Positive Phase 2a Data Update for IMM-1-104 in Pancreatic Cancer

Immuneering

Nasdaq: IMRX

January 2025

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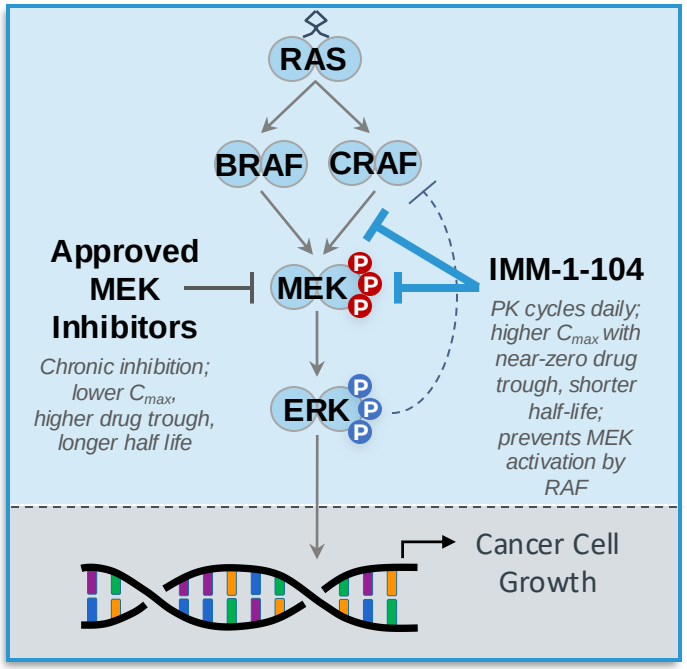
MEK Inhibitors Already Help Patients Live Longer; Drive $2.4B In Sales
Our Clinical Data Show IMM-1-104's Potential To Do Better



Goal → Expand Indications

beyond BRAF, to RAS-driven cancers and more

- **43% ORR, 86% DCR observed for 104+mGnP in 1st line pancreatic cancer** (including a complete response)
- Responses observed for 104+mFFX in 1st line (-100% PR), 104 in 2nd line (-67% PR) pancreatic cancer
- Planning for 104+mGnP pivotal trial underway; additional Phase 2a combo arms planned for 2025

Goal → Improve Tolerability

in existing and new indications

- **Observed highly differentiated tolerability in 96 patients treated with IMM-1-104 alone or in combination with mGnP**
- Broad potential of IMM-1-104 to enable new combinations, and replace existing MEK inhibitors in established combinations, for patients with tumors driven by BRAF, RAS, and beyond

Unless otherwise noted, all data reported as of Dec 5, 2024. Adding MEKINIST to TAFINLAR increased overall survival by ~6 months per COMBI-d results in MEKINIST label. TAFINLAR+MEKINIST combination net sales were ~$1.9B in 2023 per Novartis annual report. Additional ~$500M in net sales in 2023 from 3 other MEK inhibitors MEKTOVI, KOSELUGO, and COTELLIC per reports of their respective manufacturers.

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The First 5 Arms Of Our Ongoing Phase 2a Study Seek To Expand Beyond Approved MEK Inhibitor Indications

INDICATION	TYPE	DISCOVERY	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	Bench-mark (ORR)	FDA Designations for IMM-1-104
Pancreatic	Combination	1L – 104 + mGem/nab-Pac					23%[a]	Orphan Drug Fast Track 1L Fast Track 2L
	Combination	1L – 104 + mFOLFIRINOX					32%[b]	
	Monotherapy	2L (or 1L)					3%[c]	
Melanoma (RAS^{mut})	Monotherapy	2L, 3L post-IO (or 1L)						Fast Track
NSCLC (RAS^{mut})	Monotherapy	2L, 3L						

75+ pancreatic cancer patients enrolled as of December 5th, 2024

[a]Phase III MPACT trial (link) [b]Phase III PRODIGE/ACCORD 11 trial (link) [c]Phase II QUILT-3.010 trial (link)

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To Date, 1st Line Pancreatic Cancer Patients Have Faced A Difficult Choice: Live Longer OR Feel Better

	FOLFIRINOX[1]	Gemcitabine + nab Paclitaxel (GnP)[1]	IMM-1-104 + mGnP
Efficacy			We aim to give patients a better option
Tolerability			

