

# Helping Cancer Patients Live Longer and Feel Better

November 2026

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NASDAQ: IMRX

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This presentation contains forward-looking statements, including within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements including, without limitation, statements regarding: Immuneering Corporation's (the "Company") plans to develop, manufacture and commercialize its product candidates; the treatment potential of its product candidates, including atebimetinib (also referred to as "atebi" and formerly known as IMM-1-104); the design, enrollment, and conduct of the Phase 3 clinical trial for atebimetinib; the ability of interim Phase 2a clinical data to support further development of atebimetinib and be confirmed as the trial progresses, including the safety, tolerability and potential efficacy of atebimetinib, alone or in combination with other therapeutic agents including modified gemcitabine/nab-paclitaxel ("mGnP"); the potential advantages and effectiveness of the Company's clinical and preclinical candidates; the timing of enrollment, completion and topline readout of MAPKeeper 301 and other earlier trials; the filing with, and approval by, regulatory authorities of the Company's product candidates; the evolving treatment and competitive landscape and how atebimetinib may fit in that treatment landscape; the sufficiency of funds to operate the business of the Company; statements regarding the Company's ability to advance its pipeline and further diversify its portfolio and make progress towards its goal of helping cancer patients live longer and feel better; the Company's cash needs and availability, including related to the Company's projected cash runway and current operating plans; and the plans and objectives of Company management for future operations, including with respect to the planning and execution of combination or potential pivotal clinical trials.

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Unless otherwise specified, all clinical data in the following slides is based on an interim data collection from the intent-to-treat population of 55 patients dosed at the 320 mg once-daily dose level of atebimetinib in combination with modified gemcitabine/nab-paclitaxel ("mGnP" = 1,000 mg/m2 (Gem) + 125 mg/m2 (nab-Pac) days 1 & 15, every 4 weeks) in the Company's ongoing Phase 1/2a clinical trial, as of April 24, 2026. The median follow-up for overall survival (OS) was estimated by the reverse Kaplan–Meier method. All data remains subject to follow-up and database updates.


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# We Aim to Develop Cancer Medicines that Drive Long Survival with Outstanding Quality of Life for All-Comers

| Our Aspirations | Atebi+mGnP Phase 2 Reported at ASCO, 1L PDAC | |
|---|---|---|
| **Long Survival** | **17.3** | **months median overall survival** (~2X benchmark) |
| **Outstanding Quality of Life** | **0** | **categories of Gr3+ TRAEs in ≥10% attributed to atebimetinib**, only 2 attributed to chemo |
| | **84%** | **of evaluable patients maintained or gained weight** at 3 months |
| **All-Comers** | **No genetic testing required** | **Responses** in G12D, G12V, G12R, G12L, G12A, Q61H, RAS other/unknown |
| | **Broadly Combinable** | **+mGnP:** reported<br>**+FOLFIRINOX:** pending |

## What's Next

**Clinical Guidance:**

Phase 2 update in 1H 2027

Phase 3 now enrolling, NCT07562152

Phase 3 topline expected mid-2028

**Lung cancer:** atebi + anti-PD-1, dosing soon

**Pancreatic cancer:** atebi + CLDN18.2-targeted

**Anaplastic thyroid cancer:** atebi + chemo, BRAF-mutant and non-mutant

**Other MAPK-driven tumors:** *in planning*

**Other oncogenic pathways:** *preclinical pipeline*

Phase 2 data presented at ASCO in June 2026, data cutoff April 24, 2026. 1L = first-line; PDAC = pancreatic ductal adenocarcinoma; TRAE = treatment-related adverse event.



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CANCER RESEARCH | IN THE SPOTLIGHT

# MEKing Room: On the Quest for New Sources of Therapeutic Index in RAS/MAPK-Driven Cancers

Bijaya Gaire and Poulikos I. Poulikakos

CANCER RESEARCH | THERAPEUTIC DEVELOPMENT AND CHEMICAL BIOLOGY

## Dual-MEK Inhibitor Atebimetinib Displays Broad Activity in *RAS*- and *RAF*-Mutant Tumors via Deep Cyclic Inhibition and Resisting RAF Bypass

Sarah Kolitz[1], Anna Travesa[2], Amy Axel[2], Jason M. Funt[2], Matthew S. Nord[2], Amy Yamamura[2], Kevin D. Fowler[2], Praveen Nair[2], Benjamin Zeskind[3], Brett M. Hall[2], and Peter King[2]



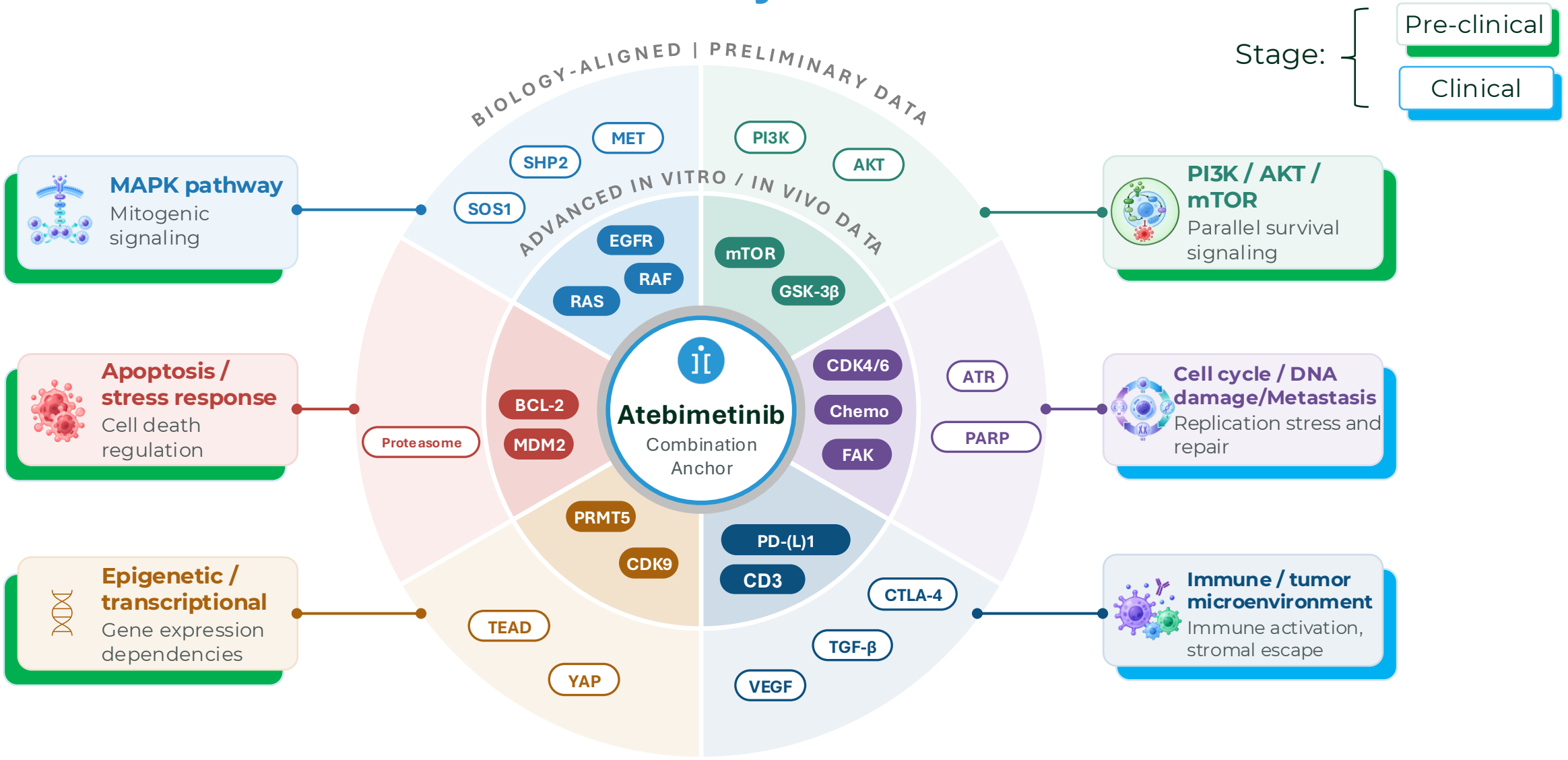
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# Expanded Immuneering Strategy

- Test, develop and gain approval for a broad set of new combinations in PDAC and other solid tumors
- Establish Atebimetinib as a backbone treatment in all MAPK-related tumors, including RAS and BRAF
- Advance our first-mover platform capability in DCI-designed inhibitors to address other oncogenic pathways


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# We Believe Atebimetinib is Broadly Combinable




*Supporting preclinical data to be presented at 2026 EORTC-NCI-AACR Symposium, November 19, 2026, 14:00–14:30 CET*

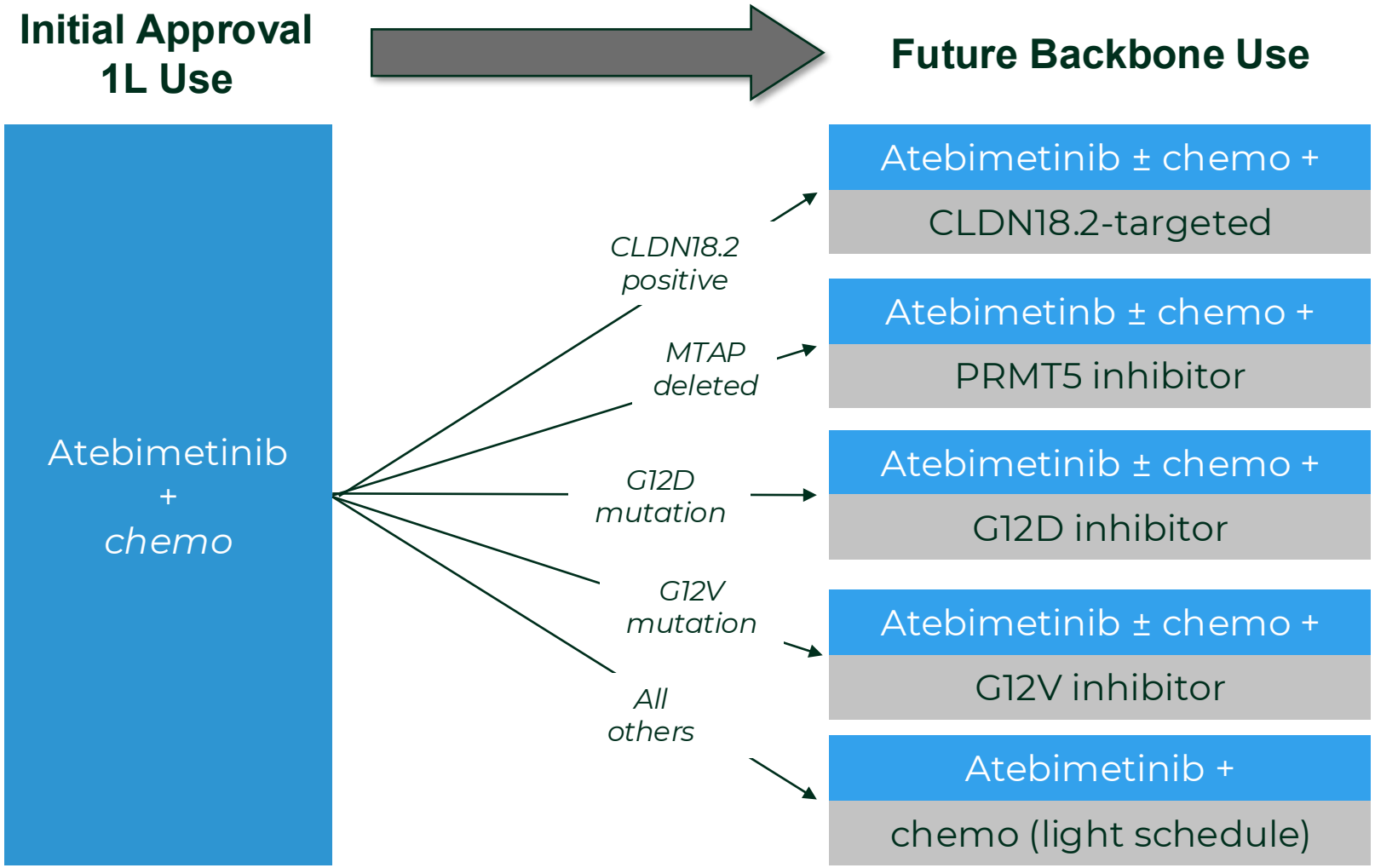


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# Atebimetinib: The Future Backbone in Pancreatic Cancer

*CONCEPTUAL*






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# Unlocking Atebimetinib's Full Potential

| Indication | Regimen | Phase 1/2 | Phase 3 | Reg. | Collaboration |
|---|---|---|---|---|---|
| **1L PDAC** | Atebimetinib + mGnP vs. GnP | Phase 3 – registrational intent | | | Immuneering only |
| **1L PDAC** | Atebi + FFX | Phase 2 · Efficacy | | | Immuneering only |
| **1L PDAC** | CLDN18.2-targeted + atebi + mGnP (biomarker-positive) | Phase 1b · Efficacy | | | Astellas |
| **2L, 3L PDAC (chemo-free)** | CLDN18.2-targeted + atebi (chemo-free; biomarker-positive) | Phase 1/2 · Efficacy | | | Astellas |
| **1L RAS-mut NSCLC** | Atebi + cemiplimab ± chemo | Phase 2 · Efficacy | | | Regeneron |
| **2L/3L RAS-G12C NSCLC** | Atebi + olomorasib | Phase 2 · Efficacy | | | Eli Lilly |
| **2L Anaplastic Thyroid Cancer** | Atebi + chemo | Phase 2 – reg'l intent | | | Immuneering only |

More combinations under discussion

atebi, atebimetinib (IMM-1-104); PDAC, pancreatic ductal adenocarcinoma; NSCLC, non-small cell lung cancer; (m)GnP, (modified) gemcitabine + nab-paclitaxel; (m)FFX, (modified) FOLFIRINOX; ATC, anaplastic thyroid cancer, SoC, standard of care; KoL, key opinion leader; 1L/2L/3L, first/second/third line.


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# 1L PDAC:

- Atebimetinib and mGnP (Phase 2a)
- Atebimetinib and FFX (Phase 2a)

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# Phase 2a Atebimetinib + Gemcitabine nab-Paclitaxel in 1L PDAC

**NCT05585320 |** active, not recruiting

## Eligibility

- 1L metastatic or locally advanced PDAC
- No prior systemic therapy for advanced disease
- ECOG PS 0–1
- ≥1 measurable lesion (RECIST 1.1)
- Adequate organ function
- All RAS/KRAS mutation subtypes permitted

**Full Cohort (N=55)**

320 mg QD atebimetinib + mGnP*

Median Follow Up = 11.6 months

* mGnP = 1,000 mg/m2 (Gemcitabine) + 125 mg/m2 (nab-Paclitaxel) days 1 & 15 of each 28-day cycle

