

Investor Presentation



Nasdaq: IMRX

October 2024

A black and white photograph of two women sitting at a table and talking. The woman on the left has curly hair and is smiling. The woman on the right has short, light-colored hair and is wearing glasses. They appear to be in a professional or educational setting.

Building a
Universal-RAS/RAF
Franchise

FORWARD-LOOKING STATEMENTS AND OTHER DISCLAIMERS

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 IMM-1-104 and IMM-6-415; the design, enrollment criteria and conduct of the Phase 1/2a clinical trials for IMM-1-104 and IMM-6-415; initial signs of clinical activity of IMM-1-104; the translation of preclinical data into human clinical data; the ability of initial clinical data to de-risk IMM-1-104 and / or IMM-6-415 and be confirmed as the trials progress, including the safety, tolerability, pharmacokinetics, pharmacodynamics and potential efficacy of IMM-1-104 and / or IMM-6-415; the potential advantages and effectiveness of the company's clinical and preclinical candidates; the timing of additional trial updates; the Company's recommended IMM-1-104 phase 2 dose; the indications to be pursued by the Company in the Phase 2a portions of the trials and timing to results; the filing with, and approval by, regulatory authorities of our product candidates; 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 longstanding goal of creating better medicines for cancer patients; the Company's cash needs and availability, including our projected cash runway and current operating plans; and the plans and objectives of management for future operations.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, without limitation: our limited operating history; our history of operating losses; our ability to raise the substantial additional capital that will be required to finance our operations; the difficulty of obtaining regulatory approval for any of our current or future product candidates; our ability to submit an Investigational New Drug application ("IND"), or IND amendments or comparable documents in foreign jurisdictions in order to commence clinical trials on the timelines we expect; our limited experience in designing and conducting clinical trials; the timing of the initiation, progress and potential results of our ongoing and planned preclinical studies and clinical trials and our research programs, including our Phase 1/2a clinical trials; our ability to successfully complete our Phase 1/2a clinical trials, or any planned or future clinical trials and for those trials to produce positive results; the risk of substantial delays in completing, if at all, the development and commercialization of our current or future product candidates; risks related to adverse events, toxicities or other undesirable side effects caused by our current or future product candidates; the risk of delays or difficulties in the enrollment and/or maintenance of patients in clinical trials; our substantial reliance on the successful development of our current and future product candidates, as well as our platform, including our proprietary technologies such as DCT and Fluency; risks related to competition in our industry; the market opportunity for our product candidates, if approved; risks related to manufacturing; risks related to our reliance on third parties; risks related to our intellectual property; and risks related to ongoing and / or future pandemics.

These and other important factors discussed under the caption "Risk Factors" in the Company's Annual Report on Form 10-Q for the six months ended June 30, 2024 filed with the SEC and its other reports filed with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management's estimates as of the date of this presentation. While the Company may elect to update such forward-looking statements at some point in the future, other than as required by law it disclaims any obligation to do so, even if subsequent events cause its views to change. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this presentation.