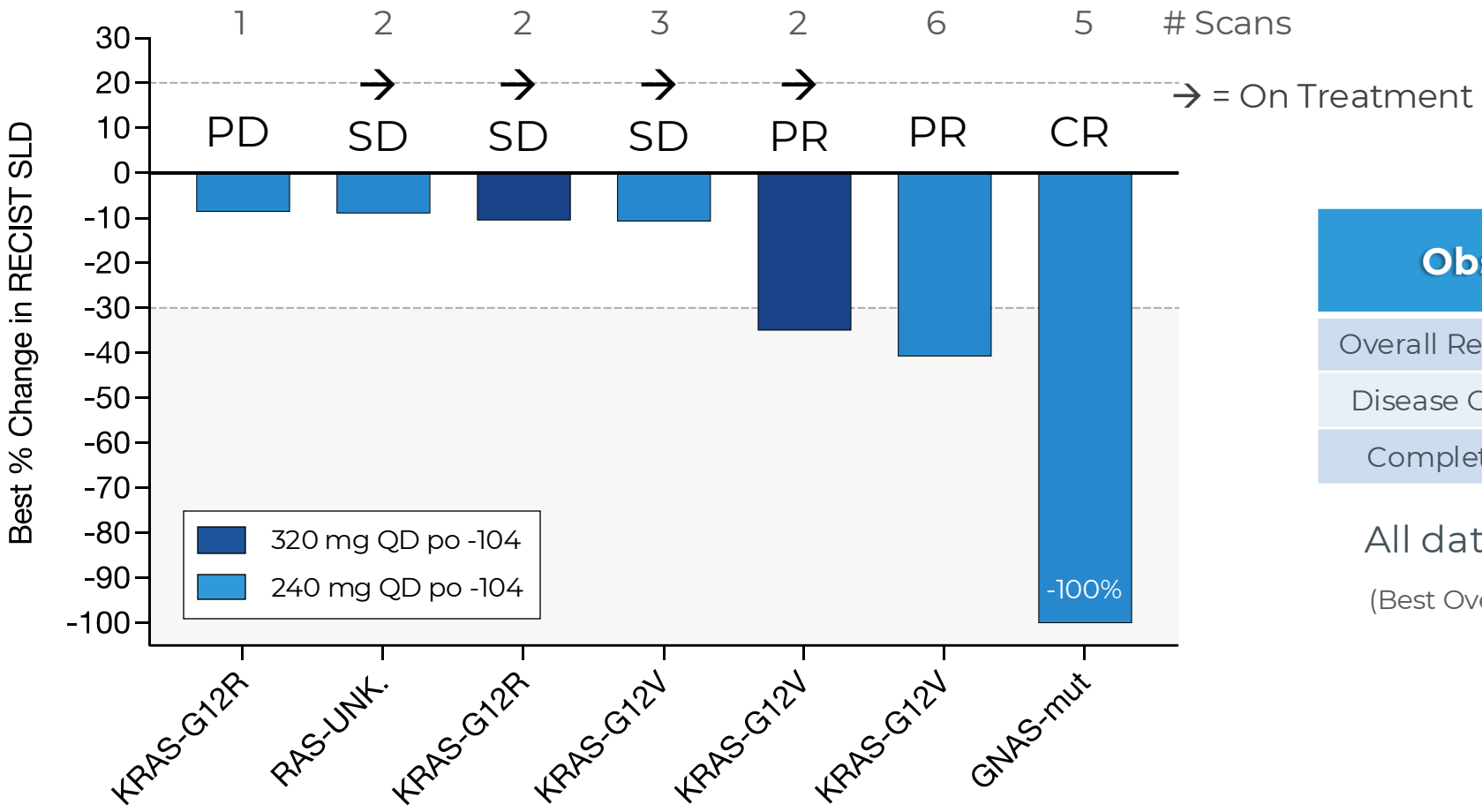
(1) Per GlobalData: in the U.S., approximately half of first-line pancreatic cancer patients are treated with FOLFIRINOX or Fluorouracil-related treatments, as compared to approximately half with GnP or Gemcitabine-related treatments

At Best, Only ~ 32% Of Patients Reported To Respond To Current Standard Of Care For 1st Line Pancreatic Cancer

	FOLFIRINOX*	Gemcitabine + nab Paclitaxel (GnP)**	IMM-1-104 + mGnP
Efficacy	⊕	⊖	We aim to give patients a better option
Objective Response Rate (ORR)	32%	23%	
Disease Control Rate (DCR)	70%	48%	
Complete Response (CR)	0.6%	0.2%	
Progression Free Survival (PFS)	6.4 months	5.5 months	
Overall Survival (OS)	11.1 months	8.5 months	
Safety	⊖	⊕	
Grade 3-4 neutropenia	46%	38%	
Grade 3-4 fatigue	24%	17%	
Grade 3-4 diarrhea	13%	6%	

*Phase III PRODIGE/ACCORD 11 trial (link) **Phase III MPACT trial (link)

43% Of Patients Responded To IMM-1-104 + Modified GnP For 1st Line Pancreatic Cancer, Including A Complete Response



Observation	IMM-1-104 + mGnP
Overall Response Rate (ORR)	**43%**
Disease Control Rate (DCR)	**86%**
Complete Response (CR)	**14%**

All data as of December 5, 2024

(Best Overall Response (BOR) to date Shown)

- ORR analyses included all evaluable patients who received their first dose of IMM-1-104 at least 14 weeks prior to data cutoff of December 5th, 2024 (to allow 2 potential scans beyond baseline scan – patients who had 2 such scans prior to 14 weeks were also included). Scans typically occur every 6 weeks (+/- 1 week)
- Glossary: PD = progressive disease; PR = partial response; SD = Stable Disease; SLD = sum of longest tumor diameter; DCR = disease control rate (CR+PR+SD)

