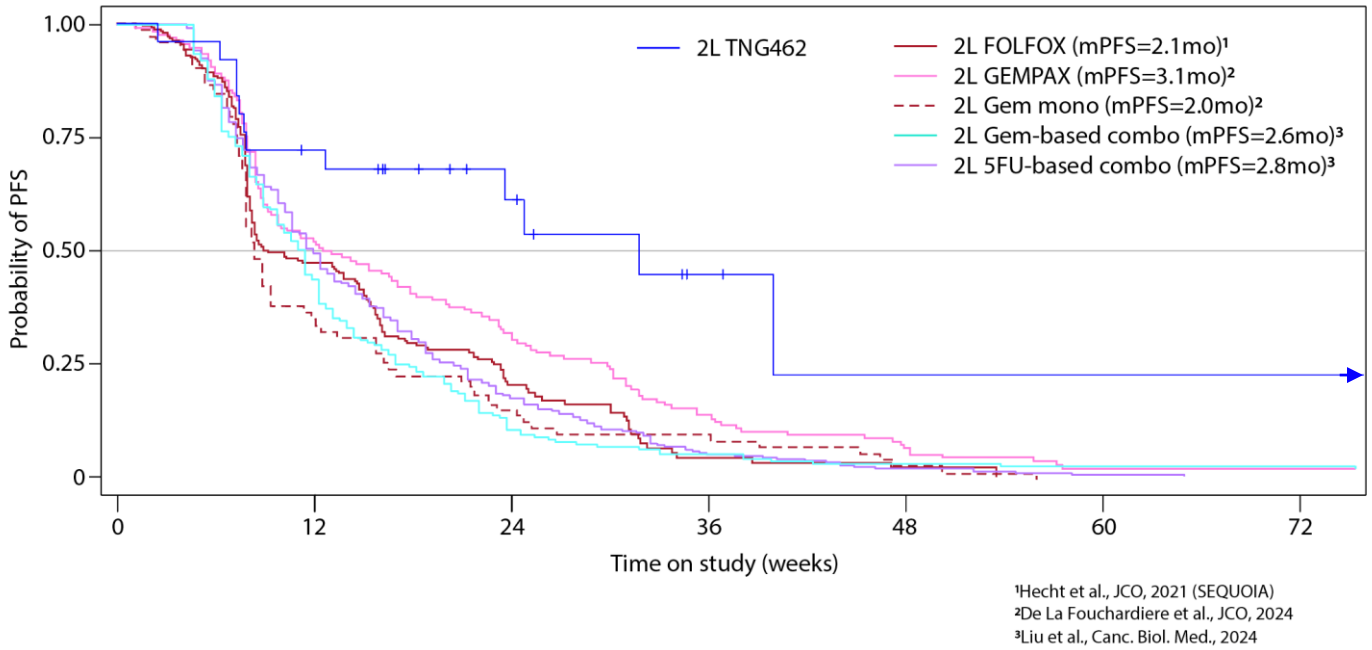
- 2L mPFS 7.2 mo
- 2L ORR 25%
  - Overall ORR 15%
- Overall DCR 71%
- Median follow-up 7.8 mo

Chemotherapy historical control trials

- 2L mPFS 2-3.5 mo
- 2L ORR ~10%*

Data extract 1 Sept 2025.
All 2L pancreatic cancer patients at 200 mg QD and above.
*ORR ranging from 3-17% reported in published literature.