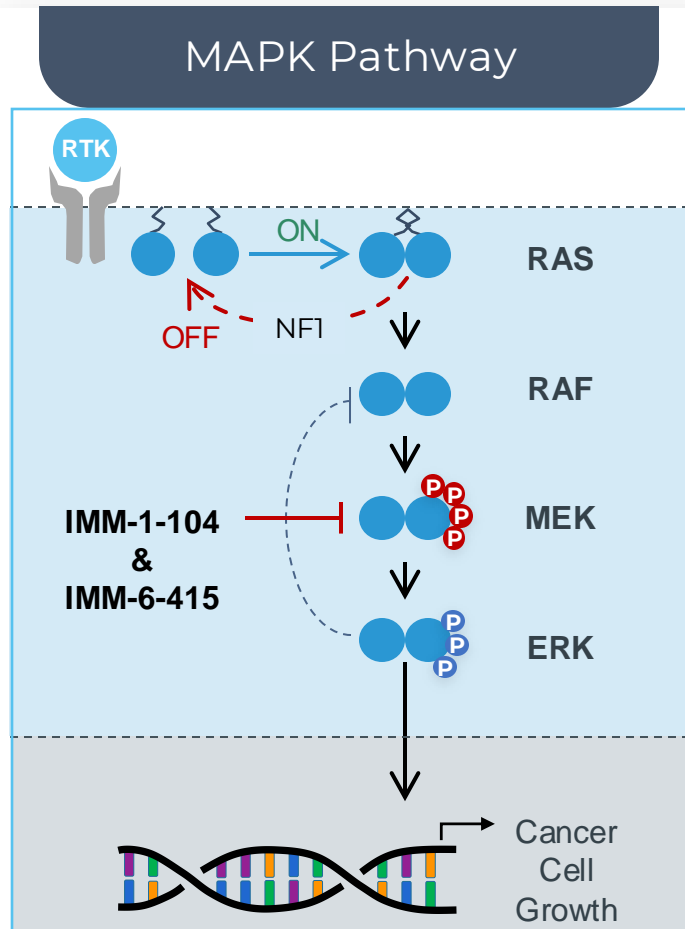
This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. Neither we nor our affiliates, advisors or representatives makes any representation as to the accuracy or completeness of that data or undertake to update such data after the date of this presentation.

Data of trametinib, cobimetinib, binimetinib, selumetinib, encorafenib, AMG-510 (now known as sotorasib) and / or other therapeutic agents as compared to IMM-1-104 presented in this presentation is based on head-to-head studies where these therapies have been purchased from commercial sources rather than the pharmaceutical company commercializing or developing, as applicable, the compound.



Immuneering Mission:

Help Many Cancer Patients Live Longer and Feel Better



✓ 200,000+ cancer patients are estimated to have RAS or RAF driven tumors.

✓ RAS, RAF, and MEK inhibitors have historically faced tolerability issues, and eventually stop working when patients develop resistance. Our uniquely designed MEK inhibitors aim to do better.

✓ In Phase 1, our lead candidate IMM-1-104 showed excellent tolerability, fewer resistance mutations, and clear activity in pancreatic cancer, a huge unmet need.

✓ Phase 2a tests IMM-1-104 alone and in combination, in 1st line pancreatic cancer and other settings.

IMM-1-104 Phase 2a



Immuneering



IMM-1-104 Clinical Development

INDICATION	TYPE	DISCOVERY	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	~ N (patients)
	Combination	1L – 104 + mGem/nab-Pac					30
Pancreatic	Combination	1L – 104 + mFOLFIRINOX					30
	Monotherapy	2L (or 1L)					30
Melanoma (RAS ^{mut})	Monotherapy	2L, 3L post-IO (or 1L)					30
NSCLC (RAS ^{mut})	Monotherapy	2L, 3L					30

Unresectable/Metastatic PDAC: Key 1L Clinical Benchmarks

Trial	Treatment	Line of Treatment	PS	OS (months)	ORR	PFS (months)	CR (%)	PR (%)	SD (%)
^a Phase III MPACT	Gemcitabine	1 st Line	0-1	6.7	7%	3.7	0	7.2	28.4
^a Phase III MPACT	nab-Paclitaxel + Gemcitabine	1 st Line	0-1	8.5	23%	5.5	0.2	22.7	27.4
^b Phase III PRODIGE/ACCORD 11	FOLFIRINOX	1 st Line	0-1	11.1	32%	6.4	0.6	31.0	38.6
^c Phase III NAPOLI-3	NALIRIFOX	1 st Line	0-1	11.1	42%	7.4	0.6	41.5	25.8
^d Modified (m) Gem/nab-Pac	(m) nab-Paclitaxel + Gemcitabine	1 st Line	0-1	10	18.6%	5.4	NR	NR	NR

NR = Not Reported

^a Phase III MPACT trial ([link](#))

^b Phase III PRODIGE/ACCORD 11 trial ([link](#))

^c Phase III NAPOLI-3 trial ([link](#))

^d Retrospective analysis – modified (m) Gem/nab-Pac 1L PDAC ([link](#))