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Favorable Tolerability Observed For IMM-1-104 In Combination With Modified Gem/nab-Pac (mGnP) For 1st Line Pancreatic Cancer

Safety: Phase 2a Combination in 1L PDAC at 240 (n=6) & 320 mg QD (n = 15)

Maximum Severity of TEAEs for combination: TEAE's observed in >10% of patients,	**Grade 1** n(%)	**Grade 2** n(%)	**Grade 3** n(%)	**Grade 4** n(%)	**Any Grade** n(%)
1. Anaemia	1 (5%)	2 (10%)	3 (14%)	0	6 (29%)
2. Fatigue	3 (14%)	3 (14%)	0	0	6 (29%)
3. Diarrhoea	1 (5%)	3 (14%)	1 (5%)	0	5 (24%)
4. Nausea	4 (19%)	1 (5%)	0	0	5 (24%)
5. Pyrexia	5 (24%)	0	0	0	5 (24%)
6. Aspartate Aminotransferase (AST) Increased	0	3 (14%)	1 (5%)	0	4 (19%)
7. Alanine Aminotransferase (ALT) Increased	1 (5%)	1 (5%)	2 (10%)	0	4 (19%)
8. Neutrophil Count Decreased	0	2 (10%)	2 (10%)	0	4 (19%)
9. Oedema Peripheral	4 (19%)	0	0	0	4 (19%)
10. Vomiting	1 (5%)	2 (10%)	1 (5%)	0	4 (19%)
11. Hyperglycaemia	2 (10%)	0	1 (5%)	0	3 (14%)
12. Neuropathy Peripheral	3 (14%)	0	0	0	3 (14%)
13. Platelet Count Decreased	1 (5%)	2 (10%)	0	0	3 (14%)
14. Rash	2 (10%)	0	1 (5%)	0	3 (14%)
15. Retinopathy	2 (10%)	1 (5%)	0	0	3 (14%)

- *TEAE = Treatment-Emergent Adverse Events*
- *All data as of December 5, 2024. All patients treated with drug combination; no Serious Adverse Events (SAE) were related to IMM-1-104*

Encouraging Response And Safety Profile Observed For IMM-1-104 + mGnP In 1st Line Pancreatic Cancer

	FOLFIRINOX	Gemcitabine + nab Paclitaxel (GnP)	IMM-1-104 + mGnP
Efficacy			✚
Overall Response Rate (ORR)			**43%**
Disease Control Rate (DCR)			**86%**
Complete Response (CR)			**14%**
Progression Free Survival (PFS)			TBD
Overall Survival (OS)			TBD
Safety			✚
Grade 3-4 neutropenia			**10%**
Grade 3-4 fatigue			**0%**
Grade 3-4 diarrhea			**5%**

We aim to give patients a better option

Efficacy analyses included all evaluable patients who received their first dose of IMM-1-104 at least 14 weeks prior to data cutoff of December 5th, 2024. All safety data as of December 5, 2024.

KOLs: IMM-1-104 + Modified Gem/nab-Pac (mGnP) May Have A Unique Profile For Response And Tolerability

Tanios (Toni) Bekaii-Saab, MD (Mayo Clinic. IMRX SAB member since 2019)

"Immuneering's Phase 2a data in first line pancreatic cancer are **very promising** … If current trends continue, the combination of IMM-1-104 with modified gemcitabine/nab-paclitaxel **may provide improved efficacy and tolerability** vs. gemcitabine/nab-paclitaxel **in the first-line pancreatic cancer setting**, where patients continue to urgently need better options. In addition, **having a MEK inhibitor that appears to be as well-tolerated as IMM-1-104 may provide new opportunities for patients with different types of cancer**."

Additional SAB Members:

Vincent Chung, MD	Shubham Pant, MD	Jordan Berlin, MD
City of Hope	MD Anderson	Vanderbilt

The First 5 Arms Of Our Ongoing Phase 2a Study Seek To Expand Beyond Approved MEK Inhibitor Indications

INDICATION	TYPE	DISCOVERY	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	Bench-mark (ORR)	FDA Designations for IMM-1-104
Pancreatic	Combination	1L – 104 + mGem/nab-Pac					23%[a]	Orphan Drug Fast Track 1L Fast Track 2L
Pancreatic	Combination	1L – 104 + mFOLFIRINOX					32%[b]	
Pancreatic	Monotherapy	2L (or 1L)					3%[c]	
Melanoma (RAS^{mut})	Monotherapy	2L, 3L post-IO (or 1L)						Fast Track
NSCLC (RAS^{mut})	Monotherapy	2L, 3L						

75+ pancreatic cancer patients enrolled as of December 5th, 2024

[a]Phase III MPACT trial (link) [b]Phase III PRODIGE/ACCORD 11 trial (link) [c]Phase II QUILT-3.010 trial (link)