Data cutoff date: April 24, 2026

## Endpoints

**Primary**

- **ORR** per RECIST 1.1

**Secondary**

- **DCR**, DOR, **PFS**, **OS**
- Safety (CTCAE v5.0)
- Patient weight and QoL

**Statistical Design**

- Simon's 2-stage optimal design
- 80% power, 1-sided $\alpha$ = 5%



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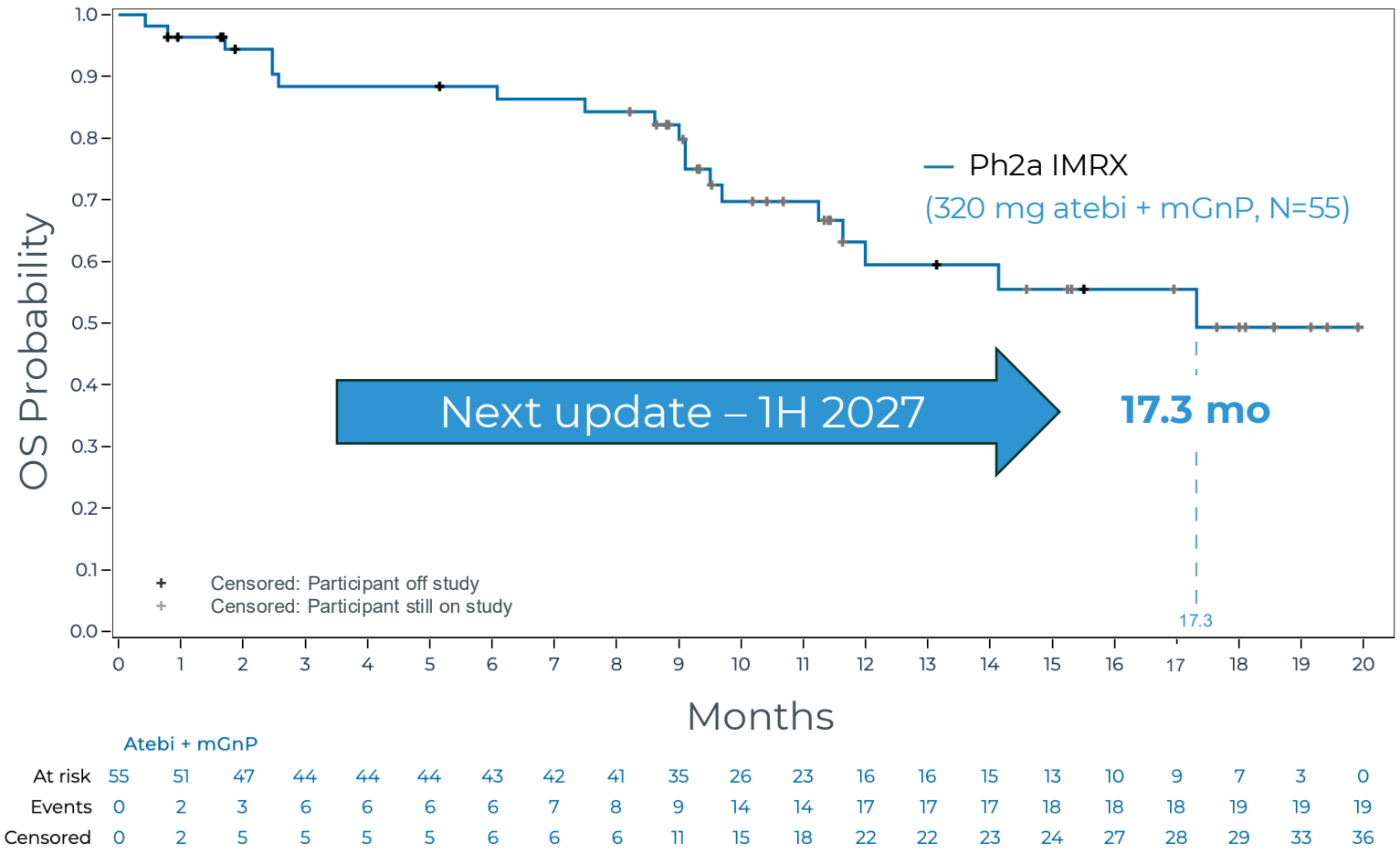
# Phase 2a Demographics and Baseline Participant Characteristics

| Characteristic | **Chung et al, ASCO 2026** atebimetinib + mGnP Phase 2a, N=55[b] | **Von Hoff et al, NEJM 2013** Gem/nab-Pac (GnP) Phase 3, N = 431[e] |
|---|---|---|
| Median age (years) | 68 | 62 |
| Age, ≥ 65 : < 65 years, % | 62% : 38% | 41% : 59% |
| Disease status, metastatic : locally advanced, % | 96% : 4% | 100% : 0% |
| Sex, female : male, % | 45% : 55% | 43% : 57% |
| ECOG status, 0:1, % | 56% : 44% | 58% : 42% |
| CA 19-9 elevated (≥ 37 U/mL) | 89%[d] | 84%[f] |
| Presence of lung metastasis[a,c], % | 27% | 35% |
| Presence of peritoneal metastasis[a] % | 36% | 4% |
| Presence of liver metastasis[a], % | 51% | 85% |
| De novo metastatic disease, % | 51% | NR |
| Received RAS inhibitor in 2nd line | 1 | N/A |
| RAS/KRAS mutational status | KRAS mutant: 48 (87%)<br>RAS unknown: 7 (13%) | NR |
| Received 2nd line treatment[b], % | 60% | 40% |

Data based on data cutoff of April 24, 2026, (a) Metastasis location sub-analyses derived from RECIST lesion pages and represent lower bounds. (b) Of the 55 participants at data cutoff, 11 were still on treatment and 44 were off-treatment. Of those 44, 21 went on to subsequent cancer therapy, 14 did not, and 9 were unknown. Of the 21 who went on to subsequent therapies, 20 went on to chemotherapy and/or radiation, and 1 to a RAS inhibitor. (c) 4 trial participants (7%) with lung as only metastatic site. (d) 40 out of 45 patients with CA 19-9 data. (e) 2013 NEJM: PMID 24131140 & 2016 BJC: PMID 27351217. (f) CA 19-9 > 35 U/mL. Note: Removal of 2 locally advanced, 4 lung only, or 1 RAS inhibitor 2L patient(s), respectively, from the Kaplan-Meier sub-analysis did not alter the mOS of the remaining patients. All of these subsets resulted in mOS of 17.3 months. OS does not differ significantly for ECOG 0 vs. 1, or for liver vs. peritoneal metastasis. NR = not reported; N/A = not applicable.


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# Compelling Survival and Tolerability in Phase 2a First Line Pancreatic Cancer




| Median OS (months) | |
|---|---|
| **Atebimetinib + mGnP** (N=55) | **17.3** |

Only 2 categories of TRAE grade ≥3 in ≥10% of participants, both chemotherapy related

MAPKeeper 301

Phase 3 Now Recruiting, NCT07562152

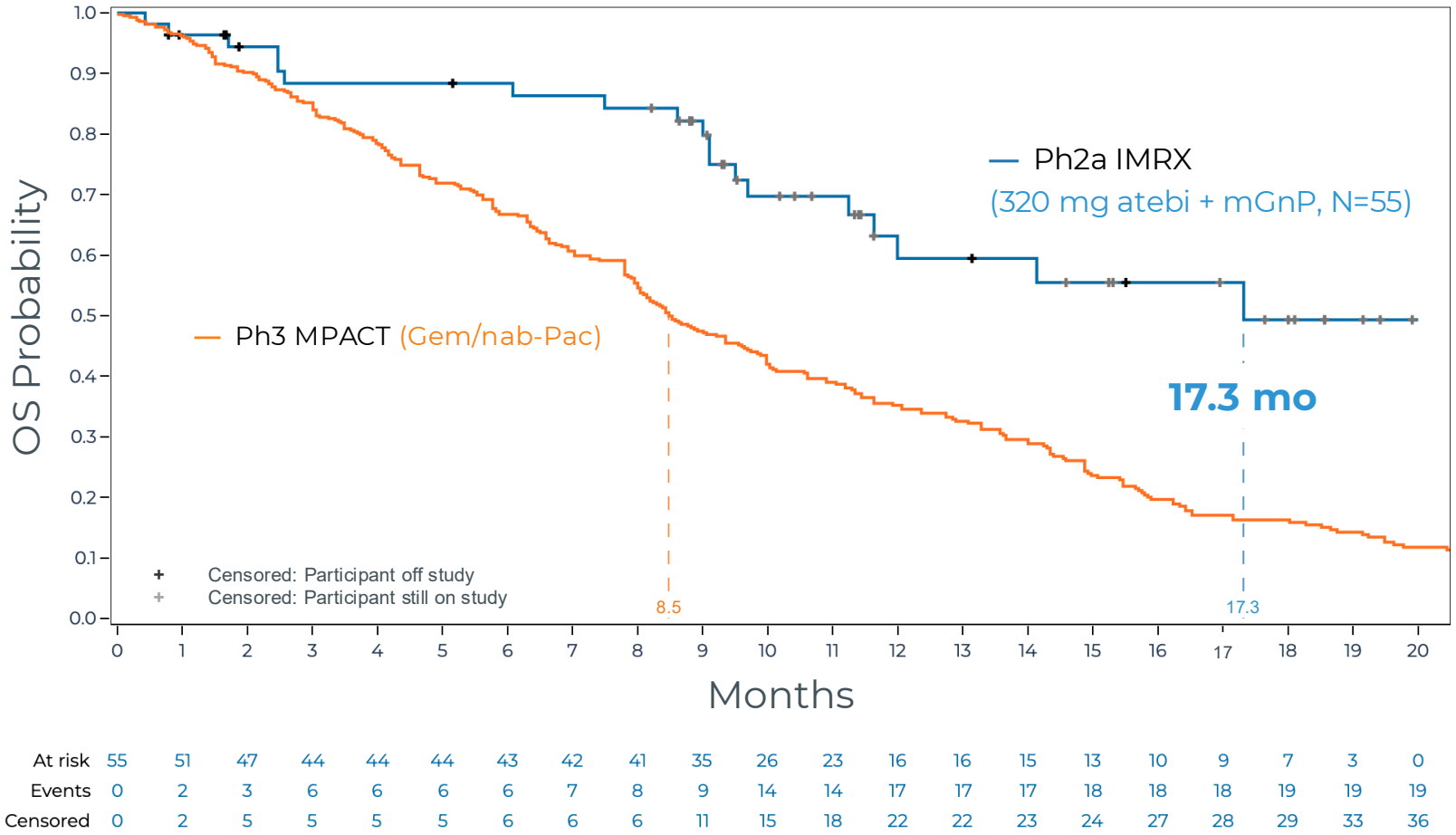
As of the April 24, 2026 data cutoff, the median follow-up was 11.6 months (N=55) as estimated by the reverse Kaplan–Meier method.



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# Consistent Separation from Standard of Care Gem/nab-Pac (GnP) in First Line Pancreatic Cancer




**Median OS**
(months)

| | |
|---|---|
| **Atebimetinib + mGnP** (N=55) | **17.3** |
| **GnP** (MPACT) | **8.5** |

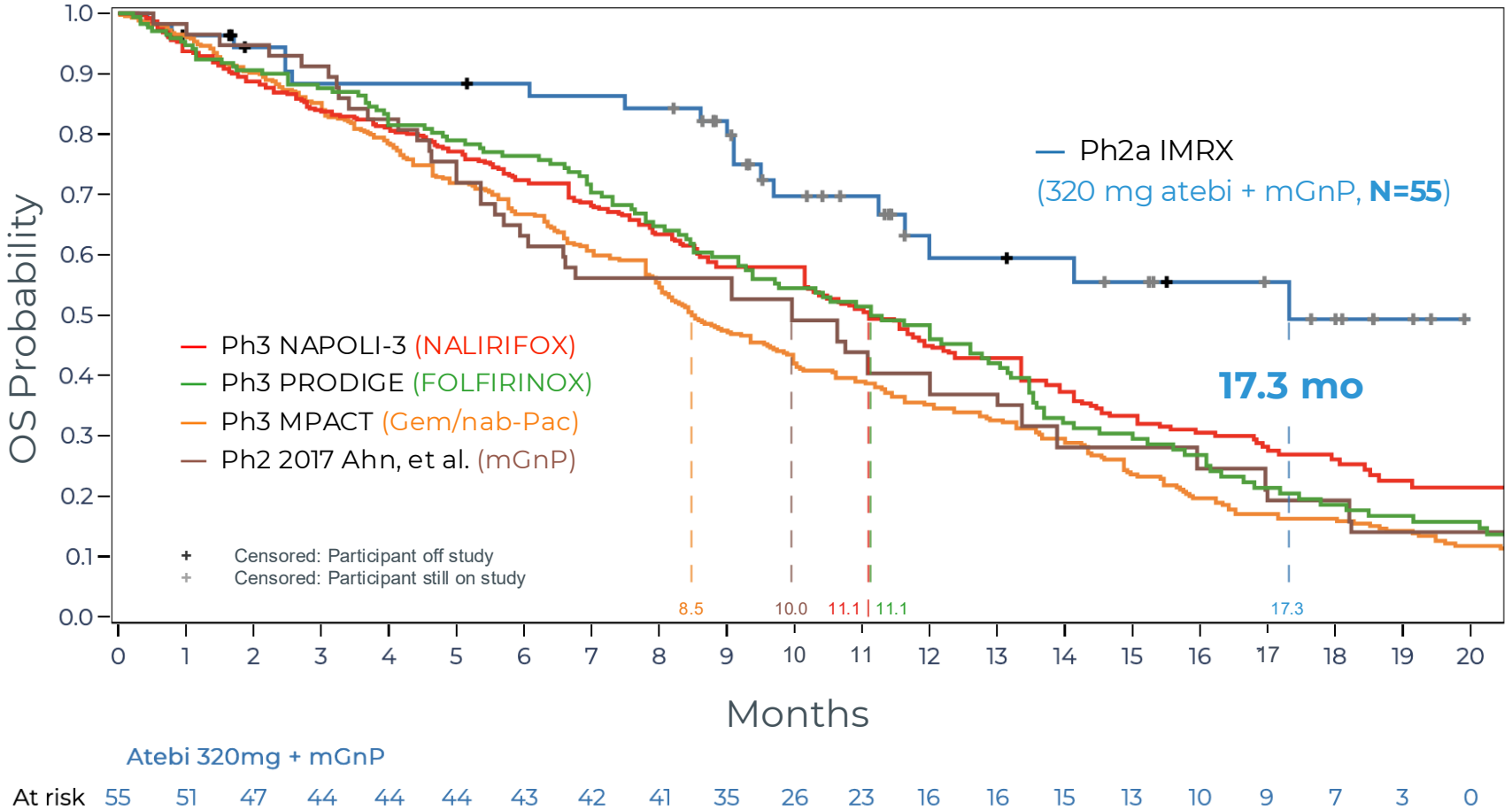
*Pivotal Studies: (1.) MPACT 2013 NEJM (PMID: 24131140) N=431.

Next Update – 1H 2027

Data based on data cutoff of April 24, 2026. Median follow up of 11.6 months (N=55) determined via reverse Kaplan-Meier method; Censored participants off study due to withdrawal of consent or lost to follow up. 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. Reconstructed Kaplan-Meier (KM) Plots of Pivotal Ph3 Studies per 2024 JAMA Nichetti, et al. 7(1):e2350756


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# Consistent Separation from Additional Standard of Care Options in First Line Pancreatic Cancer




## Median OS
(months)

| | |
|---|---|
| **Atebimetinib + mGnP** (N=55) | **17.3** |
| **GnP** (MPACT) | **8.5** |
| **FOLFIRINOX** (PRODIGE) | **11.1** |
| **NALIRIFOX** (NAPOLI-3) | **11.1** |

*Pivotal Studies: (1.) MPACT 2013 NEJM (PMID: 24131140) N=431, (2.) PRODIGE 4 / ACCORD 11 2011 NEJM (PMID: 21561347) N=171, (3.) NAPOLI 3 2023 LANCET (PMID: 37708904) N=383.

Next Update – 1H 2027

Data based on data cutoff of April 24, 2026. Median follow up of 11.6 months (N=55) determined via reverse Kaplan-Meier method; 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. Reconstructed Kaplan-Meier (KM) Plots of Pivotal Ph3 Studies per 2024 JAMA Nichetti, et al. 7(1):e2350756


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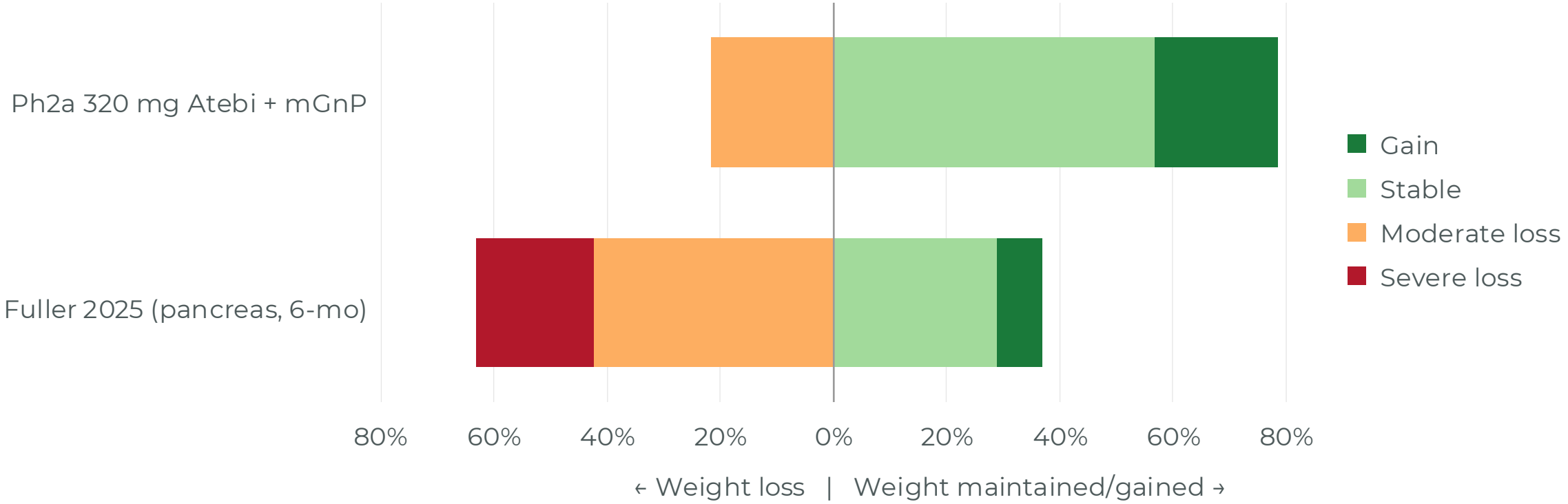
# Consistent Separation from Standard of Care Gem/nab-Pac Benchmarks on Additional Endpoints

| | **Atebimetinib + mGnP** (N = 55) | **GnP** (MPACT) |
|---|---|---|
| **Median OS** (months) | **17.3** [11.2, NR] | 8.5 |
| **Median PFS** (months) | **8.3** [5.9, 9.6] | 5.5 |
| **ORR*** | **36%** | 23% |
| **DCR*** | **82%** | 48% |
| **Participants weight stable or gained weight at 3 months^** | **84%** | NR |

*N=50 of response evaluable patients. Atebimetinib dosed at 320 mg. Scans occur approx. every 6 weeks. Patients that progressed without complete radiographic scans are not presented in graph but are counted in ORR/DCR analyses. Patients with baseline and at least one on-treatment assessment were considered evaluable.
^Weight observations from participants with weight data at ~3 mo and C1D1; weight stable defined as within 5%.