Initial Results from Phase 2a Arm Evaluating IMM-1-104 with Modified Gemcitabine/ nab-Paclitaxel in First Line Pancreatic Cancer as of September 12, 2024

Patient	MAPK Mutation Variant	Dose (p.o.) Level for IMM-1-104	% Change in SLD 1 st Scan	% Change in SLD 2 nd Scan	% Change in SLD 3 rd Scan	% Change in SLD 4 th Scan	% Change SLD 5 th Scan	ORR/ RECIST
1	GNAS-T105Vfs*3 (*)	240mg QD	-100%	-100%	-100%	-100%	<i>next scan</i>	CR
2	KRAS-G12V*	240mg QD	-8%	-10%	-40%	<i>next scan</i>		uPR^o
3	KRAS-G12V*	240mg QD	-4%	<i>next scan</i>				SD
4	Unk.#	240mg QD	+6%	<i>next scan</i>				SD
5	KRAS-G12R*	240mg QD	-9%	<i>next scan</i>				eqPD**
Initial Overall Response Rate (ORR):			40%					
Initial Disease Control Rate (DCR):			80%					

IMM-1-104 has been well-tolerated to-date in combination with modified gemcitabine/nab-paclitaxel

SLD = sum of longest diameters

* Detected in prior genetic test

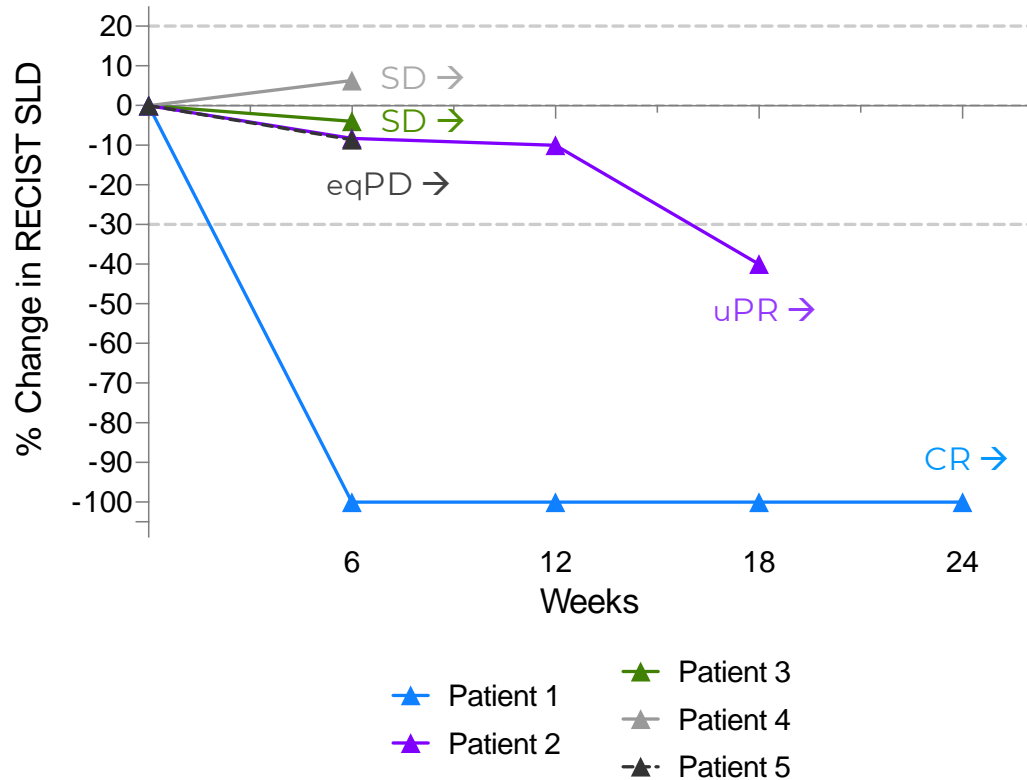
Unknown (Unk.); MAPK pathway variant not detected in plasma cfDNA or prior genomic test