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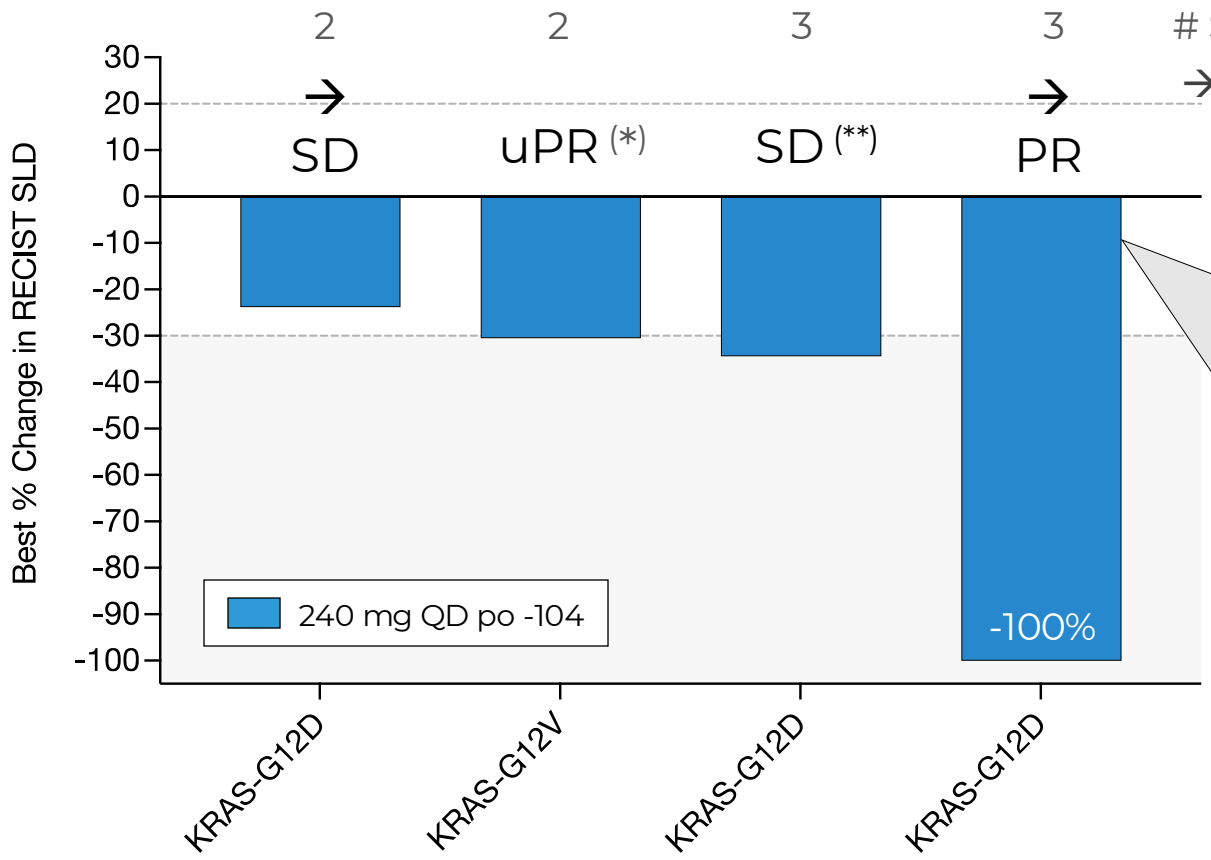
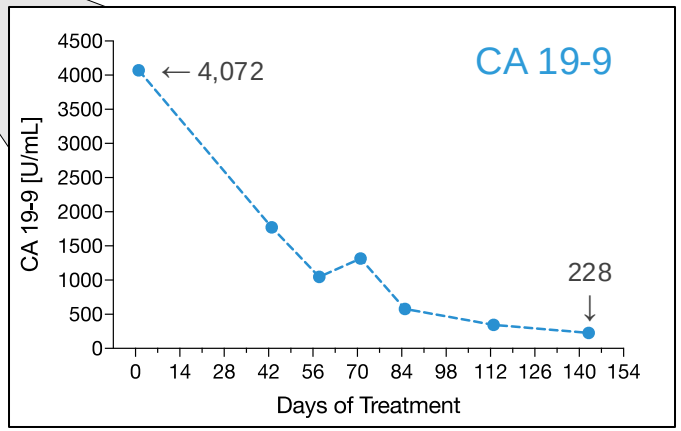
Encouraging Response To IMM-1-104 + Modified FOLFIRINOX For 1st Line Pancreatic Cancer, Including A -100% SLD Reduction



CA 19-9 = Biomarker of Pancreatic Cancer Tumor Burden and Survival



All Data as of December 5, 2024

Best Overall Response (BOR) to date shown

- Includes all evaluable patients who received their first dose of IMM-1-104 at least 14 weeks prior to data cutoff of December 5th, 2024 (to allow 2 potential scans beyond baseline scan – patients who had 2 such scans prior to 14 weeks were also included)
- Two patients with subsequently verified rare genomic variants (e.g., DPD, UGT1A1) that significantly impact ability to metabolize chemotherapy had their chemotherapy regimens dose reduced and are excluded in the analysis (both still achieved overall RECIST SLD regressions)
- (*) Patient withdrew prior to confirmatory scan or evidence of disease progression.
- (**) Patient's second scan was uPR; however, new mets observed in 3rd scan (Final BOR = SD)
- IMM-1-104 + modified FOLFIRINOX (mFFX) was observed to be generally well tolerated.

