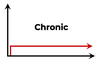
Atebimetinib (IMM-1-104) + Modified Gemcitabine/Nab-Paclitaxel (mGnP) Shows Extraordinary Overall Survival (OS) and Favorable Tolerability in First-Line (1L) Metastatic PDAC: Updated Phase 2 Results

Encore Company presentation (see Acknowledgements) Immuneering Corporation, Cambridge, MA, San Diego, CA, and New York, NY USA

Background & Methods

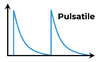
Background: Pancreatic tumors almost universally show MAPK pathway activation, most commonly through RAS mutations, making this pathway a key therapeutic target. Conventional MEK inhibitors block RAS signaling but have been limited by toxicity and short-lived efficacy. Atebimetinib (IMM-1-104) is a next-generation deep cyclic MEK inhibitor (DCI) that blocks both MEK and ERK phosphorylation, preventing CRAF bypass. Its short 2–3 h half-life and once-daily dosing enable pulsatile MEK pathway suppression that allows daily recovery in normal tissues, enhancing tolerability and reducing adaptive resistance.

Methods: This ongoing multicenter phase 2 study evaluated atebimetinib plus modified gemcitabine/nab-paclitaxel (mGnP) in 1L metastatic PDAC across 20 U.S. sites. After a 6-patient 240 mg QD lead-in, 34 patients were treated at the optimized, oral RP2D of 320 mg QD + mGnP. Safety, tolerability, and clinical activity were assessed. Data with a median follow-up of 9 months are reported.



Historical Paradigm:
- Chronic target engagement → Prioritizes fast/deep RECIST tumor shrinkage beyond -30% (limited surrogacy for OS)

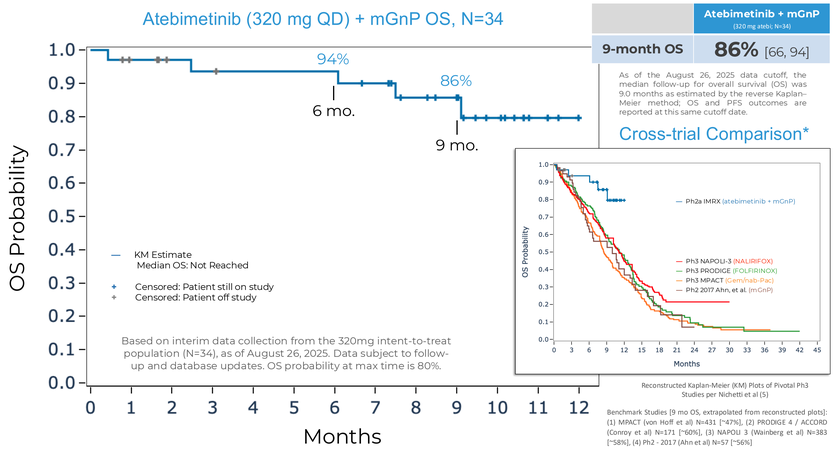
Challenges:
- High toxicity, adaptive/acquired resistance, limited durability



Alternative Approach:
- Pulsatile MEK inhibition (Deep Cyclic Inhibition) → designed to break MAPK addiction + spare healthy tissues + minimize resistance

DCI Validation:
- Observed favorable safety, clinical activity, strong 1L PDAC outcomes, expanded combinations (durability and tolerability)

Overall Survival (OS)



	Atebimetinib + mGnP (320 mg atebi; N=34)
9-month OS	86% [66, 94]

As of the August 26, 2025 data cutoff, the median follow-up for overall survival (OS) was 9.0 months as estimated by the reverse Kaplan–Meier method; OS and PFS outcomes are reported at this same cutoff date.

Cross-trial Comparison*

Reconstructed Kaplan-Meier (KM) Plots of Pivotal Ph3 Studies per Nichetti et al (5)

Benchmark Studies [9 mo OS, extrapolated from reconstructed plots]: (1) MPACT (von Hoff et al) N=431 [~47%], (2) PRODIGE 4 / ACCORD (Conroy et al) N=171 [~60%], (3) NAPOLI 3 (Wainberg et al) N=383 [~58%], (4) Ph2 - 2017 (Ahn et al) N=57 [~56%]

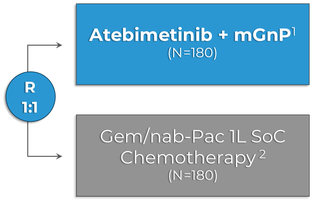
Overall Survival (OS) with Atebimetinib + mGnP in 1L PDAC. Kaplan–Meier plot showing OS in patients treated with atebimetinib (320 mg QD) plus modified gemcitabine/nab-paclitaxel (mGnP) (N=34). Median OS not reached at 9-month data cutoff (August 26, 2025); 6- and 9-month OS rates were 94% and 86%, respectively. Historical results from the Phase 3 MPACT trial of GnP report 6-month OS: 67%; 9-month OS: ~47%, Censored observations represent patients still on study (blue) or withdrew consent (gray).