^o Partial response result classified as "unconfirmed" pending subsequent scan

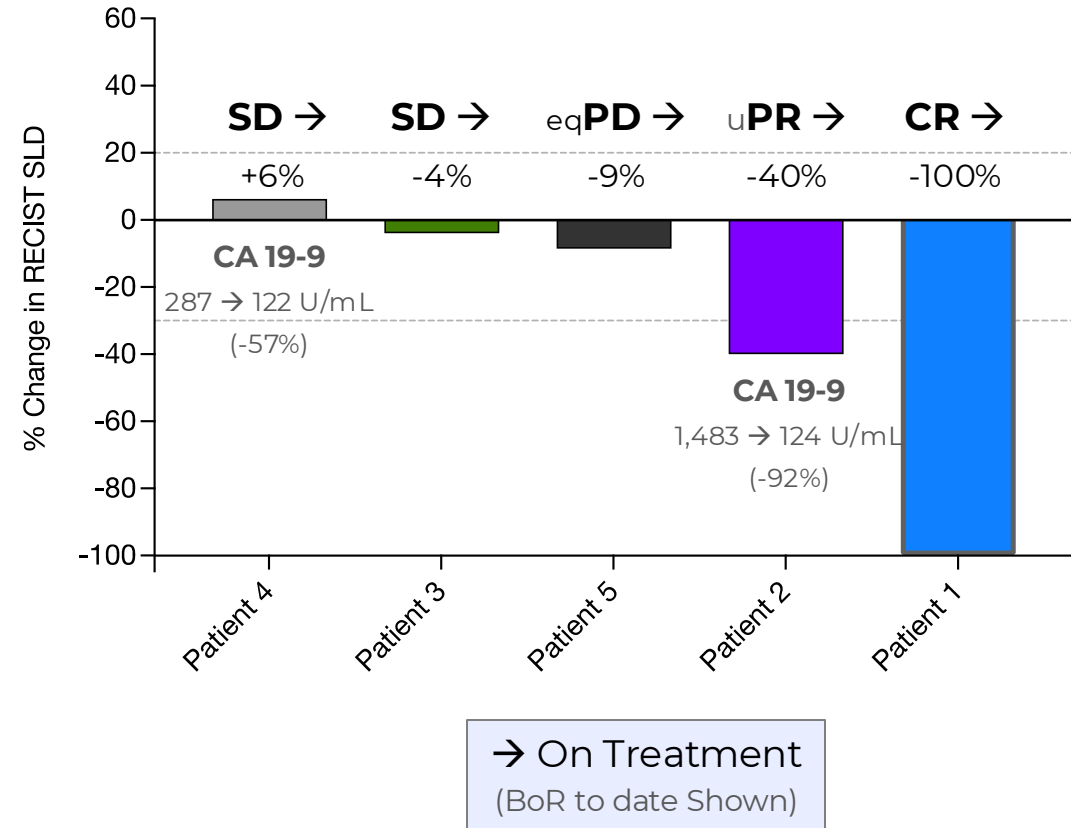
**Equivocal (eq); Patient not dosed for over two weeks during hospitalization for a preexisting condition. Scans showed ascites and a pleural effusion categorized by radiology as equivocal new lesions per RECIST 1.1. The investigator determined these to be related to the recent placement of a hepatic stent, not disease progression. The patient is improving and remains on therapy.

Promising Early Clinical Activity: Phase 2a 1L PDAC (104+mGnP)

Spider Plot (Arm B: 104 + mGnP)



Waterfall Plot (Arm B: 104 + mGnP)



- IMM-1-104 + modified Gemcitabine/nab-Paclitaxel (mGnP) combination is well-tolerated (5 evaluable patients at first dose level)
- All 5 patients at 240 mg IMM-1-104 QD p.o. + nab-Pac (125 mg/m² i.v.) and Gem (1,000 mg/m² i.v.) on days 1, 15 of every 28-day cycle
- Multiple patients now enrolled (not yet to first scan) at 320 mg IMM-1-104 + mGnP