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



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

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

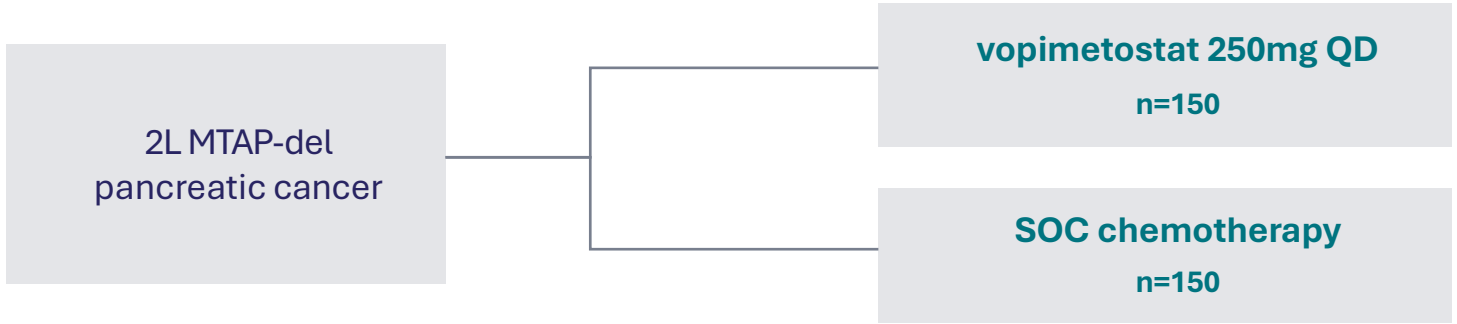
Key points

- Vopimetostat 2L mPFS 7.2 mo
- SOC chemotherapy mPFS 2-3.5 mo
- MTAP deletion likely confers worse prognosis vs WT due to concurrent CDKN2A deletion[a]
- Vopimetostat pivotal study control arm of only MTAP-del patients may have lower mPFS than historical controls, increasing probability of success

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

Vopimetostat pivotal trial in 2L pancreatic cancer

Pivotal study start planned 2026

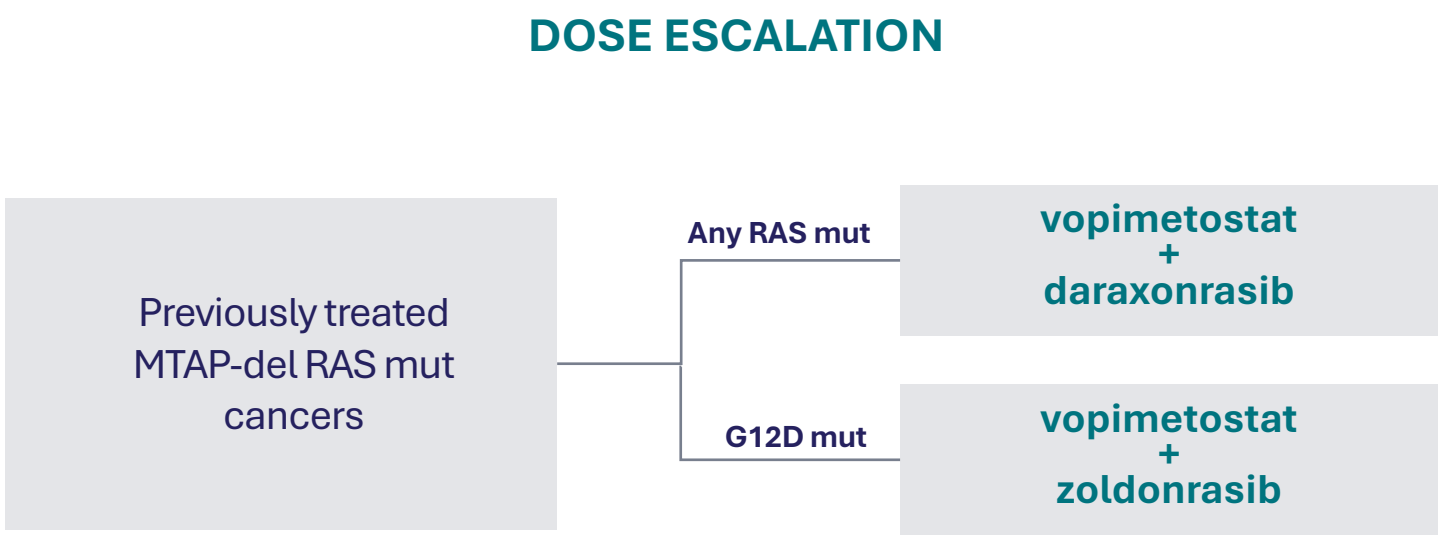


Planning for 2L registration

- Rapid enrollment of ~300 patients anticipated given high unmet medical need in this patient population
- Approval in 2L pancreatic cancer after chemotherapy and/or RAS inhibitors is expected to retain value until a PRMT5 inhibitor approval in 1L

FDA interaction to finalize trial design planned later this quarter.

Vopimetostat + RAS(ON) inhibitors may provide chemotherapy free treatment for 1L MTAP-del pancreatic cancer



Safety and efficacy data update planned 2026

Study update

- Cohort 1 complete (n=7)
  - Exposures in active range for each compound
  - Both combos well tolerated to date, early signs of activity
  - Backfill ongoing with robust enrollment
- Cohort 2 enrollment ongoing

1L pivotal study planning

- RAS inhibitors are likely to change the standard of care in 1L pancreatic cancer
- Ongoing study has the potential to support a 1L pivotal study with shorter timelines than competitors

Vopimetostat lung cancer cohort

41 lung cancer patients at active doses

One or more prior therapy for advanced disease

- n=41 patients
- 12/41 pts more than 6 months since enrollment
- Median follow-up 4.7 months

Enrollment by starting dose (QD)