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The First 5 Arms Of Our Ongoing Phase 2a Study Seek To Expand Beyond Approved MEK Inhibitor Indications

INDICATION	TYPE	DISCOVERY	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	Bench-mark (ORR)	FDA Designations for IMM-1-104
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	Combination	1L – 104 + mFOLFIRINOX					32%[b]	
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75+ pancreatic cancer patients enrolled as of December 5th, 2024

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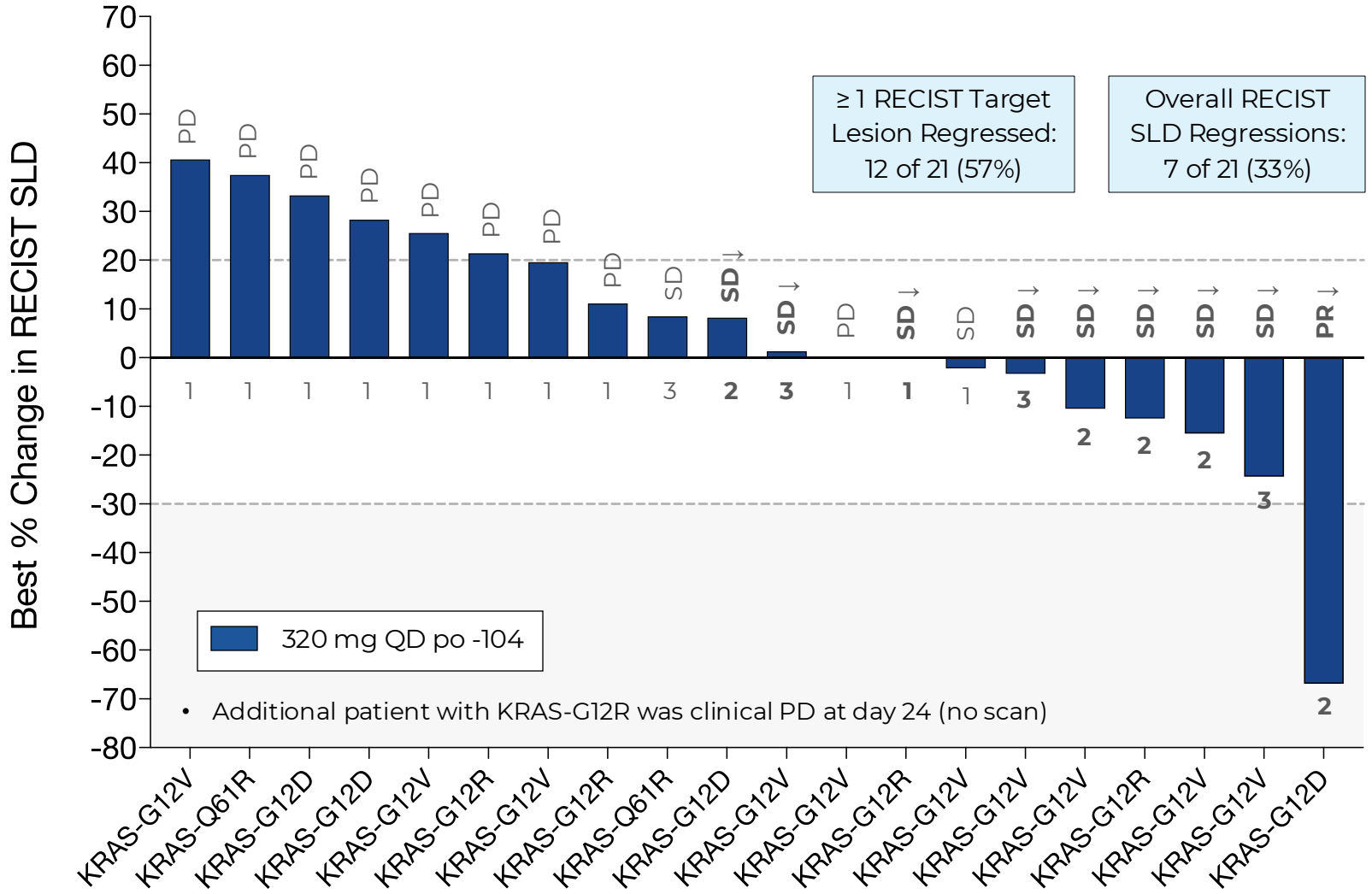
Encouraging Monotherapy IMM-1-104 Activity For 2nd Line Pancreatic Cancer Supports Observations In 1st Line Combinations