Phase 2a Initial Data Summary

- Goal of this Phase 2a trial is to evaluate IMM-1-104 in a variety of potential indications
- Early and encouraging data in 1L pancreatic cancer patients - a population with significant unmet need
- Results achieved at the IMM-1-104 lead-in dose of 240 mg
- If these early results continue, we believe there is a clear path forward for development of IMM-1-104 in 1L pancreatic cancer
- We look forward to providing additional updates

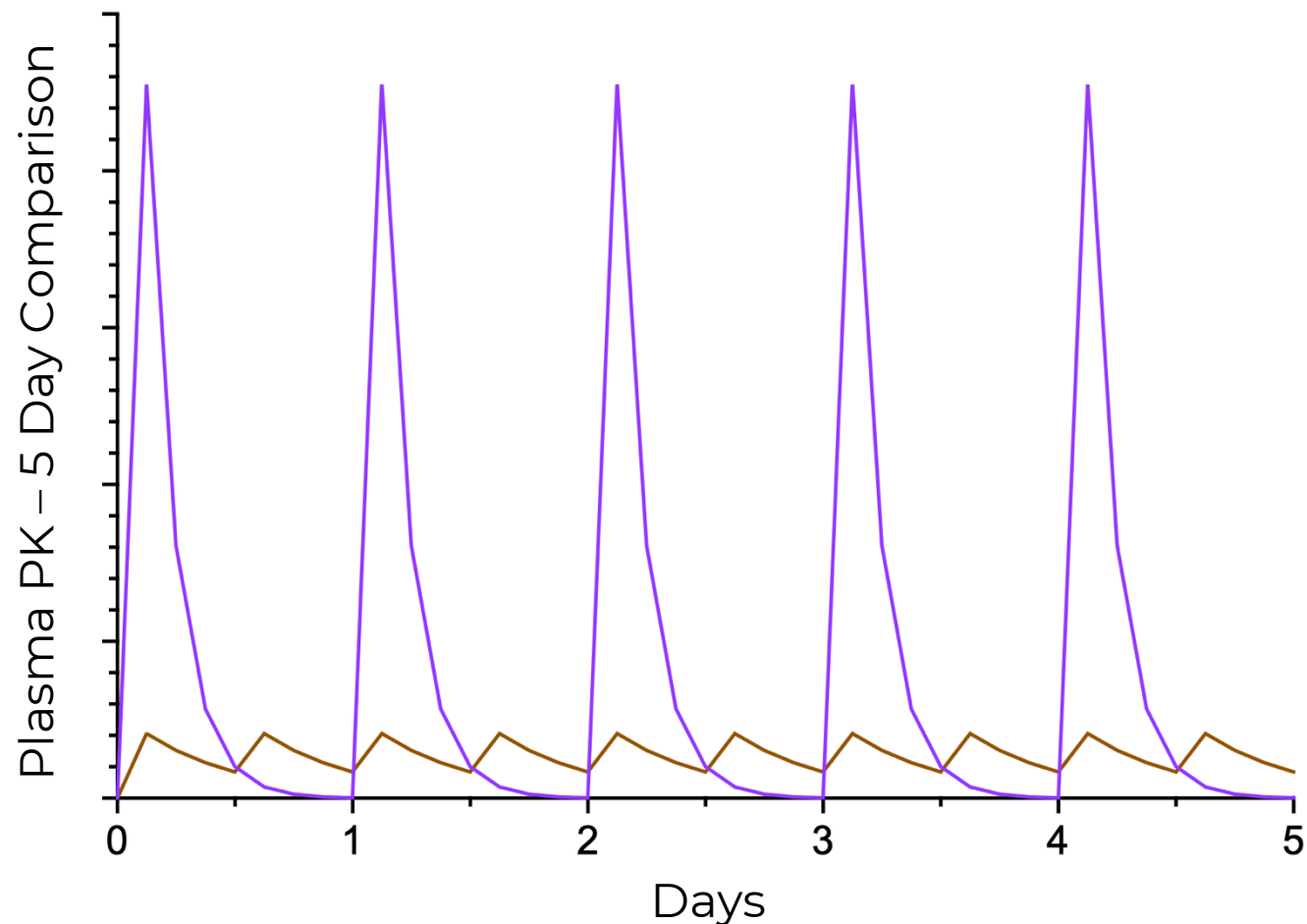
IMM-1-104 Phase 1



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IMM-1-104's Deep Cyclic Inhibition of MEK is designed to improve tolerability and broaden activity vs. chronic inhibition of MEK