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# Atebimetinib was Designed to Counteract Cachexia



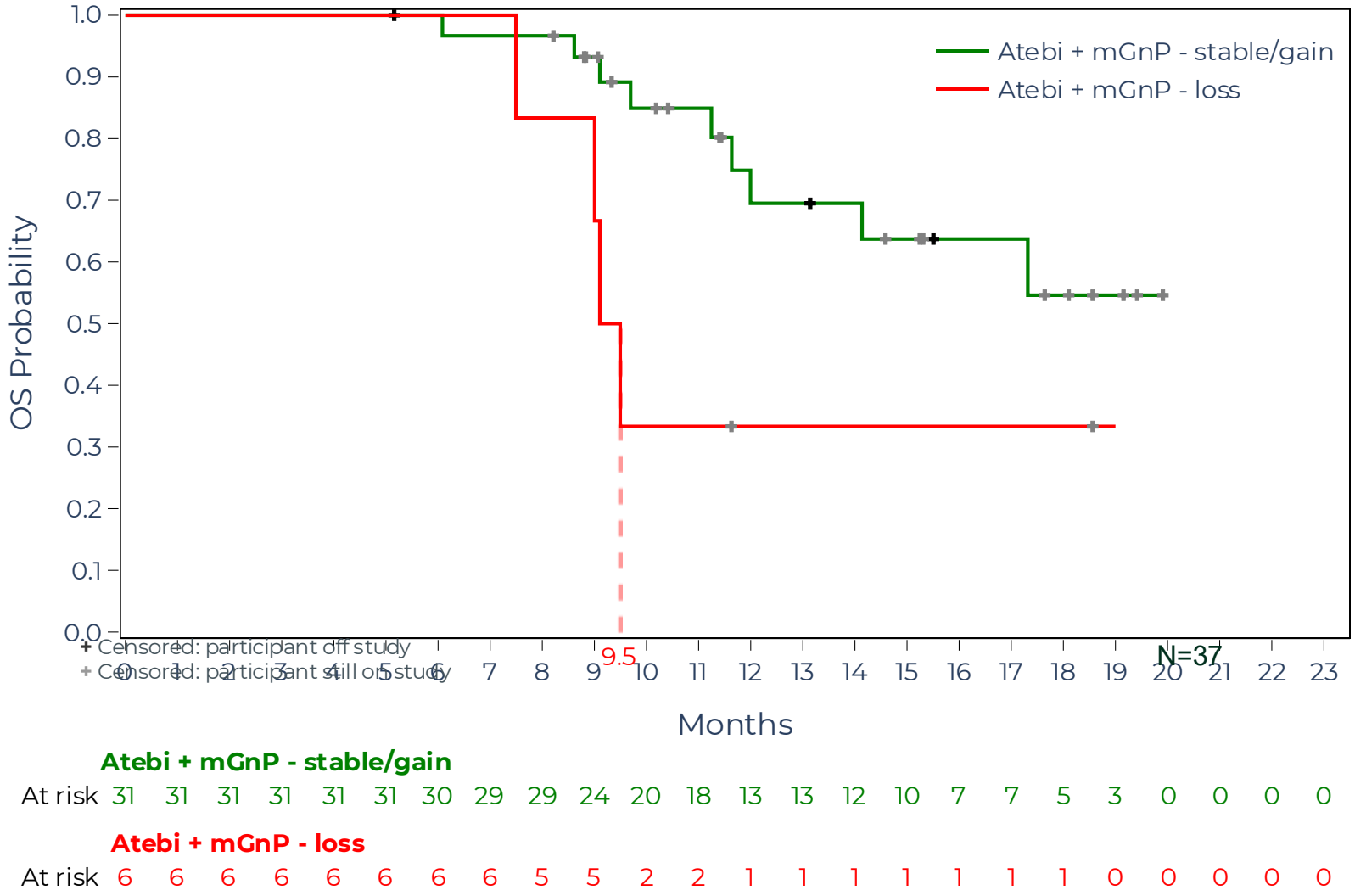

Presented at AACR Pancreatic Cancer 2026, San Diego, CA (n=23 evaluable, $p<0.001$ · Cliff's $\delta$ = +0.48) (September 2026) | Abstract Presentation #A134



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# Weight Stability Was Associated With Longer Survival



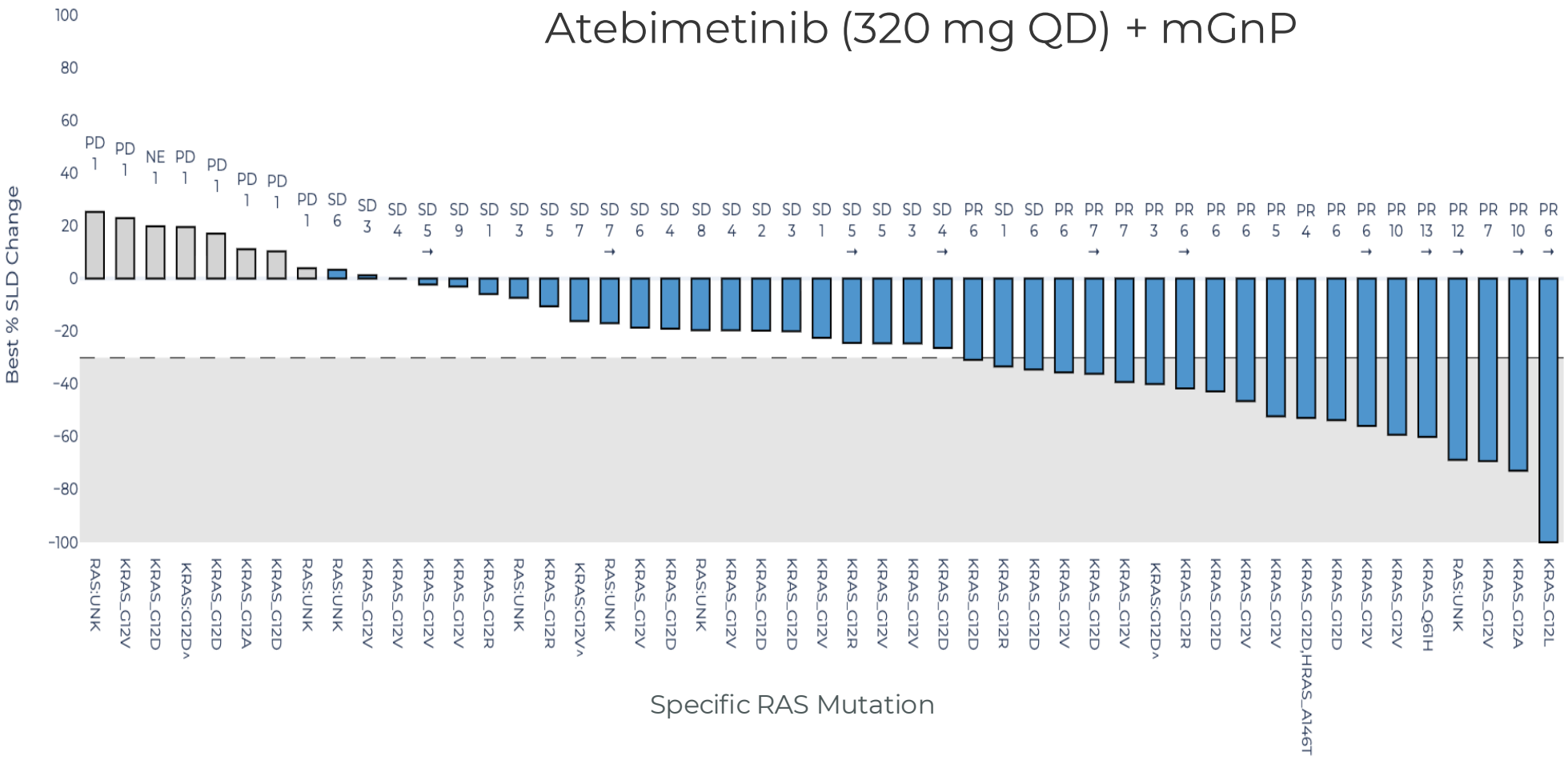

Presented at AACR Pancreatic Cancer 2026, San Diego, CA (September 2026) |
Abstract Presentation #A134



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# Overall Response Rate (ORR) and Disease Control Rate (DCR)




## Overall Response (ORR) & Disease Control (DCR) Rates

| | Atebimetinib + mGnP Ph 2a 1L PDAC |
|---|---|
| **ORR** | **36%** (18/50) |
| **DCR** | **82%** (41/50) |

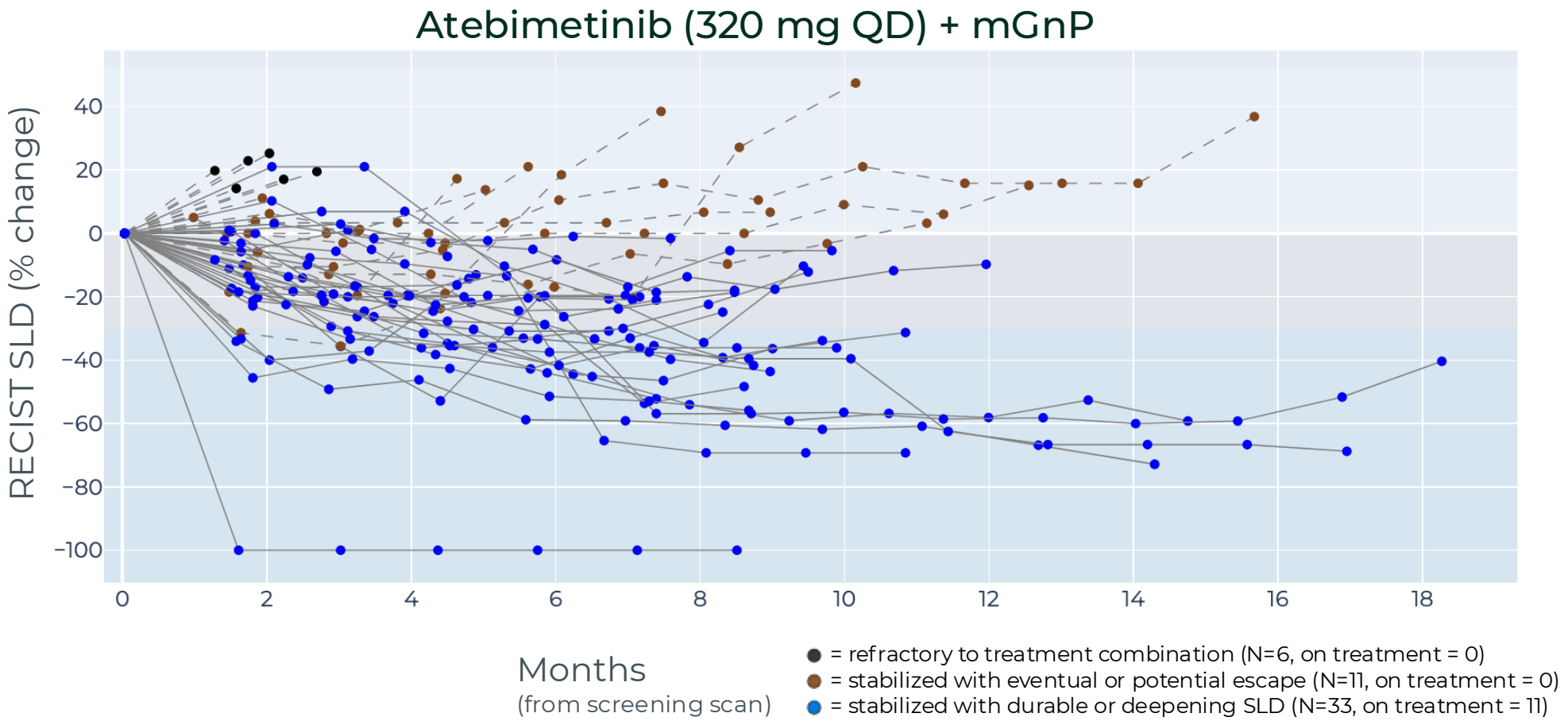
Prior Phase 3 Benchmark Overall Response (ORR) & Disease Control (DCR) Rates

| | MPACT Pivotal Study in 1L PDAC |
|---|---|
| ORR | **23%** (99/431) |
| DCR | **48%** (206/431) |

N=50 of response evaluable participants. Atebimetinib dosed at 320 mg. Scans occur approximately every 6 weeks. One participant progressed without complete radiographic scans and is not presented in graph but counted in ORR/DCR analyses. Participants deemed evaluable had screening assessment and at least one post-baseline assessment. Arrow denotes on treatment as of data cutoff date. Best overall response (BoR) shown. Data based on data cutoff of April 24, 2026.
Glossary: "^" denotation on x-axis = ctDNA-defined RAS mutation; RAS:UNK = RAS mutation status is unknown; PR = partial response; SD = stable disease; PD = progressive disease; NE = non-evaluable per RECIST v1.1


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# Deepening Durable Tumor Responses Over Time Observed




In the above graph, N=50, 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 data cutoff of April 24, 2026, of response evaluable patients from an ongoing Phase 1/2a trial of atebimetinib.



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# Atebimetinib (320 mg) + mGnP Safety: Treatment Related Adverse Events

## Safety Highlights

- Grade ≥3 Anemia and Neutropenia occurred in ≥10% of participants, both chemotherapy related

**TRAE**
(related to any drug)

| | Any Grade | Grade ≥3 |
|---|---|---|
| Fatigue | 29 (53%) | 1 (2%) |
| Nausea | 25 (45%) | 0 |
| Anaemia | 23 (42%) | 9 (16%) |
| Rash | 20 (36%) | 3 (5%) |
| Diarrhea | 20 (36%) | 0 |
| Vomiting | 16 (29%) | 1 (2%) |
| Alopecia | 15 (27%) | 0 |
| Dysgeusia | 15 (27%) | 0 |
| Oedema peripheral | 15 (27%) | 1 (2%) |
| Neutropenia | 14 (25%) | 10 (18%) |
| Neuropathy peripheral | 12 (22%) | 0 |

Data based on data cutoff date of April 24, 2026.
1 of 55 participants discontinued atebimetinib (not due to toxicity) while continuing chemotherapy. Only MEKi class effect ≥ grade 3: rash (5%), resolved with treatment; ocular, cardiac, and diarrhea events were, when observed, grade 1-2 and did not result in discontinuation

*Adverse event preferred terms related to any component of treatment, occurring in ≥ 20% of participants*

Rash = rash, dermatitis acneiform, rash maculo-papular


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# Ph 2a Atebimetinib + FOLFIRINOX (FFX) in 1L PDAC

**NCT05585320** | active, not recruiting

## Eligibility

- 1L metastatic or locally advanced PDAC
- No prior systemic therapy for advanced disease
- ECOG PS 0–1
- ≥1 measurable lesion (RECIST 1.1)
- Adequate organ function
- All RAS/KRAS mutation subtypes permitted

## Full Cohort (N=31)

320 mg or 240 mg QD atebimetinib + FFX

Eligibility and endpoints identical to the Atebi + mGnP cohort

## Endpoints

**Primary**

- **ORR** per RECIST 1.1

**Secondary**

- **DCR**, DOR, **PFS**, **OS**
- Safety (CTCAE v5.0)
- Patient weight and QoL

**Statistical Design**

- Simon's 2-stage optimal design
- 80% power, 1-sided $\alpha$ = 5%

FOLFIRINOX (FFX) was administered on Days 1 and 15 of each 28-day cycle as follows: oxaliplatin 85 mg/m² intravenously (IV) over 2 hours, folinic acid (leucovorin) 400 mg/m² IV over 2 hours, and irinotecan 150 mg/m² IV over 90 minutes, followed by fluorouracil 2400 mg/m² administered as a continuous IV infusion over 46 hours beginning on Day 1; no fluorouracil bolus was given. Dose and frequency could be adjusted per investigator judgment and institutional guidelines with Medical Monitor approval.