- 200 mg n=13*
- 250 mg n=26
- 300 mg n=2

Fully enrolled, emerging data consistent with expectations
Update planned 2026

Data extract 1 Sept 2025
*Includes two patients enrolled at 160 mg QD

Vopimetostat histology agnostic cohort

47 histology agnostic patients at active doses

Histology agnostic cohort analysis excludes pancreatic cancer, lung cancer and sarcoma

One or more prior therapy for advanced disease

- n=47 patients
- 41/47 pts more than 6 months since enrollment

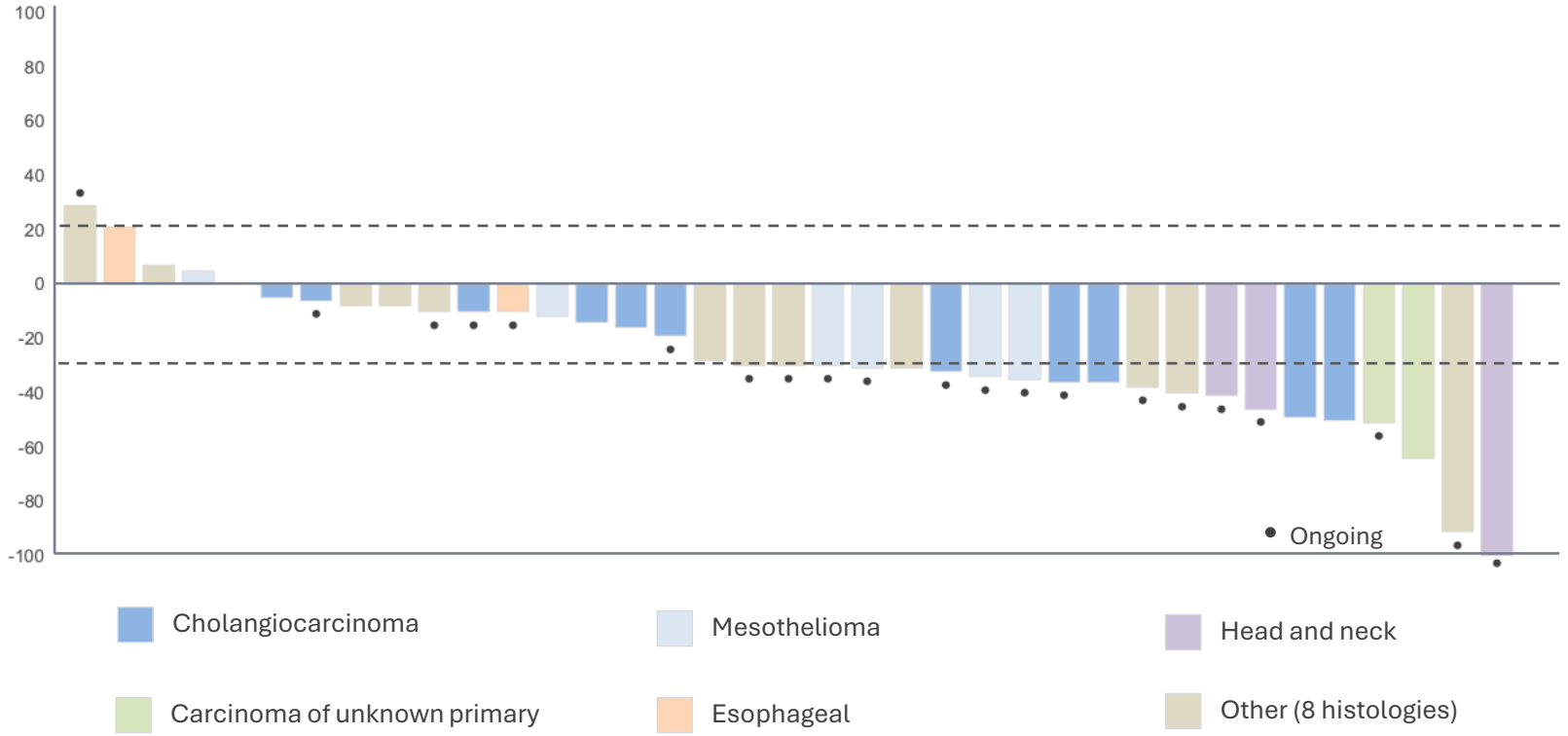
Enrollment by starting dose (QD)

- 200 mg n=15
- 250 mg n=19
- 300 mg n=11
- 600 mg n=2

Data extract 1 Sept 2025
Includes all patients enrolled in the study more than 6 months prior to the data cutoff, including those remaining on study, progressed or withdrew.