Conceptual illustration of deep cyclic inhibition (purple) vs. chronic inhibition (brown)

Dramatic PK C_{MAX} Pulse

GOAL: Achieve many fold higher drug free fraction C_{MAX} to **break tumor addiction**

Near-Zero Drug Trough

GOAL: Short plasma half-life to improve tolerability and limit adaptive resistance, so **every day is a drug holiday**

MoA Target Engagement

GOAL: Prevent MAPK-pathway bypass events, for **expanded activity into RAS mutant setting**

IMM-1-104 Phase 1 Overview

Objectives & Endpoints:

Primary

Safety (Adverse Events)

Tolerability (Dose Limiting Toxicities)

Recommendation for Phase 2 Dose (RP2D)

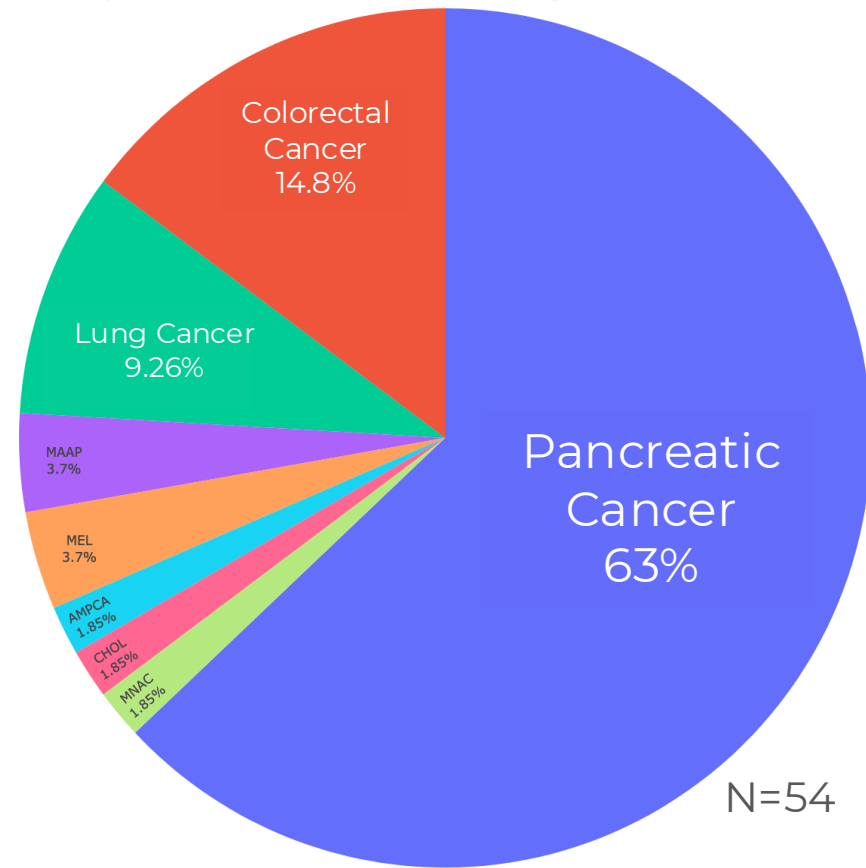
Secondary

Pharmacokinetics (PK)

Exploratory Objectives:

Pharmacodynamic (PD) & blood-based biomarkers, initial activity...

Key Patient Demographics:



• EDC snapshot as of August 19, 2024: 54 patients total, including 34 PDAC, 8 colorectal, 5 lung, 2 melanoma, 2 appendiceal, 1 cholangiocarcinoma plus 2 others.