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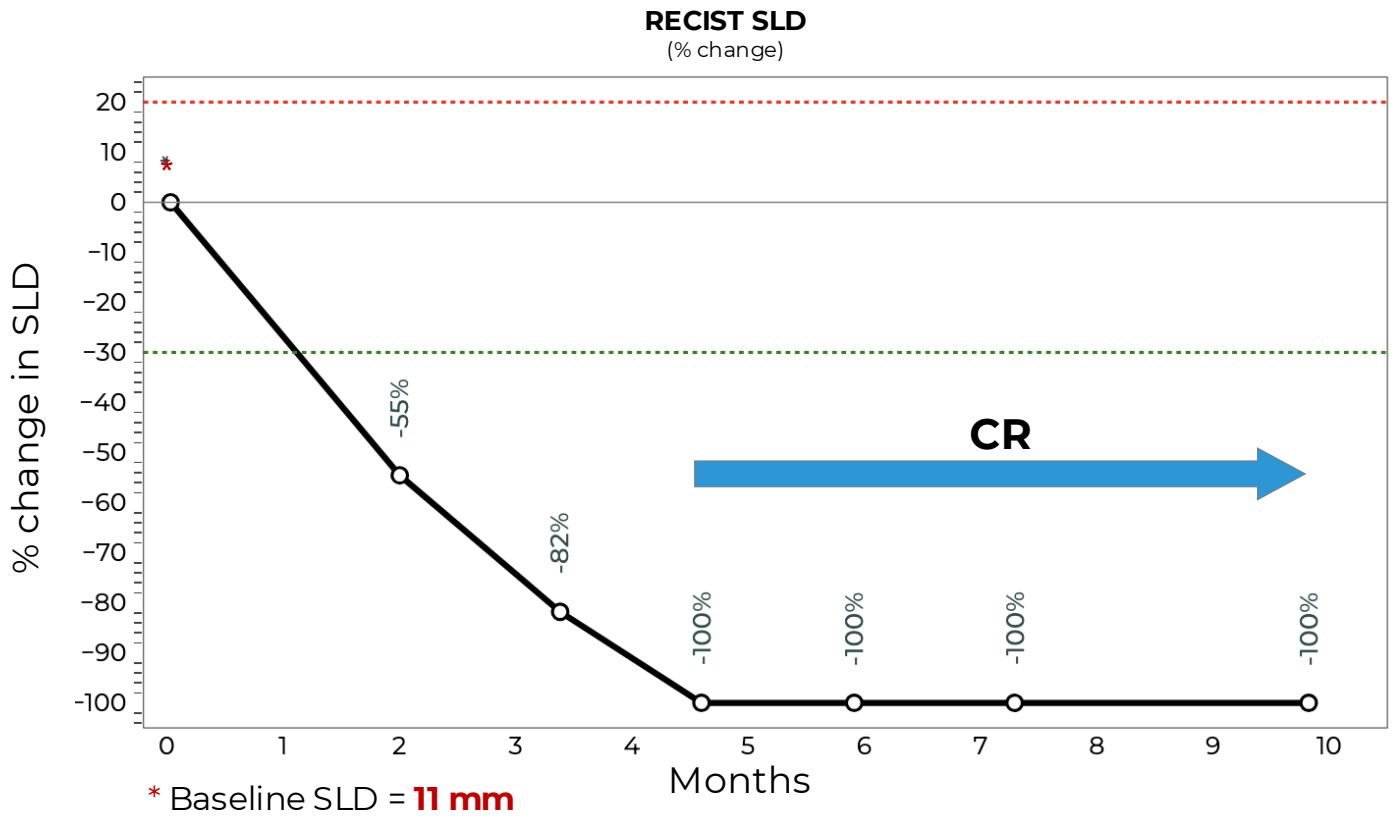
# Atebimetinib + FFX Case Study: Observed Durability and Tolerability with Complete Resolution of Liver Metastasis

**Ongoing Phase 2a Case Study**
(1L Metastatic PDAC)

1st Line (1L): Atebi + mFFX (**BOR = CR**)

- 71-year-old female
- >9 mo. on atebimetinib
  - on treatment as of data cutoff
- Improved QoL (PRO Instrument)
- Weight stable
- $KRAS^{G12D}$ mutated tumor
- ctDNA not detected (baseline or C2D15)
- Complete resolution of liver lesion

**Atebimetinib + FFX** (1L PDAC; Phase 2a)




Data based on interim data collection from a Phase 2a arm as of April 24, 2026, from an ongoing Phase 2a trial of atebimetinib. Data subject to follow-up and database updates. CR = Complete Response


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# Atebimetinib:

## Monotherapy Tolerability Supports Broad Combinability

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# Favorable Safety Results Observed for Monotherapy Atebimetinib in 2L PDAC

*Patients on atebimetinib monotherapy have described feeling almost like their pre-diagnosis selves – a truly significant outcome for individuals battling such a debilitating cancer. – Atebi Investigator*

## Safety: Phase 2a Monotherapy in 2L PDAC at 320 mg QD (n = 24)

| **Maximum Severity of TRAEs:** TRAE's observed in ≥10.0% of patients, n(%) | **Grade 1** | **Grade 2** | **Grade 3** | **Grade 4** | **Any Grade** |
|---|---|---|---|---|---|
| 1. Rash* | 6 (25%) | 1 (4%) | 0 | 0 | 7 (29%) |
| 2. Diarrhea | 4 (17%) | 2 (8%) | 0 | 0 | 6 (25%) |
| 3. Fatigue | 4 (17%) | 1 (4%) | 0 | 0 | 5 (21%) |
| 4. Aspartate aminotransferase increased | 4 (17%) | 0 | 0 | 0 | 4 (17%) |
| 5. Vision blurred | 3 (13%) | 1 (4%) | 0 | 0 | 4 (17%) |
| 6. Alanine aminotransferase increased | 3 (13%) | 0 | 0 | 0 | 3 (13%) |
| 7. Hypokalemia | 2 (8%) | 1 (4%) | 0 | 0 | 3 (13%) |
| 8. Nausea | 3 (13%) | 0 | 0 | 0 | 3 (13%) |
| 9. Vomiting | 3 (13%) | 0 | 0 | 0 | 3 (13%) |

- *TRAE = Treatment Related Adverse Event*
- *Patient population includes one 1L PDAC patient; all patients (n=24) in above table were dosed at 320 mg QD p.o.*
- **Preferred Terms within the Rash term include: Dermatitis acneiform; Rash; Rash maculo-papular; Rash pustular*

Data based on interim data collection, as of April 24, 2026, from an ongoing Phase 1/2a trial of IMM-1-104. Data subject to follow-up and database updates.


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# PDAC:

## Claudin 18.2 Combinations

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# Announcement of Our Astellas Collaboration

**Immuneering to Collaborate With Astellas on Clinical Studies of Investigational CLDN18.2 Programs in Combination with Atebimetinib for Pancreatic Cancer Patients**

*- Collaboration aligns with Immuneering's expanding strategy to provide a broad population of cancer patients with a wide set of treatment options -*

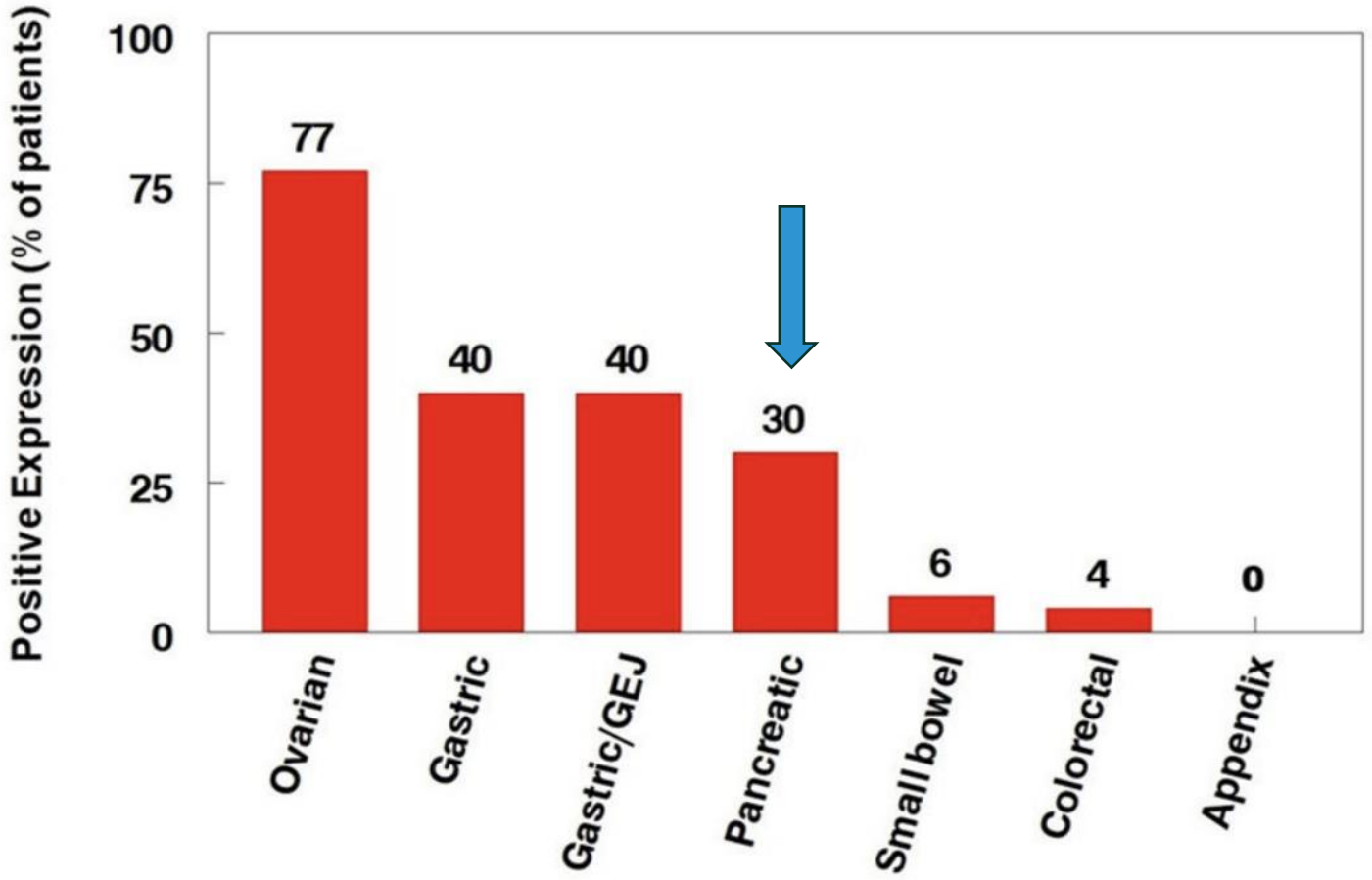
*- Represents Immuneering's fourth agreement with a pharma partner -*

*- Further expands external partnerships to bring innovative new combinations to patients -*


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# CLDN18.2 is Frequently Expressed on Solid Tumors (30% of PDAC)

## Percentage Expression by Tumor Type




## Future Combination Partner Set

- Atebimetinib + chemo (light schedule)
- Atebimetinib ± chemo + CLDN18.2-targeted
- Atebimetinb ± chemo + PRMT5 inhibitor
- Atebimetinib ± chemo + G12D inhibitor
- Atebimetinib ± chemo + G12V inhibitor

Figure modified from Nikanjam et al, 2026, Clin Cancer Res. 2026 September 01; 32(17)


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# PDAC:

## MAPKeeper 301 Pivotal Trial

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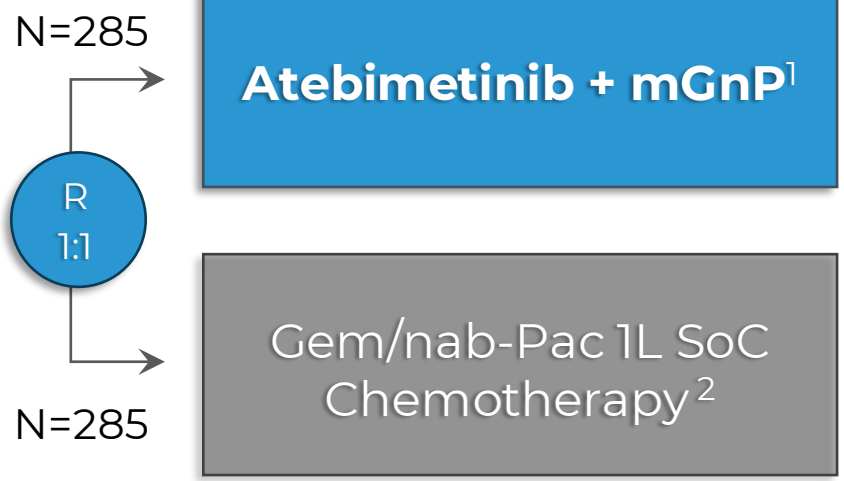
# MAPKeeper 301: Global Randomized Phase 3 Pivotal Trial Underway

**NCT07562152 | recruiting**

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

MAPKeeper 301

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




| Primary Endpoints |
|---|
| OS |
| **Secondary Endpoints** |
| PFS |
| DCR |
| ORR |
| QoL |

(R) = Randomization Stratification Factors: (1.) Geography (US vs. ROW), (2.) Liver Metastasis (present vs. absent), (3.) ECOG PS: 0 vs. 1, (4.) Denovo vs Recurrent Metastatic

- Total enrollment increased to 570
- Enrolling above plan to date
- Topline results expected mid-2028

1. 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)

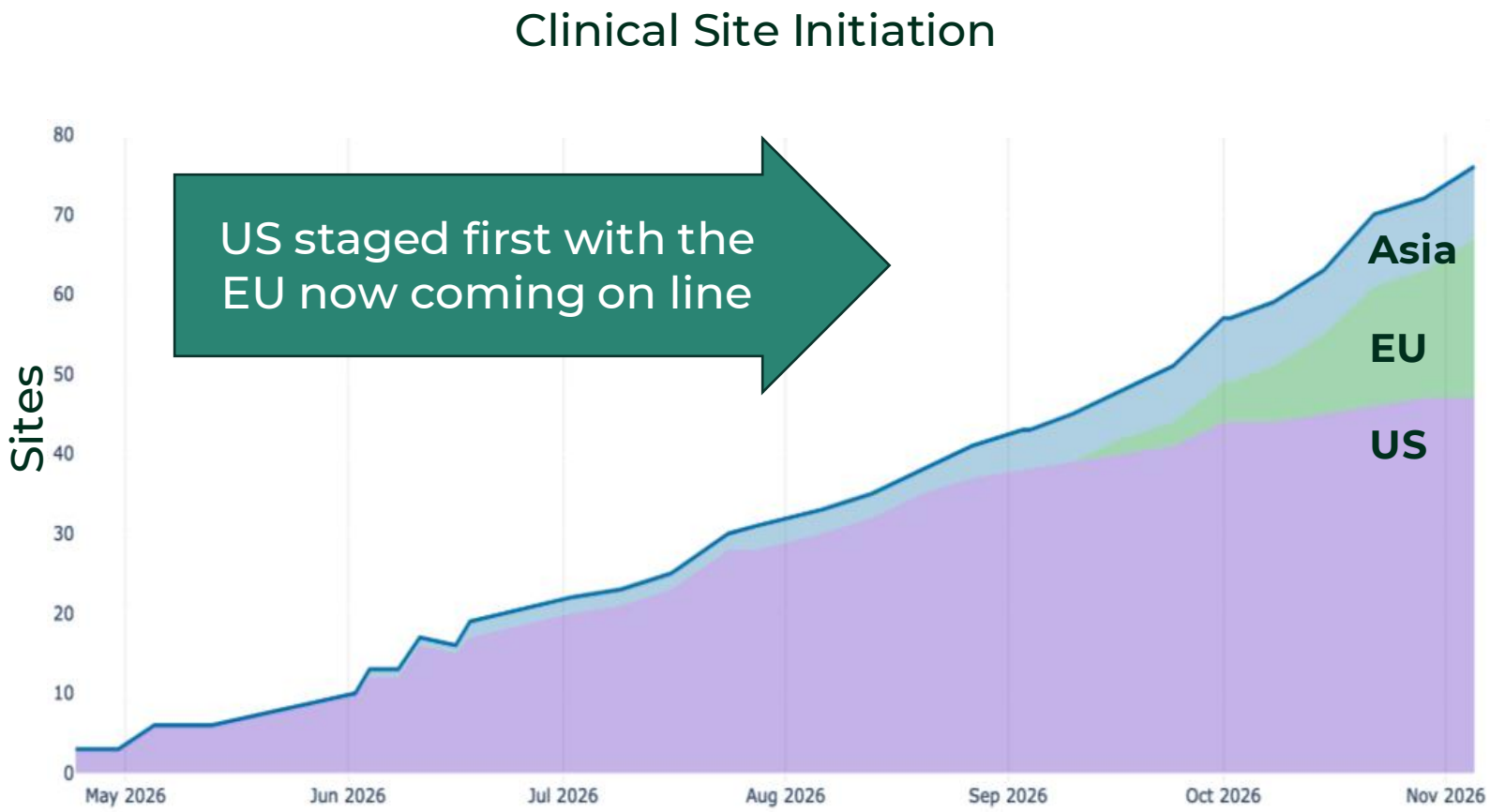
PFS = progression-free survival; OS = overall survival; ORR = overall response rate; DCR = disease control rate; QoL = Quality of Life


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# MAPKeeper 301 Execution – Patients Can't Wait

"There is an urgent need for new first-line treatment options that can improve treatment outcomes by augmenting survival and improving quality of life.
The MAPKeeper 301 trial evaluating atebimetinib with standard of care therapy represents an exciting step toward addressing that need."