ORR:	**5**%

RECIST ORR:	
CR:	0
PR:	1
SD:	10
PD:	10

DCR:	**52**%

→ On Treatment (9/21) 43%

(BOR to date Shown)

scans shown below bars

All Data as of December 5, 2024

- ORR analyses included all evaluable patients who received their first dose of IMM-1-104 at least 14 weeks prior to data cutoff of December 5th, 2024 (to allow 2 potential scans beyond baseline scan – patients who had 2 such scans prior to 14 weeks were also included). Scans typically occur every 6 weeks (+/- 1 week)
- Glossary: ORR = overall response rate; CR = complete response; PD = progressive disease; PR = partial response; SD = Stable Disease; SLD = sum of longest tumor diameter; DCR = disease control rate (CR+PR+SD); BOR = best overall response

IMM-1-104 Monotherapy In 2nd Line Pancreatic Cancer Observed To Be Very Well Tolerated

We believe IMM-1-104 is highly suitable for monotherapy and combination therapy

Safety: Phase 2a Monotherapy in 2L PDAC at 320 mg QD (n = 21)

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*	5 (24%)	1 (5%)	0	0	6 (29%)
2. Diarrhea	3 (14%)	2 (10%)	0	0	5 (24%)
3. Fatigue	3 (14%)	1 (5%)	0	0	4 (19%)
4. Nausea/Vomiting	3 (14%)	0	0	0	3 (14%)
5. Blurred Vision	2 (10%)	1 (5%)	0	0	3 (14%)

- *All data as of December 5, 2024. TRAE = Treatment Related Adverse Event*
- *IMM-1-104 TRAE's above have been reversible; no TRAEs in the table above were deemed serious*
- *Patient population includes one 1L PDAC patient; all patients were dosed at 320 (N=21) mg QD p.o.*
- *(*) Preferred Terms Included in the Rash term include: Dermatitis acneiform, Photosensitivity reaction, Rash, Rash macular, Rash maculo-papular, Rash pruritic, Rash pustular*

Additional Phase 2a Combination Arms Planned

INDICATION	TYPE	DISCOVERY	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	Bench-mark (ORR)	FDA Designations for IMM-1-104
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	Combination	1L – 104 + mFOLFIRINOX					32%[b]	
	Monotherapy	2L (or 1L)					3%[c]	
Melanoma (RAS^{mut})	Monotherapy	2L, 3L post-IO (or 1L)						Fast Track
NSCLC (RAS^{mut})	Monotherapy	2L, 3L						
Melanoma	Combination	Planned → 104 + RAF inhibitor						
Melanoma & NSCLC	Combination	Planned → 104 + anti-PD-1						

Plus, inbound investigator-initiated trial requests under consideration

[a]Phase III MPACT trial (link) [b]Phase III PRODIGE/ACCORD 11 trial (link) [c]Phase II QUILT-3.010 trial (link)

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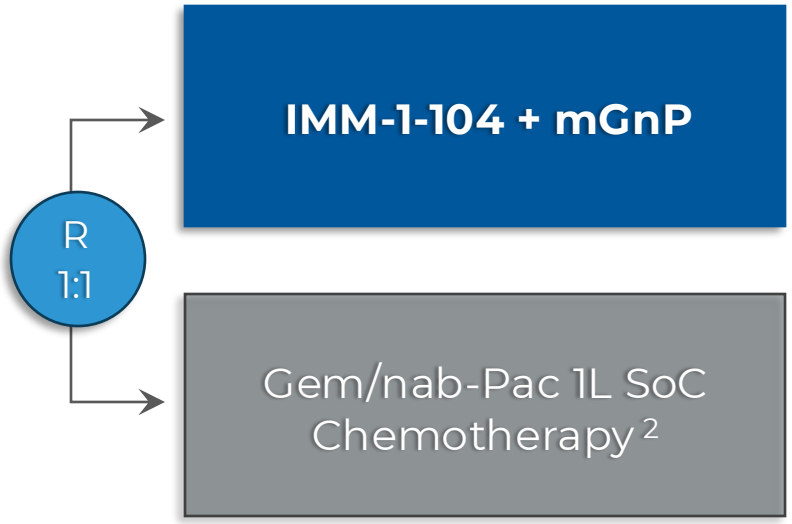
Potential Future Clinical Development Considerations

Prospective Global Randomized Phase 3 Trial Based on Trending Phase 2 Data[1]

Proposed Patient Population: First-line locally-advanced unresectable or metastatic Pancreatic Ductal Adenocarcinoma (PDAC)

- PDAC
- First-line setting
- Locally-advanced unresectable or metastatic
- ECOG PS 0-1



Primary Endpoints
PFS
OS
Secondary Endpoints
ORR
DCR
QoL

(1) Trial design and development path subject to change, including based on results of Phase 1/2a trial and regulatory authority feedback

(2) SOC chemotherapy options: full schedule Gemcitabine + nab-Paclitaxel. 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

“Is This The MEK Inhibitor We’ve Been Waiting For?” *- IMM-1-104 trial investigator*

Goal → Expand Indications

beyond BRAF, to RAS-driven cancers and more

- **43% ORR, 86% DCR observed for 104+mGnP in 1st line pancreatic cancer** (including a complete response)
- Responses observed for 104+mFFX in 1st line (-100% PR), 104 in 2nd line (-67% PR) pancreatic cancer
- Planning for 104+mGnP pivotal trial underway; additional Phase 2a combo arms planned for 2025