Source: ESMO 2024

IMM-1-104 Phase 1: Summary of Treatment-Related Adverse Events

Topline Phase 1 Safety (N = 54)

TOTAL TREATED PATIENTS (N=54)		Patients at 240 (N=19) or 320 mg (N=30) QD p.o.*			
Maximum Severity of TRAE's	Grade 1	Grade 2	Grade 3 **	Grade 4	Any Grade
TRAE's occurring in ≥10% of patients n (%)					
Rash ***	8 (15)	5 (9)	1 (2)	0 (0)	14 (26)
Diarrhea	9 (17)	3 (6)	0 (0)	0 (0)	12 (22)
Nausea	8 (15)	1 (2)	0 (0)	0 (0)	9 (17)
Fatigue	6 (11)	3 (6)	0 (0)	0 (0)	9 (17)
Vomiting	6 (11)	2 (4)	0 (0)	0 (0)	8 (15)
Subretinal fluid	7 (13)	0 (0)	0 (0)	0 (0)	7 (13)
Retinopathy	3 (6)	3 (6)	0 (0)	0 (0)	6 (11)

*54 treated patients also included 1 patient treated at 40 mg QD p.o., 1 patient treated at 80 mg QD p.o. and 3 patients treated at 160 mg QD p.o.

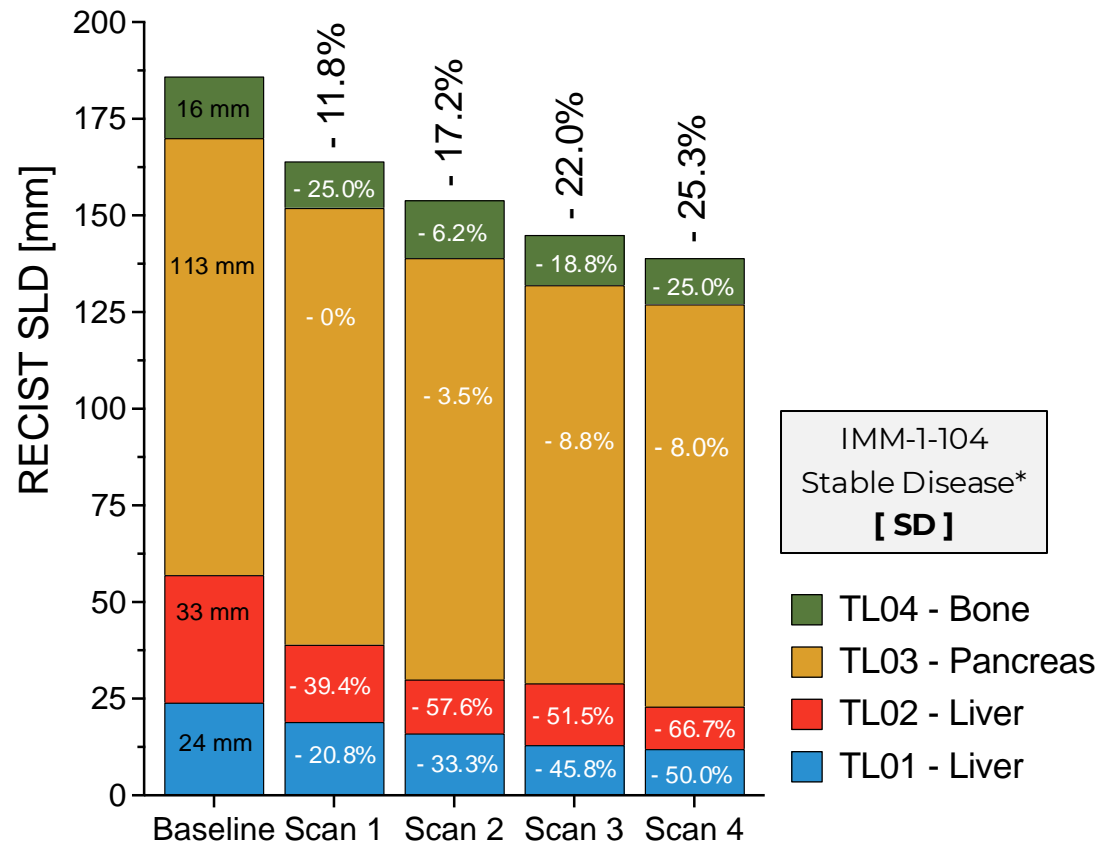
**All treatment-related adverse events (TRAE's), regardless of occurrence frequency or grade, were reversible and deemed non-serious