**Eileen M. O'Reilly, MD, FASCO,**
*Winthrop Rockefeller Endowed Chair in Medical Oncology at Memorial Sloan Kettering Cancer Center, and the lead principal investigator of the MAPKeeper 301 study*




Data source: https://clinicaltrials.gov/study/NCT07562152
Quote source: https://ir.immuneering.com/news-releases/news-release-details/immuneering-announces-first-patient-dosed-pivotal-phase-3


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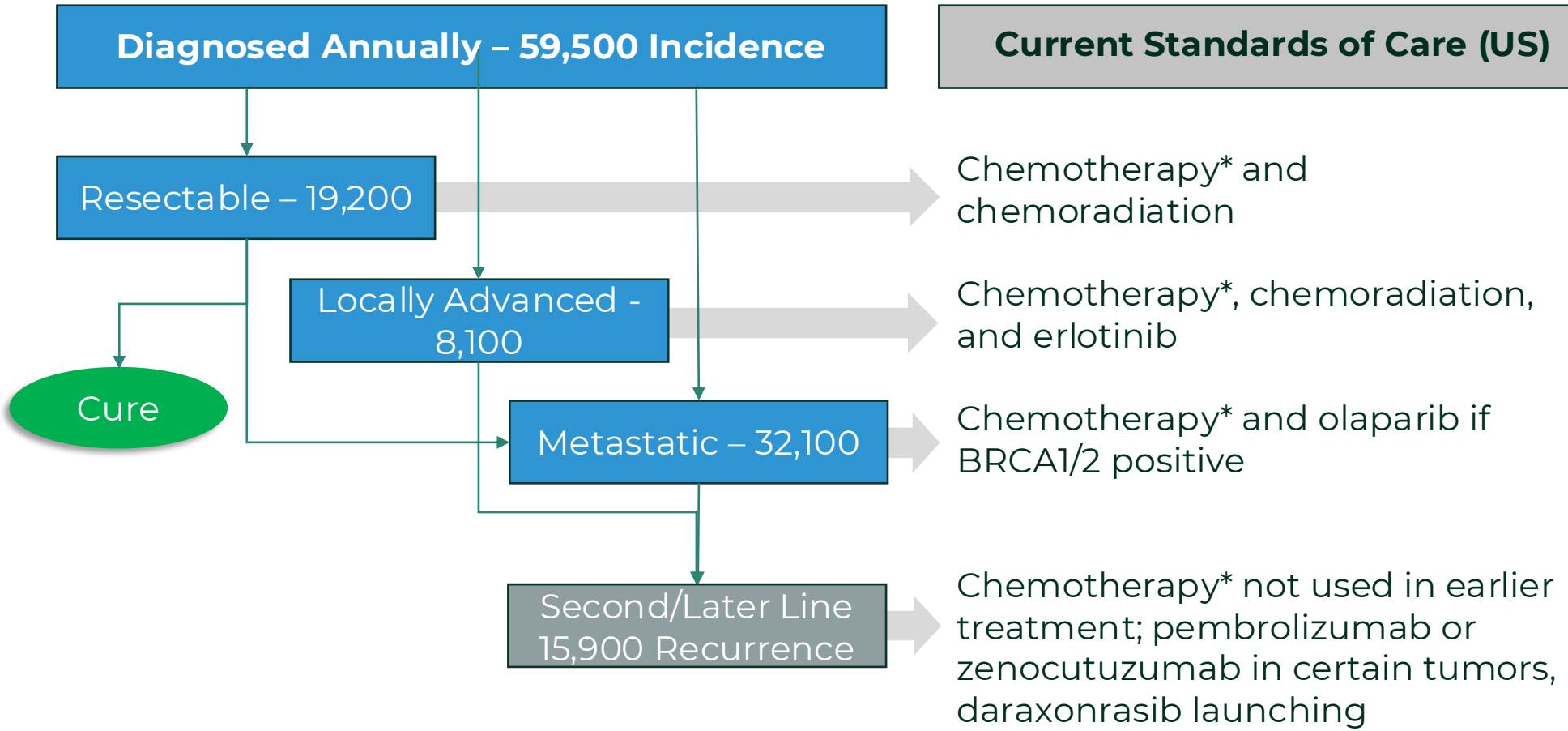
# PDAC:

## Atebimetinib Preliminary Commercial Assessment

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# Epidemiology for Pancreatic Cancer

US only 2026 Estimates




Source: Clarivate

* Chemotherapies include FOLFIRINOX/NALIRIFOX (or components thereof), Gemcitabine, Capecitabine, Nab-paclitaxel, and platinums



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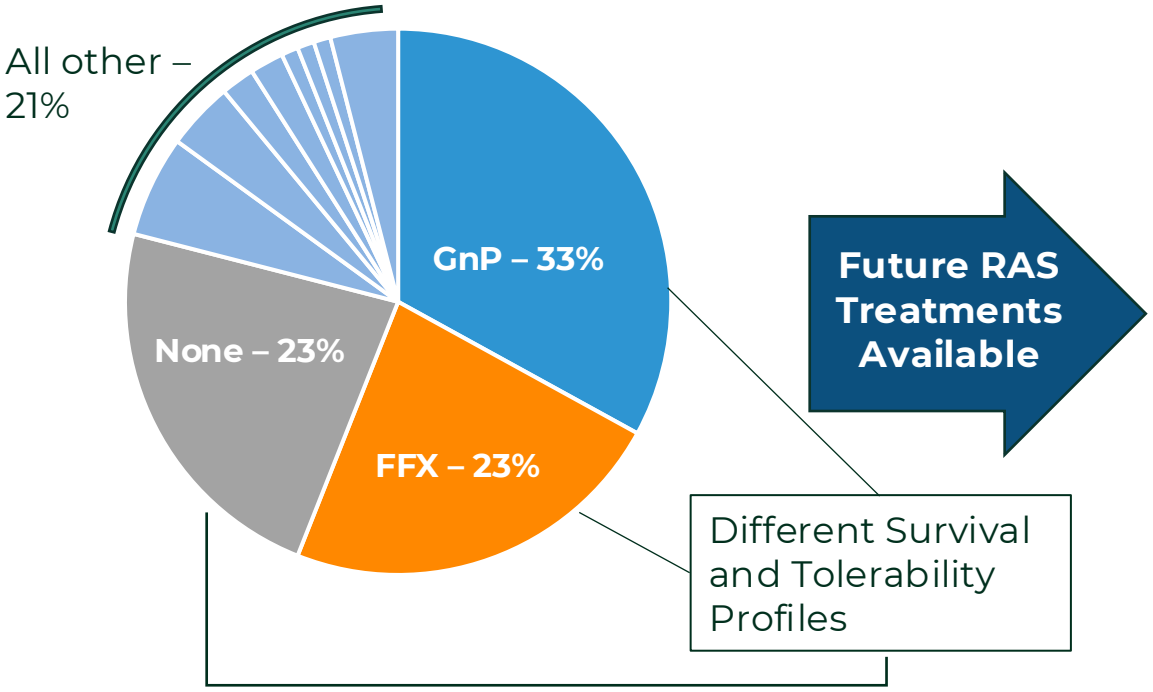
# 1L PDAC Patients Select Among Treatment Options Differently

"When the field has more than one effective first-line option, the deciding factor at the bedside will be tolerability."

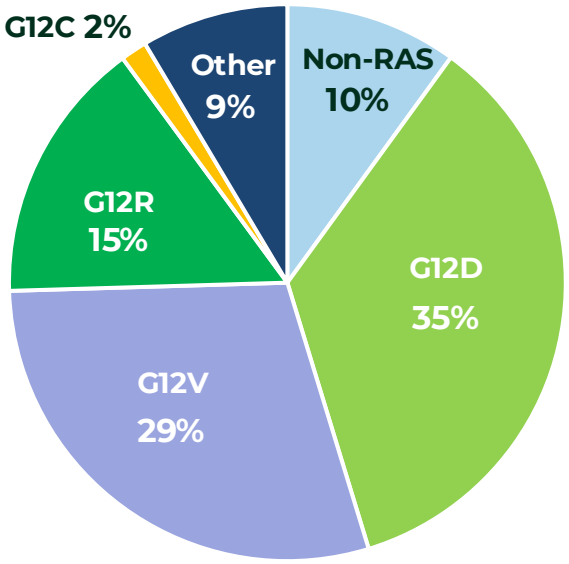
**-Daniel Ahn, D.O.**

*Mayo Clinic Arizona; investigator on the Phase 2a trial of atebimetinib.*

## 1L Pre-RAS Real World Treatment Choices - US




## RAS Status




- Mutation specific RAS inhibitors will not cover all mutant groups
- Pan-RAS inhibitors will have differential effectiveness across mutations and potential tolerability concerns
- Atebimetinib could address the broadest population with favorable OS and tolerability

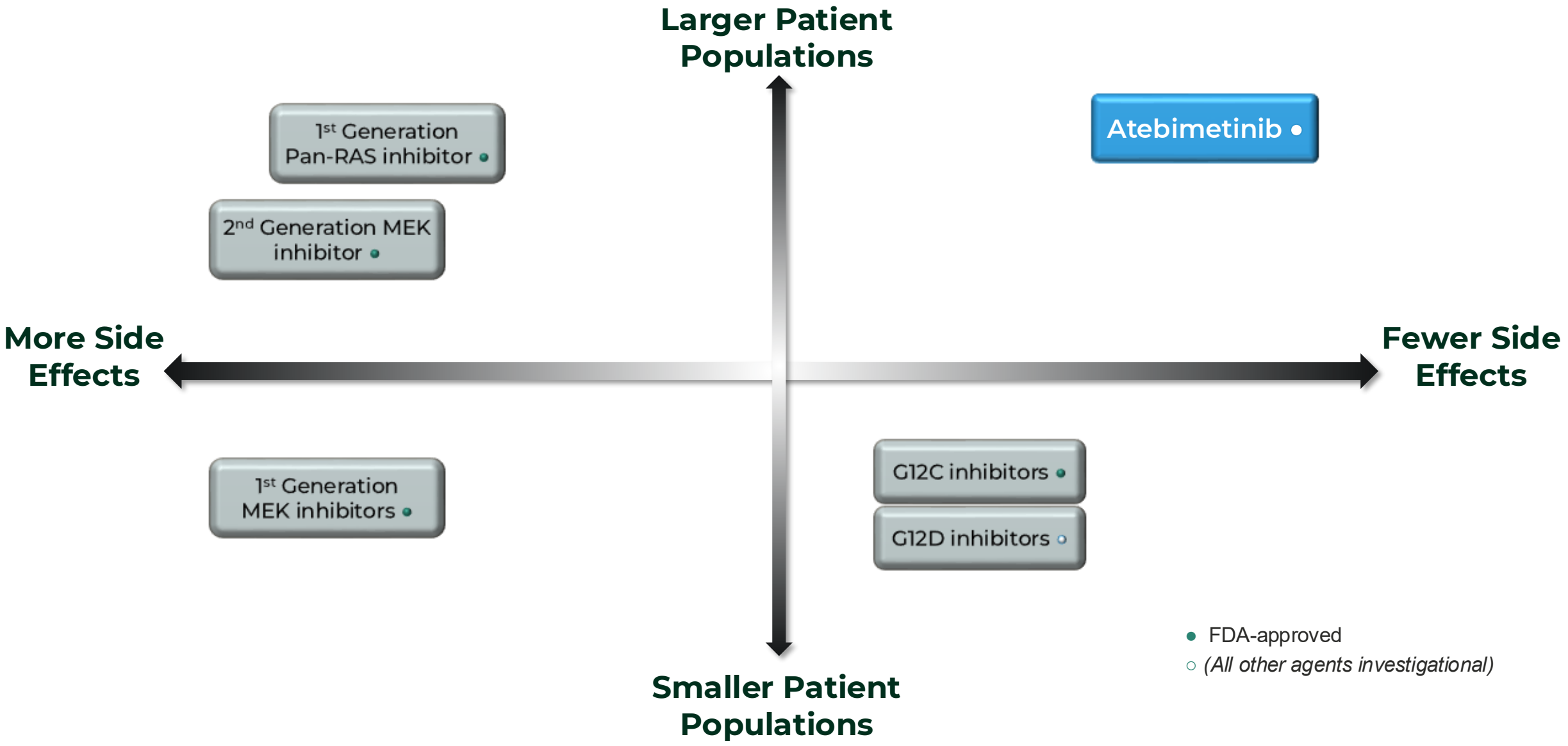
Data source: Dennen et al (2024) Journal of Clinical Oncology.



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# Atebitmetinib in the RAS / MEK Inhibitor Landscape




*Source: Kolitz S, et al. Cancer Res 2026; doi:10.1158/0008-5472.CAN-25-4907. Adapted from Figure 7.*

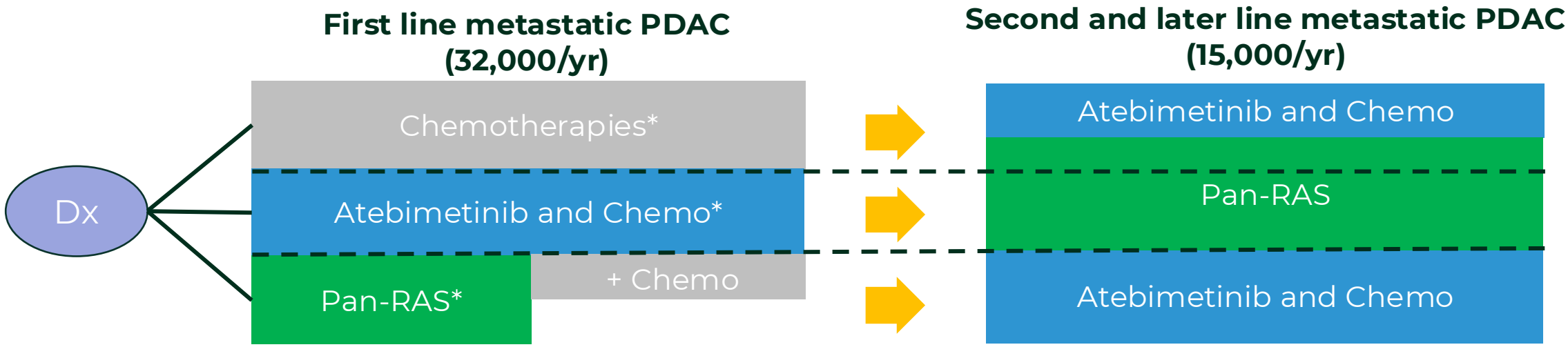


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# The Metastatic Treatment Paradigm will Evolve with the Approval of New Medicines – Pre KRAS Mutation Specific Inhibitor Approval

US-only 2026 Estimates

*CONCEPTUAL*



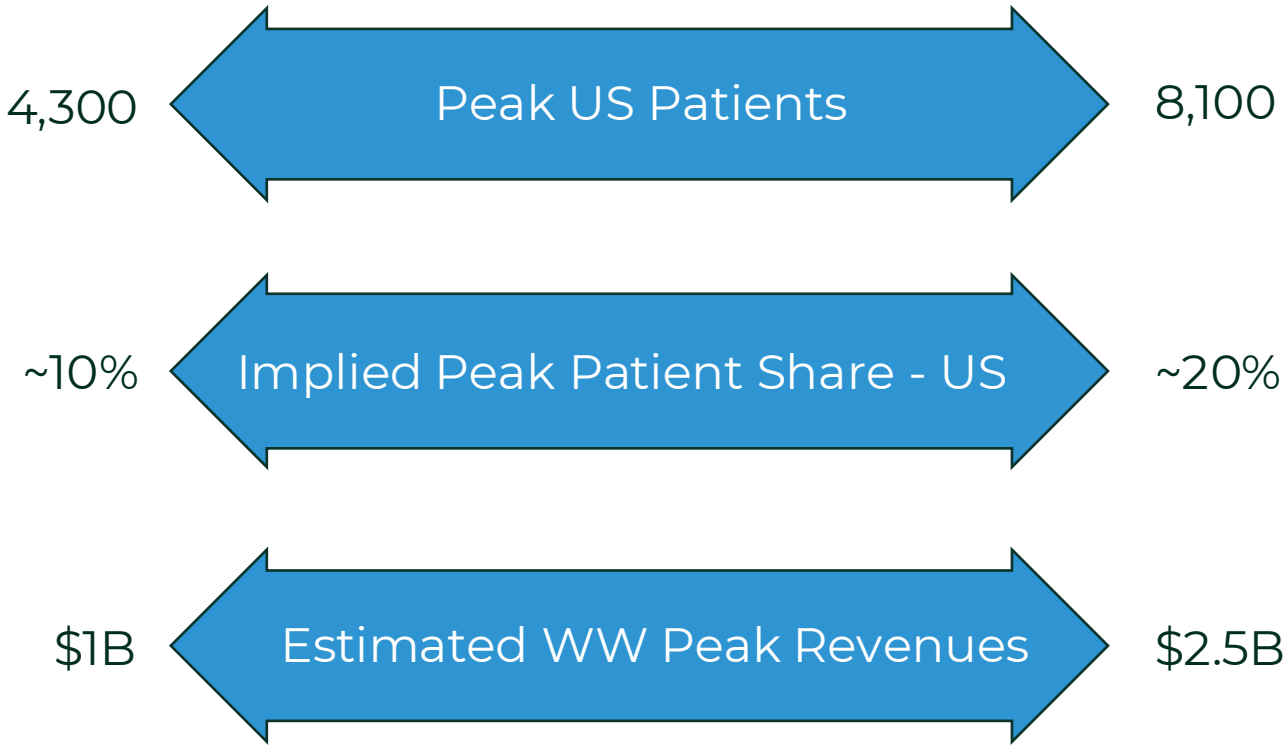

- There likely will be legacy chemotherapy use in first line that could dissipate over time
- Atebimetinib could take considerable first line share if it continues to show OS favorability over Pan-RAS inhibitors and better tolerability
- Atebimetinib could also be used in second line as there are few options for patients particularly when they fail Pan-RAS

* Possible combinations with PRMT5i, CLDN18.2, and other MOAs


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# Summary of Analyst Expectations on Future Market Dynamics

## Proprietary Analyst Models




## "The Pancreatic Cancer Drug Market"*

- "By 2034, RAS inhibitors are projected to be the top-selling class ($3.8 billion), driven entirely with daraxonrasib
- Whereas MEK inhibitors are expected to generate $1.5 billion, exclusively from atebimetinib.
- Driven by its extended use as a first-line chemotherapy regimen and its evaluation in combination with novel emerging therapies, gemcitabine plus nanoparticle paclitaxel is projected to drive sales to nearly $2 billion."