Planned Phase 3 Global Study in 1L Metastatic Pancreatic Cancer

Global Randomized Pivotal Trial Plan: Designed to Demonstrate Best-in-Class Profile in 1L PDAC

Planned Patient Population: First-line (1L) metastatic Pancreatic Ductal Adenocarcinoma (PDAC)

- First line (1L) PDAC
- Metastatic setting
- ECOG PS 0-1



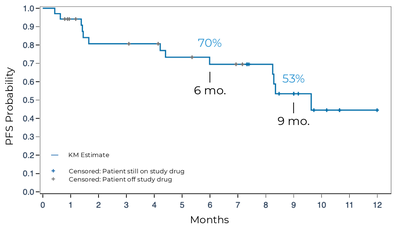
Primary Endpoint
OS
Secondary Endpoints
PFS
ORR
DCR
QoL

SOC = standard of care; R = randomize; PFS = progression-free survival; OS = overall survival; ORR = overall response rate; DCR = disease control rate; QoL = Quality of Life
(1.) Atebimetinib 320 mg PO QD + mGnP = 1,000 mg/m2 (Gem) + 125 mg/m2 (nab-Pac) days 1 & 15, every 4 weeks
(2.) SOC chemotherapy = full schedule Gemcitabine + nab-Paclitaxel (3 wk on/ 1 wk off)

Planned Phase 3 Global Randomized Trial Design. Upcoming pivotal study expected to enroll first-line (1L) metastatic PDAC patients with ECOG PS 0–1 and randomize (1:1) to atebimetinib (320 mg QD po) + mGnP (N=180) or standard-of-care gemcitabine/nab-paclitaxel (N=180). The primary endpoint is overall survival (OS); key secondary endpoints include progression-free survival (PFS), overall response rate (ORR), disease control rate (DCR), and quality of life (QoL). Trial design and development path subject to change, including based on results of ongoing Phase 1/2a trial and regulatory authority feedback.

Progression-Free Survival (PFS)

Progression-Free Survival (PFS) Supports Extraordinary Overall Survival in First-Line Pancreatic Cancer



Based on interim data collection from the 320mg intent-to-treat population (N=34), as of August 26, 2025. Data subject to follow-up and database updates.

	Atebimetinib + mGnP (320 mg atebi-; N=34)
9-month PFS	53% [31, 71]

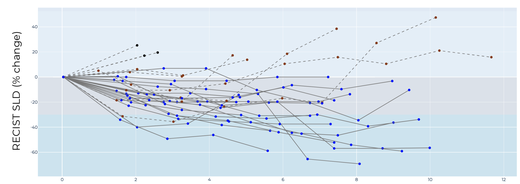
As of the August 26, 2025 data cutoff, the median follow-up for overall survival (OS) was 9.0 months as estimated by the reverse Kaplan-Meier method; OS and PFS outcomes are reported at this same cutoff date.

Median PFS (mPFS) SoC Benchmarks

	Reported mPFS	Target 1L Population
Atebi + mGnP	9.6 months	Broad
Gem/nab-Pac (GnP)	5.5 months	Broad
FOLFIRINOX	6.4 months	High-fitness
NALIRIFOX	7.4 months	High-fitness

Tumor RECIST SLD Over Time

Deepening Tumor Responses Over Time Observed



Sept 2025 corporate deck confirmed RECIST overall response rate **(ORR) of 39%** & disease control rate **(DCR) of 81%**, which included the 240 mg QD dose safety lead-in group as well.

In the above graph, N=29, consisting of response evaluable patients who also had ≥ 1 matched RECIST-evaluable post-baseline scan. Color coded categorization based on Company's initial assessment. SLD = RECIST sum of longest diameter for target lesions. Data based on interim data collection, as of August 26, 2025, of response evaluable patients from an ongoing Phase 1/2a trial of atebimetinib. One patient's target lesion measurement was corrected by the clinical site between the 6-month and 9-month median follow-up data cuts, resulting in a change in percent SLD reduction from approximately ~60% to ~40%. This correction did not affect the calculated ORR, DCR, PFS, or OS for the study population.