Vopimetostat 49% ORR in histology agnostic cohort

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

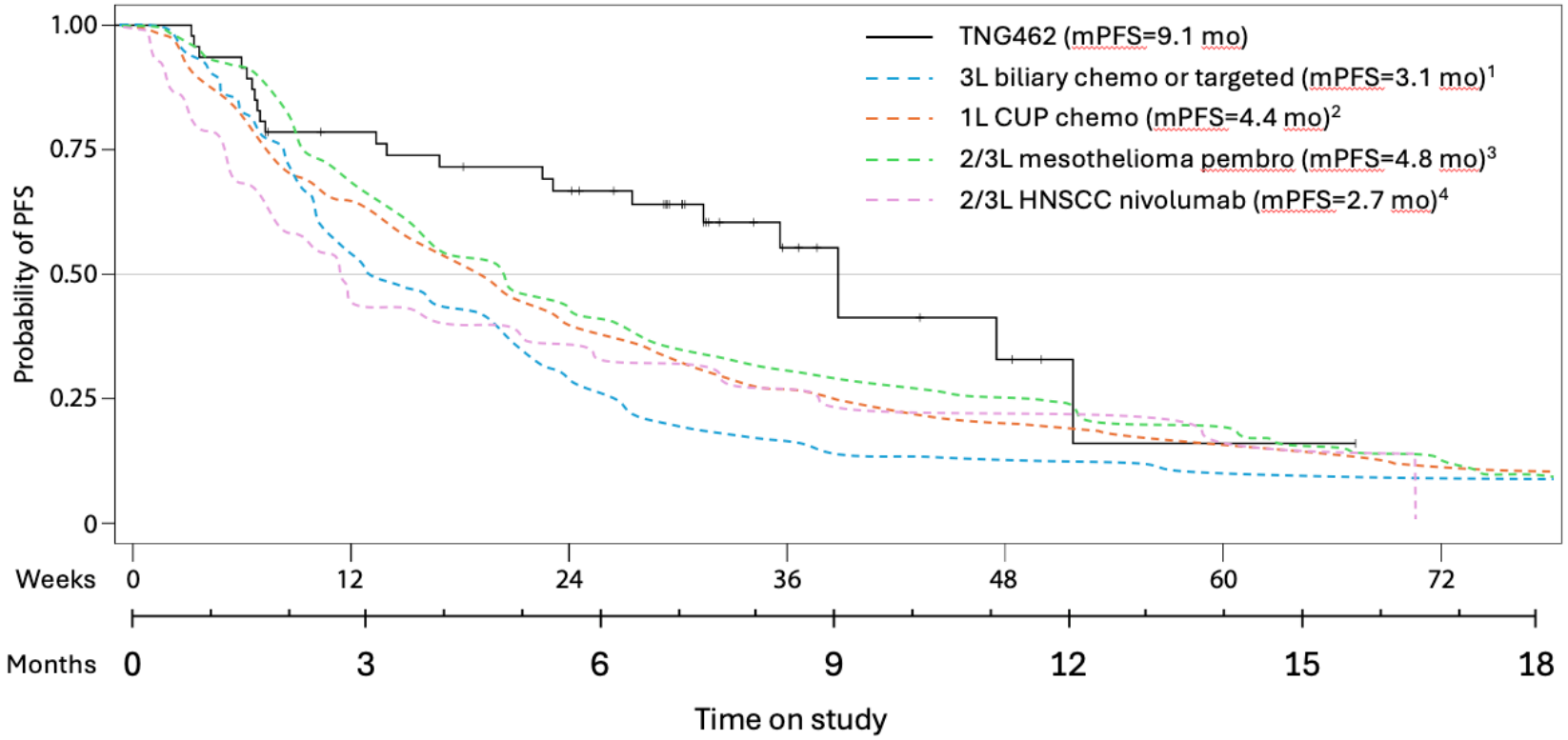


Key points

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

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

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



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

mPFS (95% CI)

9.1 months
(6.5 – 12.0)

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

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

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

Vopimetostat has the potential to be best-in-class and first-to-market for large patient populations with high unmet need

- FDA alignment on 250 mg QD go-forward dose
- Strong activity across cancer types
  - All histologies ORR 27%, mPFS 6.4 months
  - 2L pancreatic cancer ORR 25%, mPFS 7.2 months
  - Histology agnostic cohort ORR 49%, mPFS 9.1 months
  - Lung cancer data immature but promising, data update with development plans 2026
- 2L pancreatic cancer pivotal study start planned 2026
- Ongoing combination studies of vopimetostat + either daraxonrasib or zoldonrasib provide potential path to 1L registration pancreatic and lung cancer
- Potential best-in-class safety and tolerability profile supports potential for good combinability with other agents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