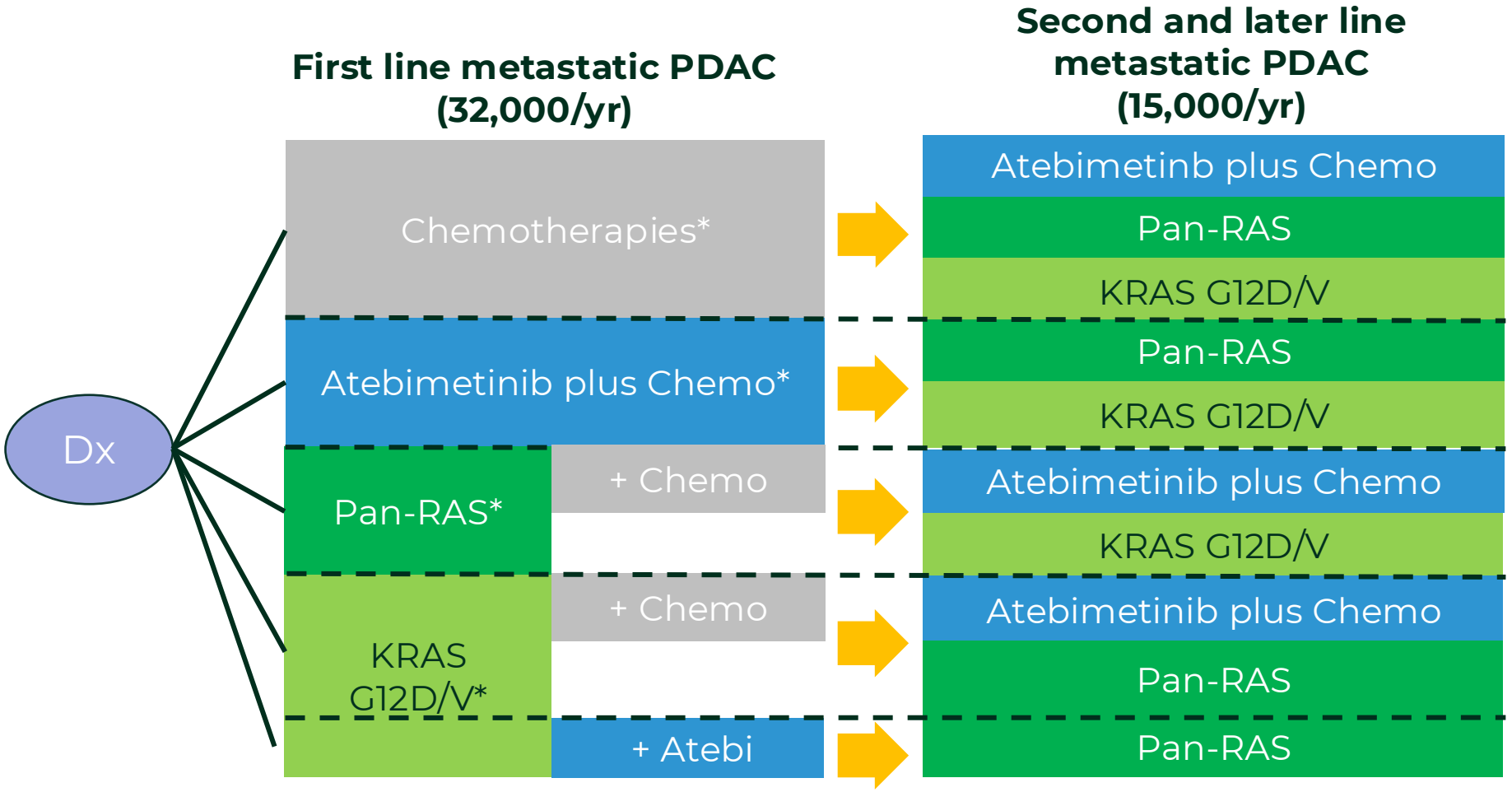
* *Nature reviews drug discovery*, Tripathi et al. 20 Feb 2026


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# The Metastatic Treatment Paradigm will Evolve with the Approval of New Medicines – Post KRAS Mutation Specific Inhibitor Approval

US only 2026 Estimates

*CONCEPTUAL*




- The treatment use picture becomes more complicated if KRAS mutation specific inhibitors are approved
- Atebimetinib could maintain first line use with chemotherapies and can be combined with KRAS mutation specific inhibitors in first line to increase depth and durability of treatment
- Atebimetinib could also be used in second line as there are fewer options for patients particularly when they fail Pan-RAS or KRAS mutation specific inhibitors

* Possible combinations with PRMT5i, CLDN18.2, and other MOAs

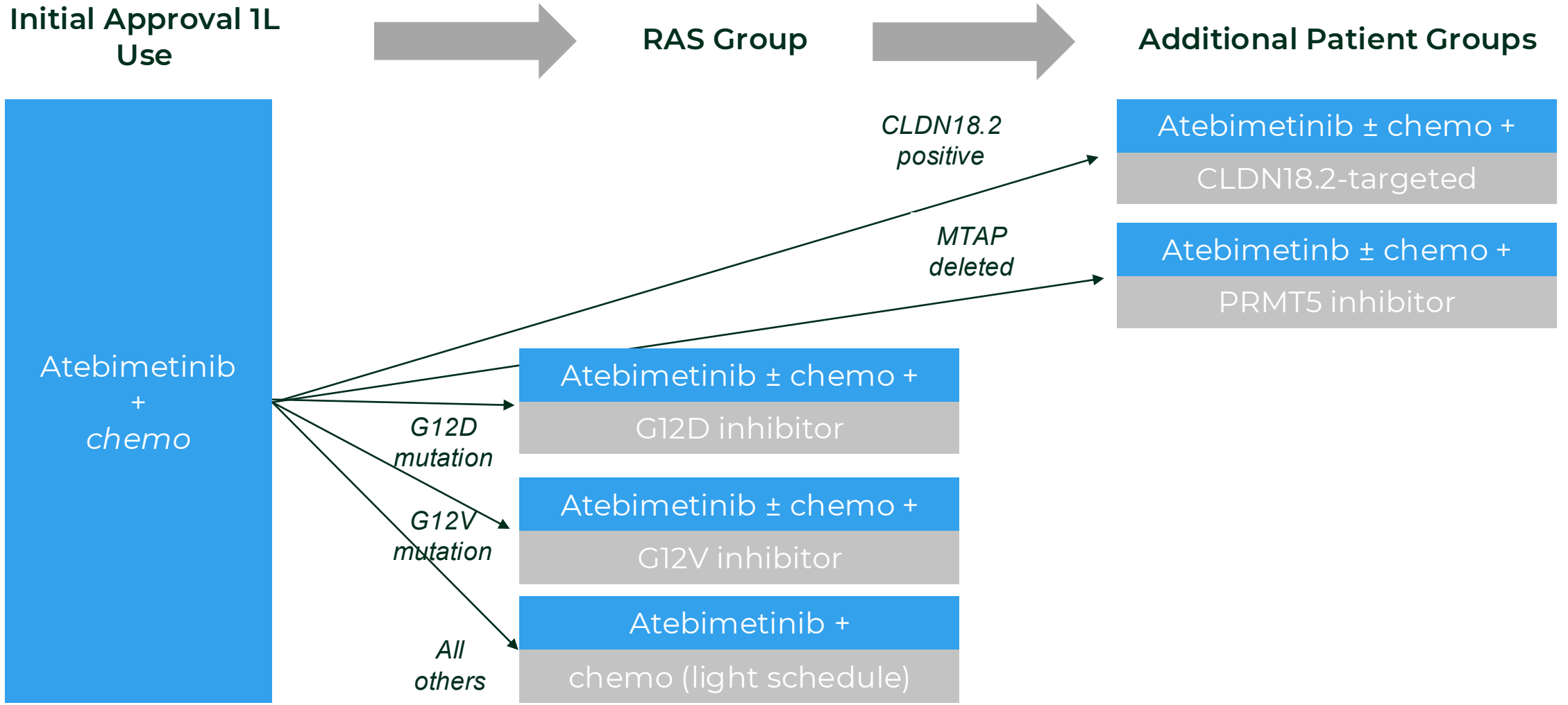


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# CLDN18.2 and MTAP Status May Impact 1L Treatment as Well

*CONCEPTUAL*






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# NSCLC, ATC and Beyond

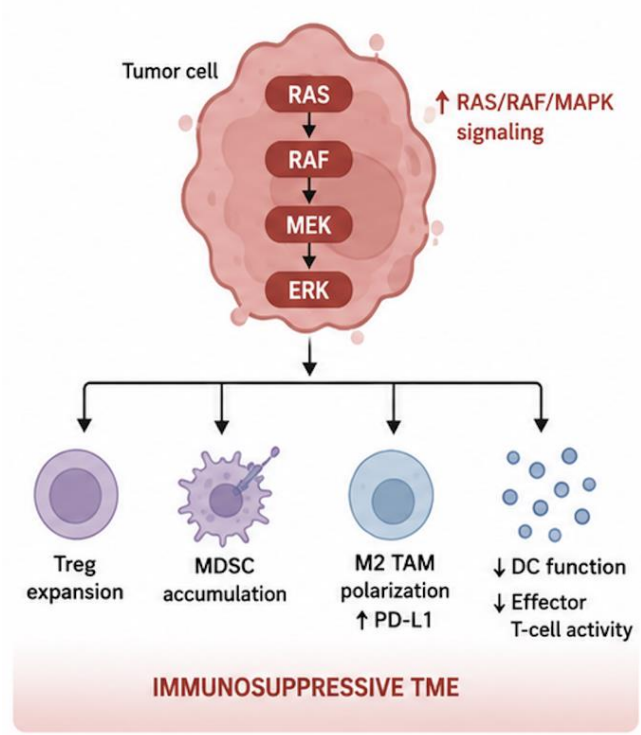
Atebimetinib+PD-1 in NSCLC

Atebimetinib+chemo in ATC

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# Atebimetinib + PD-1 Blockade: DCI-Based Rationale for Immune Synergy

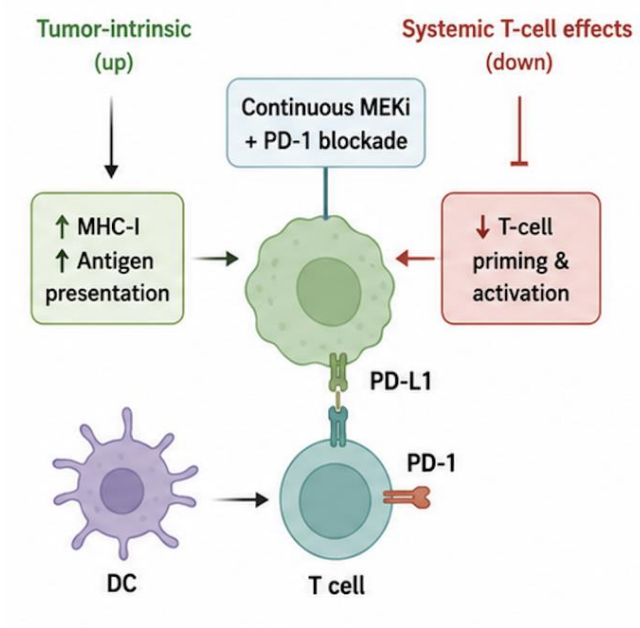
**1** Hyperactive RAS/MAPK establishes an immunosuppressive TME




**MAPK-driven signaling programs an immunosuppressive microenvironment that blunts anti-tumor immunity**

*Jung et al., Int J Mol Sci 2021 (review)*
*Loi et al., Clin Cancer Res 2016*

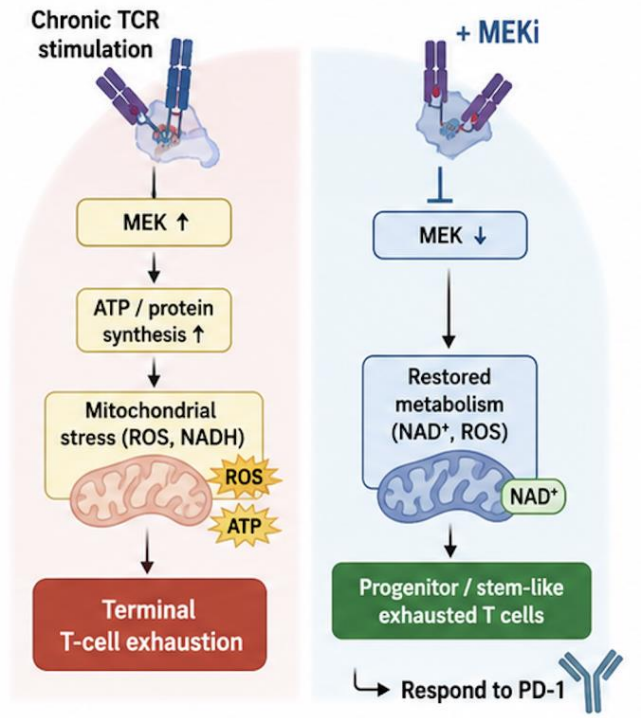
**2** Continuous MAPK inh (MEKi) + PD-1 blockade disappointed clinically




**Tumor-intrinsic gains are masked by reduced T-cell priming and activation, limiting the benefit of chronic MEKi + PD-1**

*Ebert et al., Immunity 2016 (combo rationale)*
*Dennison et al., Cancer Immunol Res 2021 (failure mechanism)*
*IMblaze370 / IMspire170*