Safety & Tolerability

Favorable Tolerability Profile in 1L Pancreatic Cancer

Safety Data for Pivotal Trials and for Atebimetinib + mGnP in 1L PDAC*

PIVOTAL STUDY	Gem/nab-Pac (MPACT; N=431)	FOLFIRINOX (PRODIGE/ACCORD 11; N=171)	NALIRIFOX (NAPOLI 3; N=383)	Atebimetinib + mGnP (320mg atebi-; N=34)
Adverse Event (AE)	Grade ≥ 3 Incidence (%)	Grade ≥ 3 Incidence (%)	Grade ≥ 3 Incidence (%)	Grade ≥ 3 Incidence (%)
Neutropenia	38%	45.7%	14.1%	18%+
Fatigue	17%	23.6%	6.2%	6%
Diarrhea	6%	12.7%	20.3%	0%
Sensory Neuropathy	17%	9%	3.2%	0%
Leukopenia	31%	NR	NR	0%
Vomiting	NR	14.5%	7%	3%
Febrile Neutropenia	3%	5.4%	NR	3%
Thrombocytopenia	13%	9.1%	NR	0%
Anemia	13%	7.8%	10.5%	24%+
Hypokalemia	NR	NR	15.1%	3%
Nausea	NR	NR	11.9%	3%

- *Pivotal Studies: (1.) MPACT 2013 NEJM (von Hoff et al) N=431, (2.) PRODIGE 4 / ACCORD 11 2011 NEJM (Conroy et al) N=171, (3.) NAPOLI 3 2023 LANCET (Wainberg et al) N=383, (4.) FFX pivotal study follow up (Peron et al), and NR = not reported or not clearly reported*
- *Not all pivotal trials reported on all AE's or used fully consistent terminology*
- *(b) = only AE groups in this atebi + mGnP arm (N=34) that reached ≥ 10% Gr3 event level. For Anemia, all Grade 3, not SAE's, older patient population vs. historical benchmarks*
- *Neutropenia: Neutropenia, Neutrophil Count Decreased*
- *Sensory Neuropathy: Peripheral Sensory Neuropathy; Neuropathy: Peripheral*
- *No Gr 5 events; Patients received combination of 320mg atebi + mGnP (N=34)*

*FOR ILLUSTRATIVE PURPOSES ONLY: No head-to-head clinical trial has been conducted evaluating atebimetinib and other candidates or products. Differences exist between trial designs, subject characteristics and other factors, and caution should be exercised when comparing data across studies. mGnP = 1,000 mg/m2 (Gem) + 125 mg/m2 (nab-Pac) days 1 & 15, every 4 weeks

Patient Demographics

Atebimetinib + mGnP Evaluated in Older Patient Population

Characteristic	IMRX Ph2a (320 mg) Atebimetinib + mGnP	MPACT Gem/nab-Pac	PRODIGE/ACCORD 11 FOLFIRINOX	NAPOLI 3 NALIRIFOX
Trial Phase	Phase 2a	Phase 3	Phase 2/3	Phase 3
Patient Population	Metastatic PDAC (>90%)	Metastatic PDAC	Metastatic PDAC	Metastatic PDAC
N (treatment arm)	34	431	171	383
Median Age (years)	69	62	61	64
Age ≥ 65 (%)	68%	41%	28%	50%
ECOG PS 0 or 1 (%)	100%	92%	99%	100%
Male (%)	65%	57%	62%	53%
Liver, Lung and/or Peritoneal (%)	88%	85%	88%	80%
CA 19-9 Elevated (≥ 37 U/mL)	90% (N = 27/30)	84%*	85%	84%

Pivotal Studies: (1.) MPACT (von Hoff et al, 2013) N=431, (2.) PRODIGE 4 / ACCORD 11 (Conroy et al, 2011) N=171, (3.) NAPOLI 3 (Wainberg et al, 2023) N=383; FOR ILLUSTRATIVE PURPOSES ONLY: No head-to-head clinical trial has been conducted evaluating atebimetinib and other candidates or products. Differences exist between trial designs, subject characteristics and other factors, and caution should be exercised when comparing data across studies. [* = CA 19-9 > 35 U/mL]

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References

1. Von Hoff DD, Ervin T, Arena FP, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. N Engl J Med. 2013;369(18):1691-1703. doi:10.1056/NEJMoa1304369
2. Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N Engl J Med. 2011;364(19):1817-1825. doi:10.1056/NEJMoa1011923
3. Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. Lancet. 2023;402(10409):1272-1281. doi:10.1016/S0140-6736(23)01366-1
4. Ahn DH, Krishna K, Blazer M, et al. A modified regimen of biweekly gemcitabine and nab-paclitaxel in patients with metastatic pancreatic cancer is both tolerable and effective: a retrospective analysis. Ther Adv Med Oncol. 2017;9(2):75-82. doi:10.1177/1758834016676011
5. Nichetti F, Rota S, Ambrosini P, et al. NALIRIFOX, FOLFIRINOX, and Gemcitabine With Nab-Paclitaxel as First-Line Chemotherapy for Metastatic Pancreatic Cancer: A Systematic Review and Meta-Analysis. JAMA Netw Open. 2024;7(1):e2350756. Published 2024 Jan 2. doi:10.1001/jamanetworkopen.2023.50756
6. Péron J, Roy P, Conroy T, et al. An assessment of the benefit-risk balance of FOLFIRINOX in metastatic pancreatic adenocarcinoma. Oncotarget. 2016;7(50):82953-82960. doi:10.18632/oncotarget.12761

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