Goal → Improve Tolerability

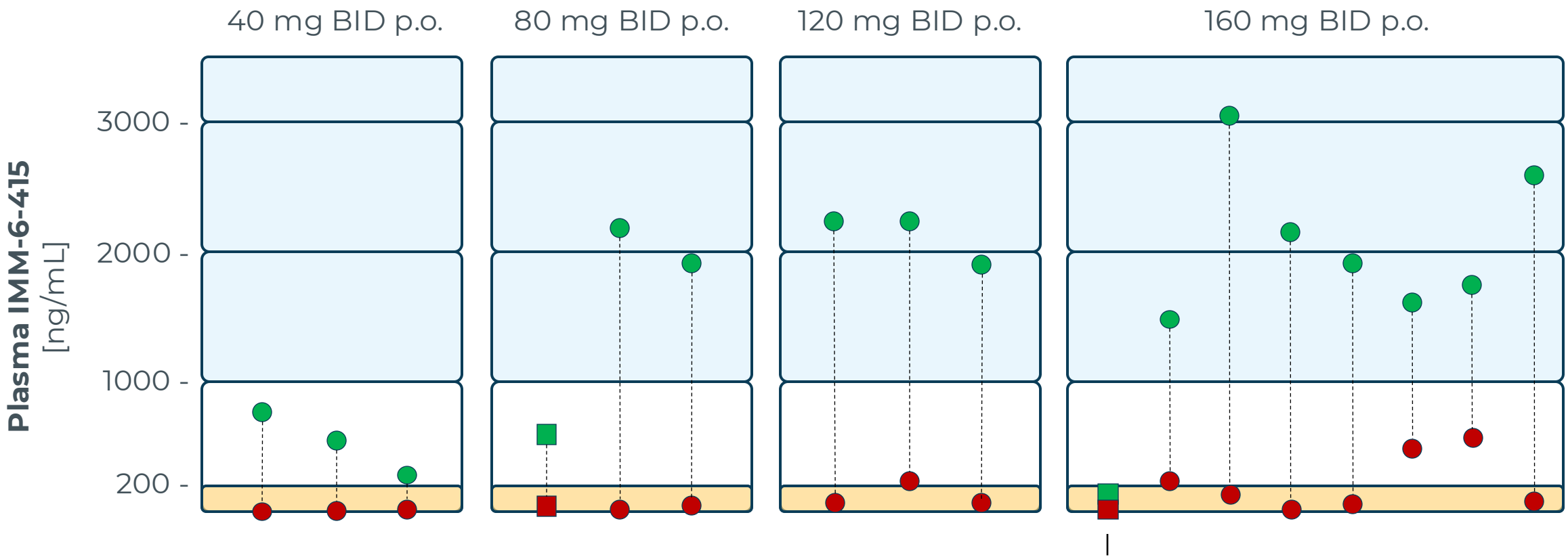
in existing and new indications

- **Observed highly differentiated tolerability in 96 patients treated with IMM-1-104 alone or in combination with mGnP**
- Broad potential of IMM-1-104 to enable new combinations, and replace existing MEK inhibitors in established combinations, for patients with tumors driven by BRAF, RAS, and beyond

Appendix

January 2025

IMM-6-415 Phase 1: Monotherapy PK/PD Summary



- C1D15/16 used when C1D1/2 was: below quantification limit (<1.00); not collected; or otherwise not available
- Maximum pERK inhibition = normalized to C1D1 pre-dose value (%)
- Currently in dose expansion at 120 mg BID po (N= 15 to 20 patients total)
- Cleared DLT (dose limiting toxicity) assessments at 40, 80, then 160 mg BID po (MTD not reached)
- PK = pharmacokinetics; PD = pharmacodynamics; BID p.o. = twice per day oral administration

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IMM-6-415 Phase 1: Monotherapy Safety/Tolerability Summary

Observed safety profile suggests that IMM-6-415 is well-tolerated and we believe highly suitable for monotherapy and combination therapy

Safety Summary: Phase 1 Monotherapy at 40, 80, 120, 160 mg BID p.o. (n = 22)

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*	5 (23%)	0	0	0	5 (23%)
2. Peripheral Edema	3 (14%)	0	0	0	3 (14%)

- *All data as of December 23, 2024. TRAE = Treatment Related Adverse Event*
- *IMM-6-415 TRAE's have been reversible; no reported TRAEs deemed serious*
- *Patient population includes diverse tumor types; patients dosed at 40 (N=3), 80 (N=3), 120 (N=8) 160 (N=8) mg BID p.o.*
- *(*) Preferred Terms Included in the Rash term include: Dermatitis acneiform, Photosensitivity reaction, Rash, Rash macular, Rash maculo-papular, Rash pruritic, Rash pustular*

EDC Snapshot as of 23DEC2024

Promising IMM-1-104 Monotherapy Durability: Ph-1 in 3L PDAC

Patient with longest Phase 1 monotherapy treatment to date (>11 months)