**3** Chronic MEK signaling via prolonged TCR stimulation drives terminal T-cell exhaustion




**MEKi disrupts continuous TCR signaling and metabolic stress, restoring exhausted T cells that can respond to PD-1**

*Mitra et al., Immunity 2026*
*Verma et al., Nat Immunol 2021*

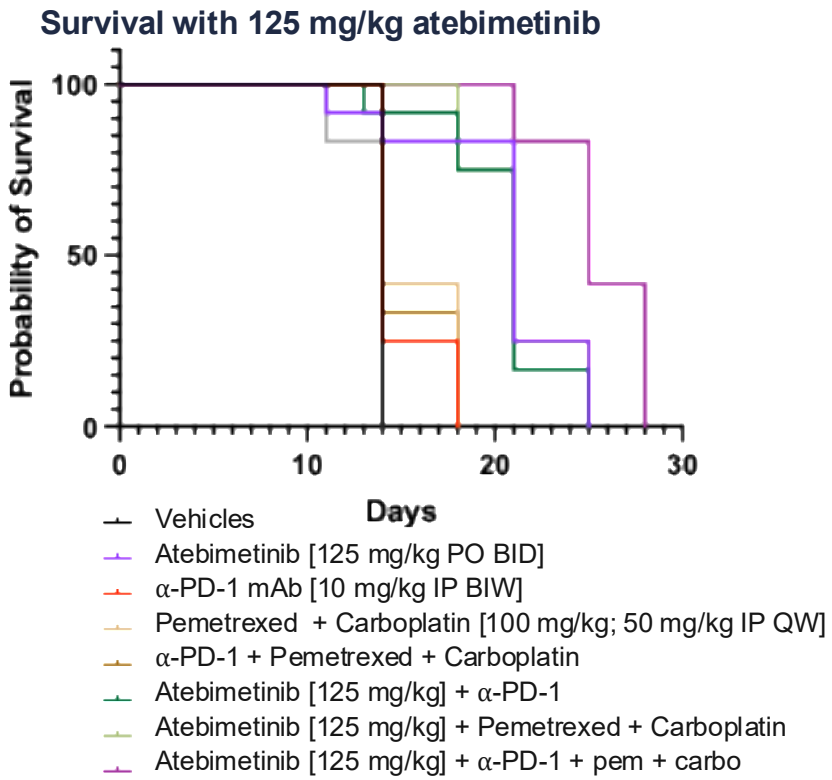


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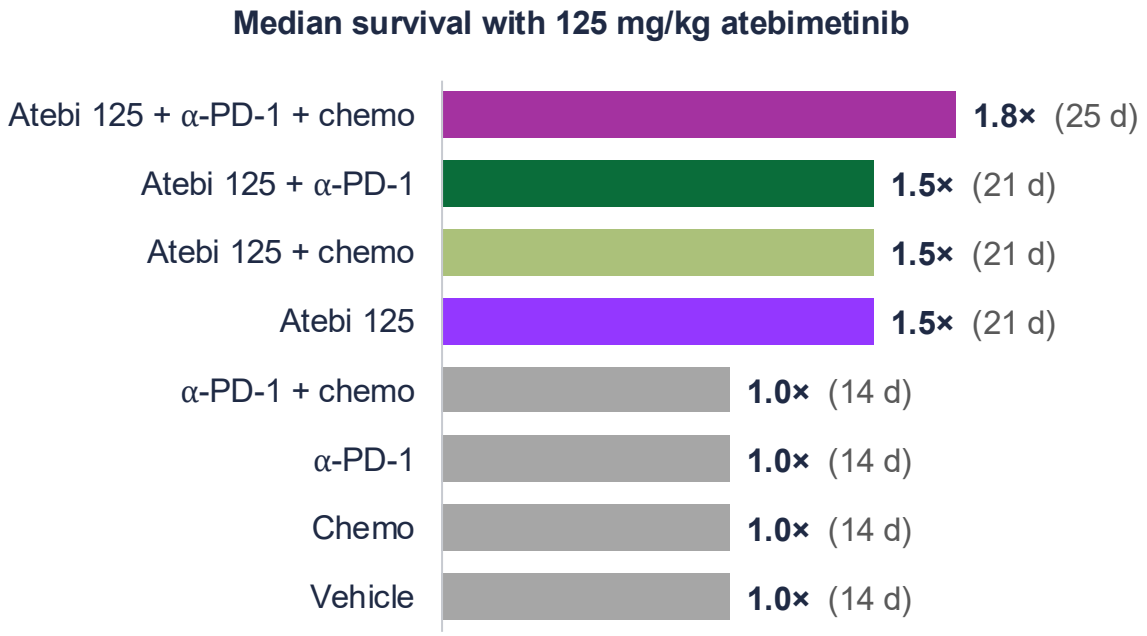
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# Atebimetinib Plus PD-1 is Effective in a Cold Lung Cancer Model

## Lewis Lung Carcinoma (LL2 model)




## Median Survival Time Advantage vs Control




Fold-change in MST vs α-PD-1 + chemo (MST in days), n = 12 per group

Atebi: atebimetinib 125 mg/kg PO BID; Chemo: carboplatin + pemetrexed

Presented at SITC 2026, Phoenix, AZ (November 6, 2026) | Abstract Presentation #377



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# NSCLC Phase 2 Trial Design

Patient Population: First-line (1L) RAS-mutant Non-Small Cell Lung Cancer (NSCLC)

## Key Eligibility Criteria

- First-line (1L) treatment for NSCLC
- Advanced, unresectable, or metastatic
- Presence of RAS mutation

## Dose Optimization Phase

**Cohort 1: Atebimetinib** (160 mg QD) + **Libtayo[1]** + **chemo[2]** (N=up to 20)

**Cohort 2: Atebimetinib** (240 mg QD) + **Libtayo[1]** + **chemo[2]** (N=up to 20)

**Cohort 3: Atebimetinib** (320 mg QD) + **Libtayo[1]** + **chemo[2]** (N=up to 20)

## Expansion Phase

(optimal dose from dose optimization)

**Arm A** (Expansion)

- PD-L1 ≥ 50%
- Atebi[3] + Libtayo
- N = 20

**Arm B** (Expansion)

- PD-L1 < 50%
- Atebi[3] + Libtayo + chemo
- N = 20

1. Libtayo (cemiplimab) = 350 mg Q3W
2. Chemotherapy (chemo) = carboplatin (AUC 5 IV Q3W) + pemetrexed (500 mg/m$^2$ IV Q3W)
3. Atebimetinib = at dose selected from safety lead-in (160, 240 or 320 mg QD p.o.)



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# Emerging Pre-clinical Data will Support the Combination of Atebimetinib and Chemotherapy in Anaplastic Thyroid Cancer

*Anaplastic Thyroid Cancer – Preclinical Poster Presentation*

**Title**: Atebimetinib, a deep cyclic inhibitor of MEK, combined with chemotherapy: preclinical rationale for treatment of anaplastic thyroid cancer (ATC)

**Abstract Number**: 144

**Poster Number**: PB-144

**Presenter**: Praveen Nair, Immuneering Corporation

**Date**: November 18, 2026

**Session**: Translational Studies

Supporting preclinical data to be presented at 2026 EORTC-NCI-AACR Symposium, November 18, 2026



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# Anaplastic Thyroid Cancer Phase 2 Trial Design

Patient Population: Second-line (2L) anaplastic thyroid cancer (ATC)

## Eligibility

- Histopathologically confirmed ATC with MAPK pathway alteration
- Molecular profiling by FDA-approved test
- ECOG performance status 0–2 (both cohorts)

- **Cohort A**: Progression on prior BRAF inhibitor plus MEK inhibitor required
- **Cohort B**: All Comers NOT otherwise eligible for Cohort A progressing on standard of care.

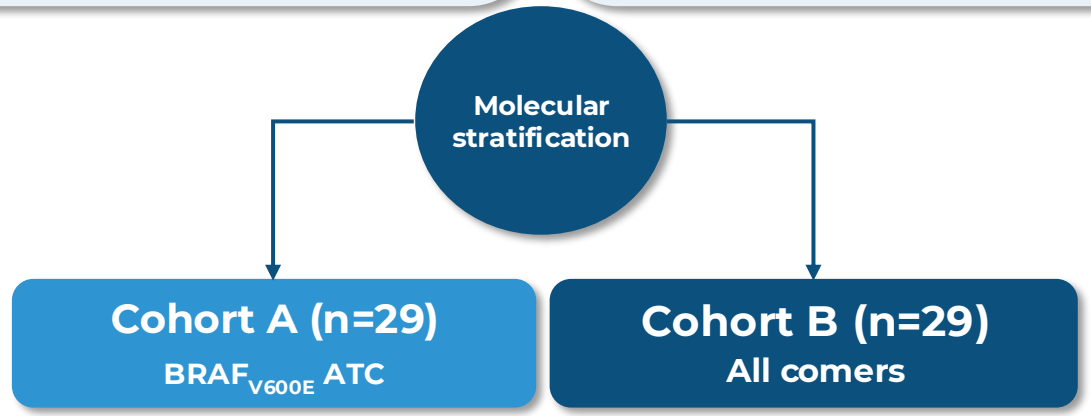
### Safety Run-in (n=6)

Atebimetinib 320 mg PO QD (continuously)
+ Carboplatin AUC 5 IV Day 1 q21 days
+ Pemetrexed 500 mg/m² IV Day 1 q21 days

### DLT evaluation period:

patients will be monitored for dose-limiting toxicities (DLTs) to assess tolerability of the combination and inform dose selection.

**The 6 patients in the safety run-in will be counted towards Cohort A and B




### TREATMENT

Treatment regimen for Cohorts A and B will be the same as the Safety Run-In

**Atebimetinib dose will be determined from the Safety Run-In**

## Endpoints

**Primary**
- ORR

**Secondary**
- DOR
- DCR
- PFS
- Safety
- OS

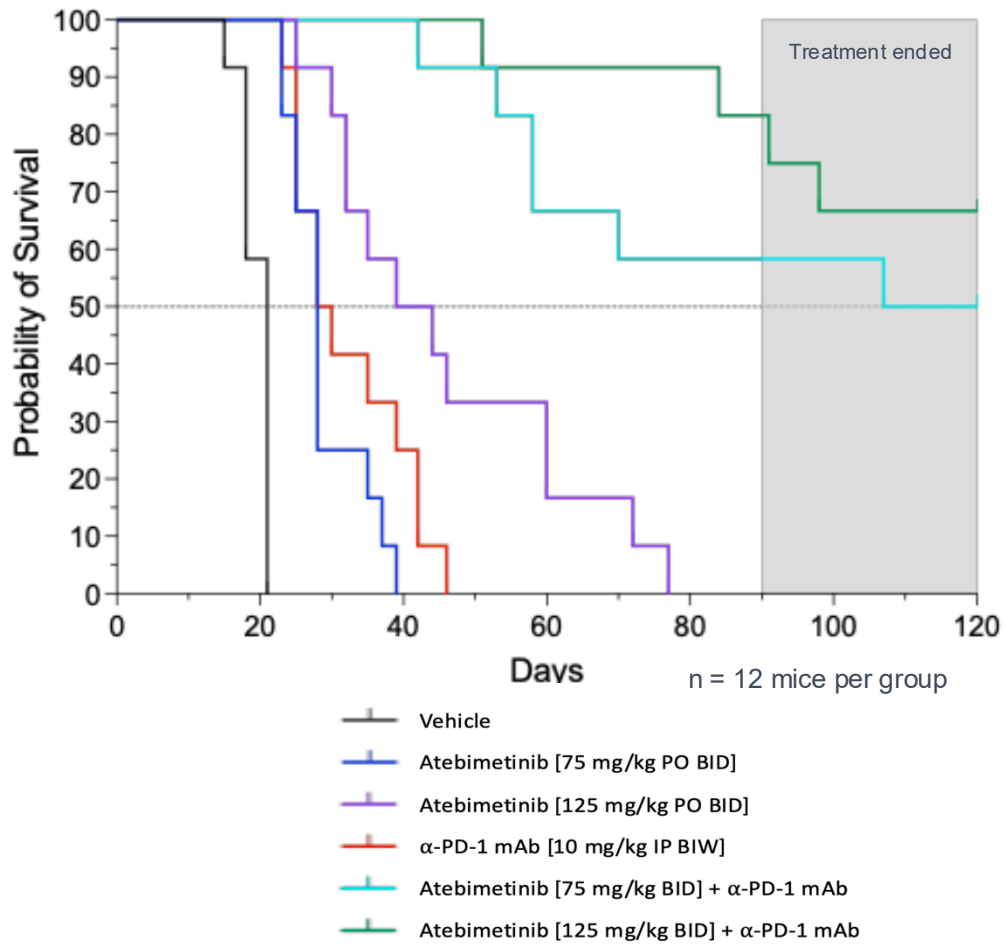

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# Future Atebimetinib Indications – a Pipeline in a Product

- **CRC**
  - 1L Metastatic: Atebi+EGFR(/MET)
  - 1L Metastatic: Atebi+BRAF
  - 2L Metastatic: Atebi+ASP3082+chemo
- **Gastric**
  - 1L Metastatic: Atebi+CLDN18.2+chemo
- **Melanoma**
  - 2L/3L Metastatic: Atebi+BRAF
- **Cholangiocarcinoma** (CCA)
  - 1L Metastatic: Atebi+FGFR
- **Heme** (AML, MM)

Example

**Atebimetinib + anti-PD-1 extends survival in CRC KRAS$^{G12D}$ CT26***




* Presented at SITC 2026, Phoenix, AZ (November 6, 2026) | Abstract Presentation #377



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# Atebimetinib

## Mechanism of Action

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# Three Mechanisms Well-Established to Improve Survival

| | Shrinking Tumors | Preserving Body Mass (Countering Cachexia) | Minimizing Side Effects |
|---|---|---|---|
| **Atebimetinib+mGnP – Clinical Evidence** | Disease Control Rate (DCR) = 82% | 84% of patients stable or gain weight | Only 2 categories of Grade 3+ AEs in ≥10% of patients |
| **Published Studies Linking Mechanism to Overall Survival in PDAC** | OS correlation coefficient[1] with DCR = 0.74 ($p < 0.001$) | Weight Loss[2] HR = 1.55<br><br>"1/3 of pancreatic cancer patients die from complications of cachexia"[3] | Decline to ECOG 2 HR = 1.48<br>No 2L treatment[4] HR = 1.51 |

Atebimetinib + mGnP Clinical Evidence in 1L PDAC, N = 55, data cutoff April 24, 2026. 84% of patients with weight data at baseline and 3 months showed either stable weight (within 5%) or gain weight at 3 months.

References: [1] Makris et al, 2017. [2] Wang et al, 2025. [3] Yoo et al, 2021 [4]Weiss et al, 2024



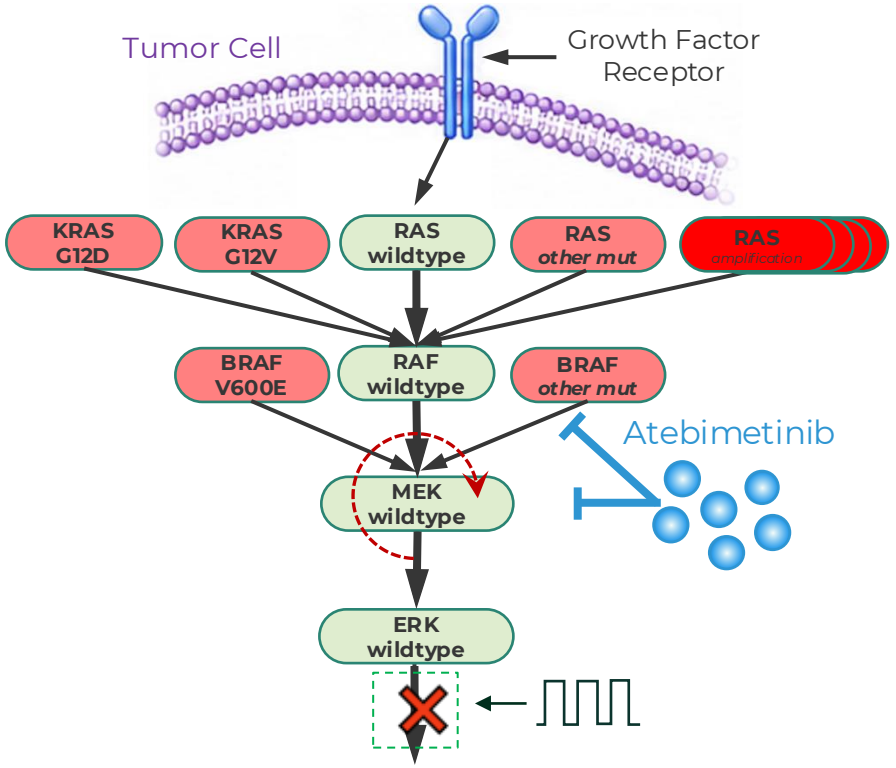
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# Atebimetinib Addresses Two Key Liabilities in MEK Inhibition

## Our First Target: MEK

*Pulsatile ≥$IC_{90}$ Inhibition with Once-Daily Oral Dosing*




**Healthy Cells = Intermittent**

**Cancer Cells = Continuous**

## Goals: Improve Tolerability, Expand Applicability to RAS Mutant Cancers

| | Liabilities | | Strengths | |
|---|---|---|---|---|
| **1st Generation MEK inhibitors** | Ineffective in cancers driven by **RAS** | Poorly tolerated | Effective in cancers driven by **RAF** | Counters Cachexia to preserve body mass |
| | corrected | improved | retained | retained |
| **3rd Generation MEK inhibitor: Atebimetinib** | **Block RAF-mediated MEK phosphorylation** | **Immuneering's Deep Cyclic Inhibitor (DCI) Technology** | | |

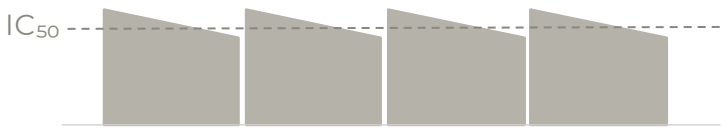


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# Immuneering's DCI Technology – Designed to Shrink Tumors but Allow Healthy Cells Necessary Access to Target Pathway

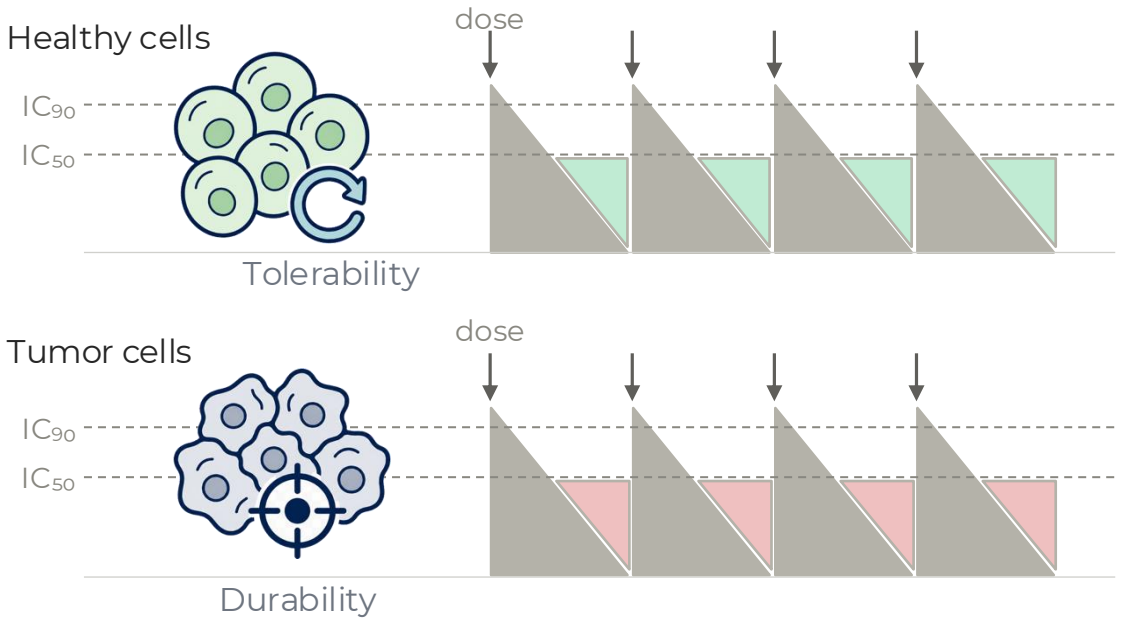
## Conventional Wisdom: Chronic Inhibitors




**All cell signaling suppressed**
= toxicity, resistance

## Immuneering's Deep Cyclic Inhibitor Technology

*Pulsatile ≥$IC_{90}$ Inhibition with Once-Daily Oral Dosing*




*High Free-Fraction CMax, Fast Off Rate, Short Half Life (~2 hours)*

### 1. Tolerability

Provides Recovery Window for Healthy Cells

### 2. Durability

Limits Adaptive and Acquired Resistance

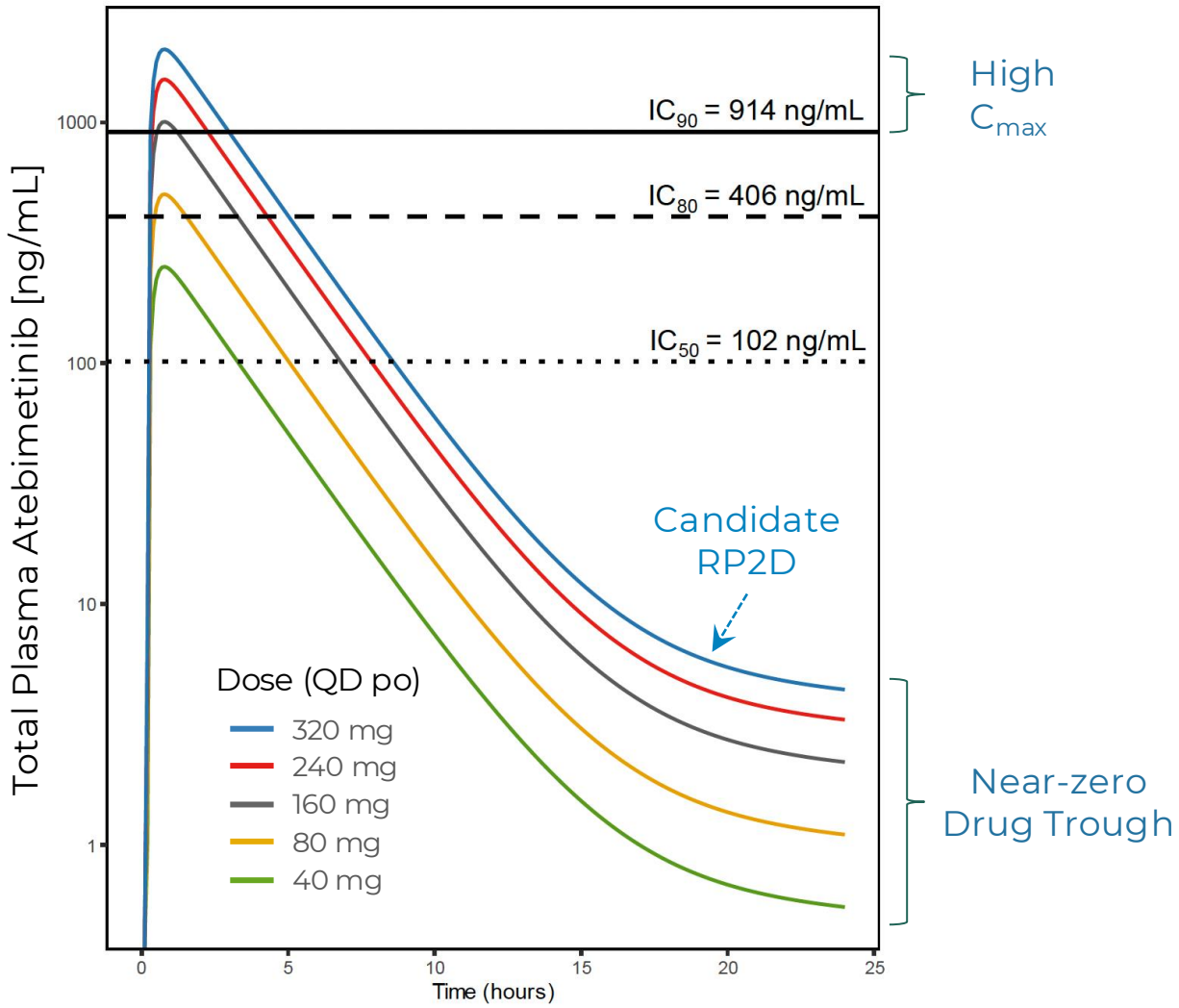


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# DCI Achieves >90% Target Inhibition Peak and Near Zero at Trough

## Topline PK/PD Data for atebimetinib




## Deep Cyclic Inhibition (DCI) Profile Maximized at Candidate RP2D of 320 mg

- Longer time above pERK $IC_{90}$ at 320 mg (2.7 hr) vs. 240 mg (1.9 hr)
- Lower variance in PD (p-ERK) profiles at 320 mg vs. 240 mg

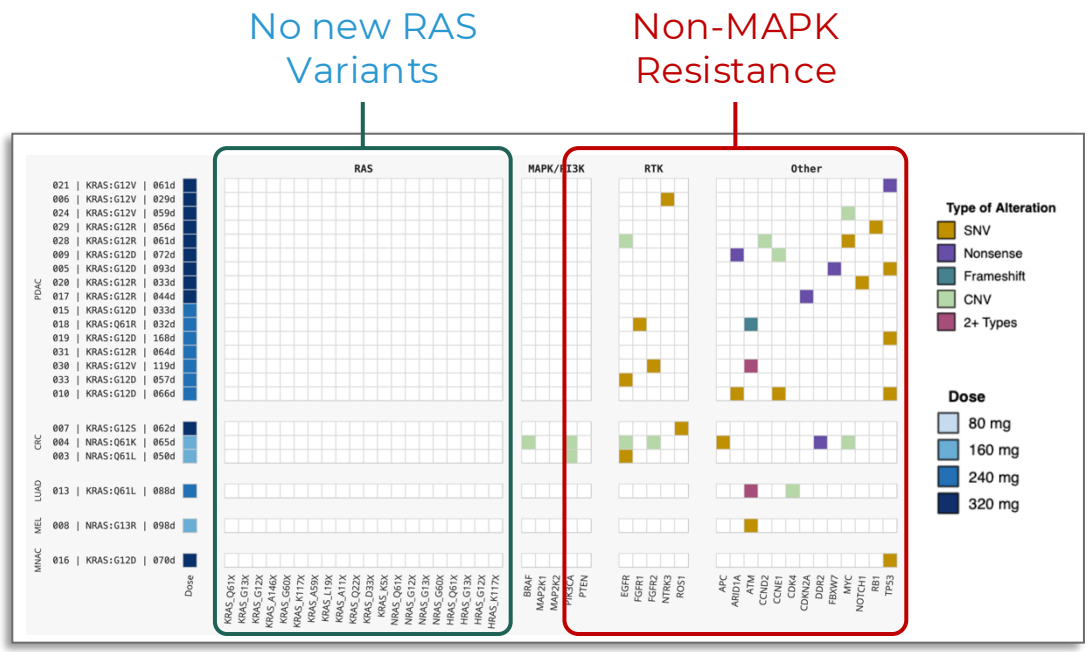
**Both DCI requirements met in patients: a deep pulse above $IC_{90}$, then daily clearance**

*Modeled typical profiles based on 19 patients of atebimetinib plasma concentrations (ng/mL) versus time (h) on a semilogarithmic scale for the different dose groups. Direct measure of time above PD $IC_{level}$ does not consider $k_{off}$ PD shadow. Approximately dose linear from 40 to 320 mg PO QD; no drug accumulation. Tight relationship observed between plasma concentrations and phosphorylated ERK (p-ERK) to total ERK (t-ERK) ratios; Longer time above pMEK IC90 at 320 mg (4.0 hr) vs. 240 mg (3.3 hr)*


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# Atebimetinib Rarely Drives Acquired Alterations in the MAPK Pathway; RAS Inhibition Drives RAS Amplifications Which May Increase Risk of Death

## (1.) Atebimetinib rarely drives acquired alterations in RAS or other MAPK pathway genes




*Newly arising variants detected by Guardant Health circulating tumor DNA (ctDNA) test on ~day 28 or end of treatment (EoT). Data received by February 20, 2024*

*2024 AACR King, et al.*

## (2.) RAS amplifications are a common acquired alteration in pan-RAS-treated patients

"Treatment-emergent genomic alterations in the RAS signaling pathway were observed in more than half (26 of 44; 59%) of these patients, including, most notably, mutant KRAS amplifications in one-third (16 of 44; 36%)" [Aronchik et al, Nature Medicine, 2026]

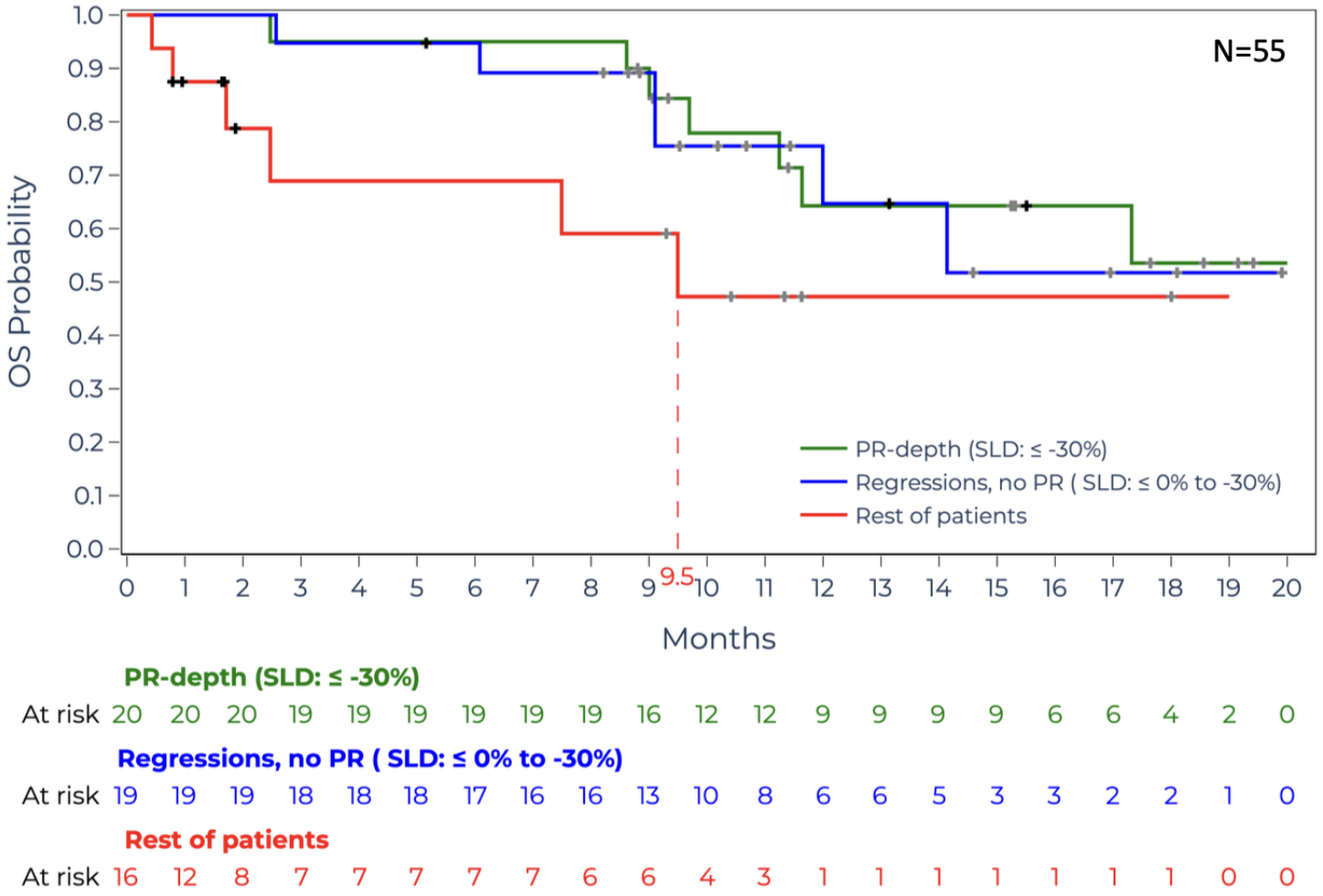
## (3.) RAS amplifications are associated with higher risk of death in pancreatic cancer (HR = 1.7)

"patients with tumors with any gain of KRAS-MUT allele had significantly lower OS compared to those with tumors with one mutant allele" [Varghese et al, Nature Medicine, 2025]


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# Presence of Tumor Volume Reductions More Important than Depth

Phase 2a Data (atebi 320mg QD + mGnP)




There was no difference in survival between patients who had

- A "RECIST partial response (PR)" (green bar) and
- Tumor control but did not achieve a PR (blue bar)

ORR, which measures the rate of PRs, was not a predictor of survival

Makris et al, 2017 showed that in pancreatic cancer, response rate is a weaker predictor of OS than disease control rate or PFS

Presented at AACR Pancreatic Cancer 2026, San Diego, CA (September 2026) | Abstract Presentation #A134



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# Conclusion

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# Immuneering's Pipeline

| Indication | Regimen | Phase 1/2 | Phase 3 | Reg. | Collaboration |
|---|---|---|---|---|---|
| **1L PDAC** | Atebimetinib + mGnP vs. GnP | **Phase 3 – registrational intent** | | | Immuneering only |
| **1L PDAC** | Atebi + FFX | **Phase 2 · Efficacy** | | | Immuneering only |
| **1L PDAC** | CLDN18.2-targeted + atebi + mGnP (biomarker-positive) | **Phase 1b · Efficacy** | | | Astellas |
| **2L, 3L PDAC (chemo-free)** | CLDN18.2-targeted + atebi (chemo-free; biomarker-positive) | **Phase 1/2 · Efficacy** | | | Astellas |
| **1L RAS-mut NSCLC** | Atebi + cemiplimab ± chemo | **Phase 2 · Efficacy** | | | Regeneron |
| **2L/3L RAS-G12C NSCLC** | Atebi + olomorasib | **Phase 2 · Efficacy** | | | Eli Lilly |
| **2L Anaplastic Thyroid Cancer** | Atebi + chemo | **Phase 2 – reg'l intent** | | | Immuneering only |

More atebimetinib combinations under discussion;

Preclinical pipeline applying deep cyclic inhibition platform to additional targets and parallel pathways in oncology

atebi, atebimetinib (IMM-1-104); PDAC, pancreatic ductal adenocarcinoma; NSCLC, non-small cell lung cancer; (m)GnP, (modified) gemcitabine + nab-paclitaxel; (m)FFX, (modified) FOLFIRINOX; ATC, anaplastic thyroid cancer, SoC, standard of care; KoL, key opinion leader; 1L/2L/3L, first/second /thirdline.



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# News Flow Guidance

## 2026

**4Q 2026**

### First patient dosed Ph 2 NSCLC

Atebimetinib + anti-PD-1 (cemiplimab) in non-small cell lung cancer

**4Q 2026**

### Submit IND for Ph 2 ATC

Atebimetinib + chemotherapy

## 2027

**1H 2027**

### Updated Ph 2 PDAC data

1L Phase 2 atebimetinib + mGnP (N=55)

**Mid-2027**

### First patient dosed Ph 2 ATC

Atebimetinib + chemotherapy

**Mid-2027**

### Begin IND-enabling studies

Next DCI drug program

**Late 2027**

### Preliminary Ph 2 data NSCLC

Atebimetinib + anti-PD-1 (cemiplimab) in non-small cell lung cancer

## 2028

**Mid-2028**

### Topline readout

Phase 3 MAPKeeper 301

***Cash runway*** **Into 4Q 2028**



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