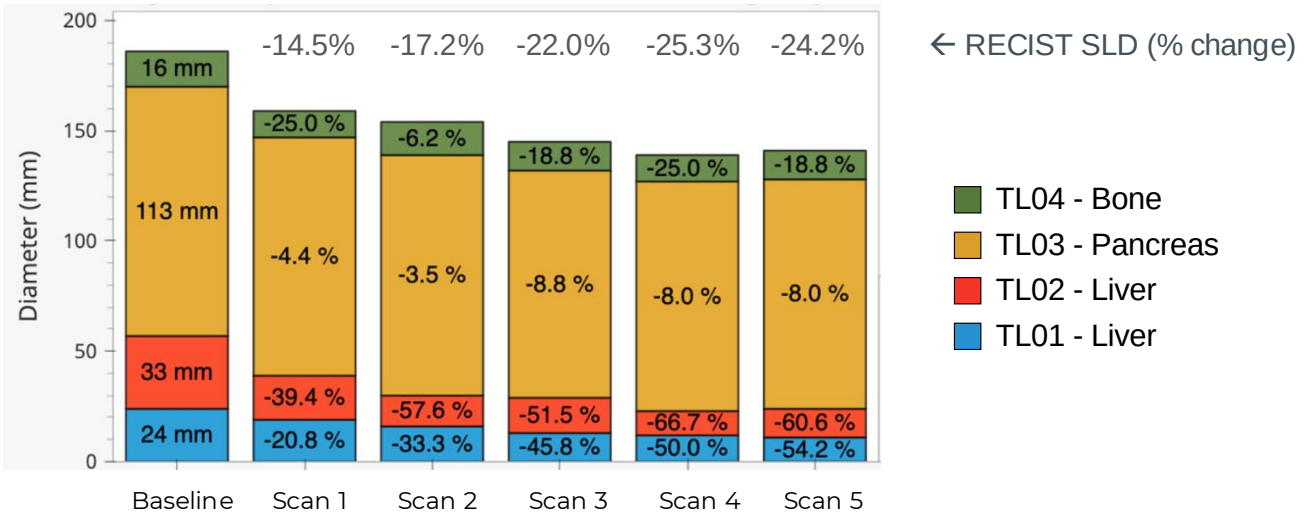
IMM-1-104 monotherapy

3L PDAC $KRAS^{G12D}$

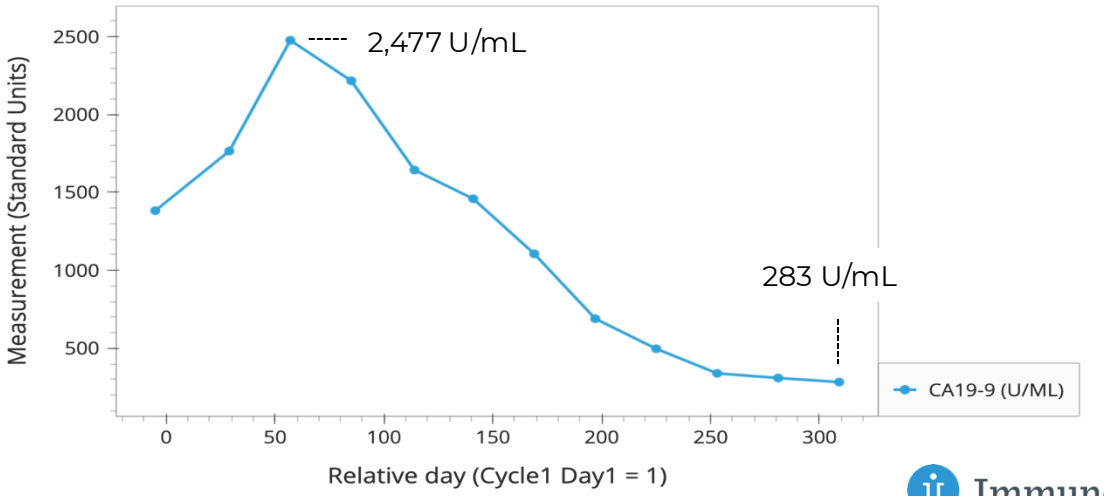
- Metastatic Pancreatic Cancer (PDAC)
- 70-year-old Caucasian male
  - 1st Line: FOLFIRINOX (**BOR = PD**)
  - 2nd Line: Gem/Cis/nab-Pac (**BOR = PD**)
- **3rd Line: 240 mg QD p.o. IMM-1-104**
  - IMM-1-104 BOR = Stable Disease (SD)
  - >11 months on IMM-1-104 (remains on treatment)
  - Reduction in $KRAS^{G12D}$ ctDNA[1]
  - 89% reduction in peak CA 19-9 levels
  - Improved QoL[1] and weight gain (+12%)

[1] *Update on patient '4' from 2024 ESMO (Chung, et al.); January 6th, 2025*

RECIST Lesions



CA 19-9



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- Nasdaq: IMRX