***Preferred Terms Included in the Rash term include Dermatitis acneiform, Photosensitivity reaction, Rash, Rash macular, Rash maculo-papular, Rash pruritic, Rash pustular

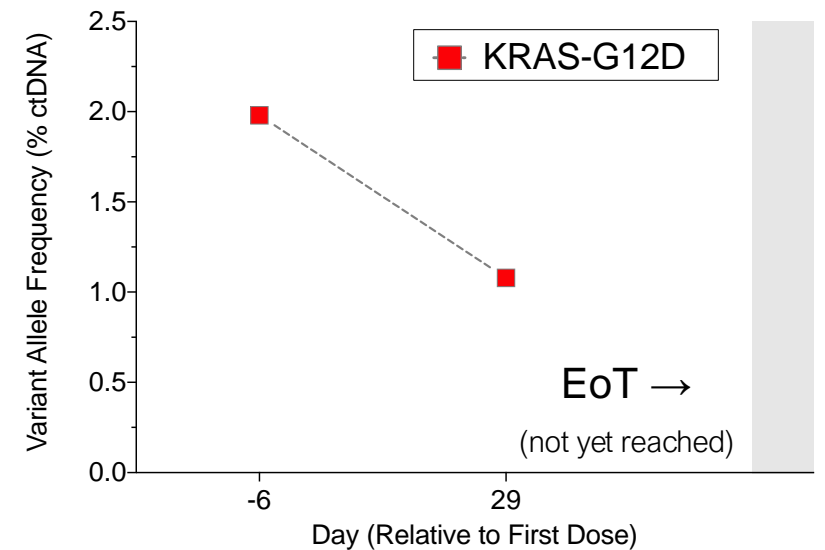
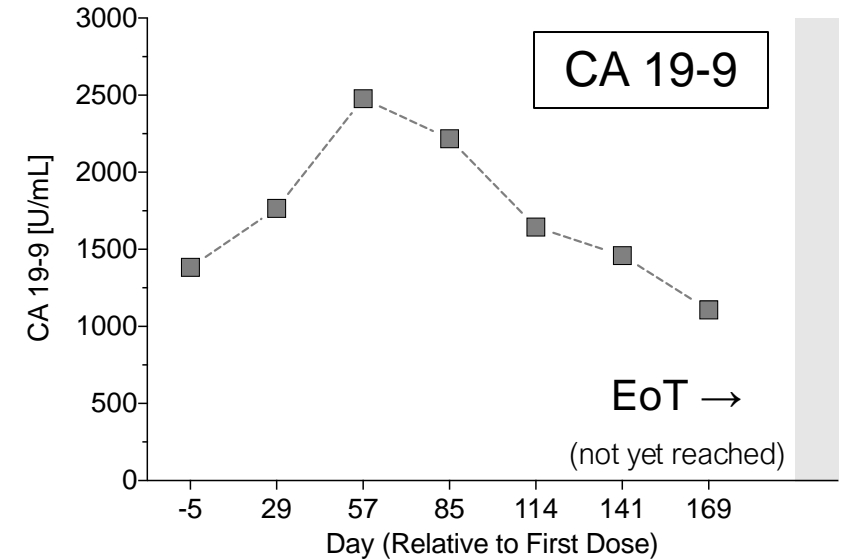
Source: ESMO 2024

Phase 1 Data – Highlighted Case Study (Patient 4)

- Patient 4: **KRAS^{G12D} PDAC**
- Metastatic Pancreatic Cancer (adeno)
- 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 (on study) = ***Stable Disease**
- Improved QoL² and weight gain (+7%)

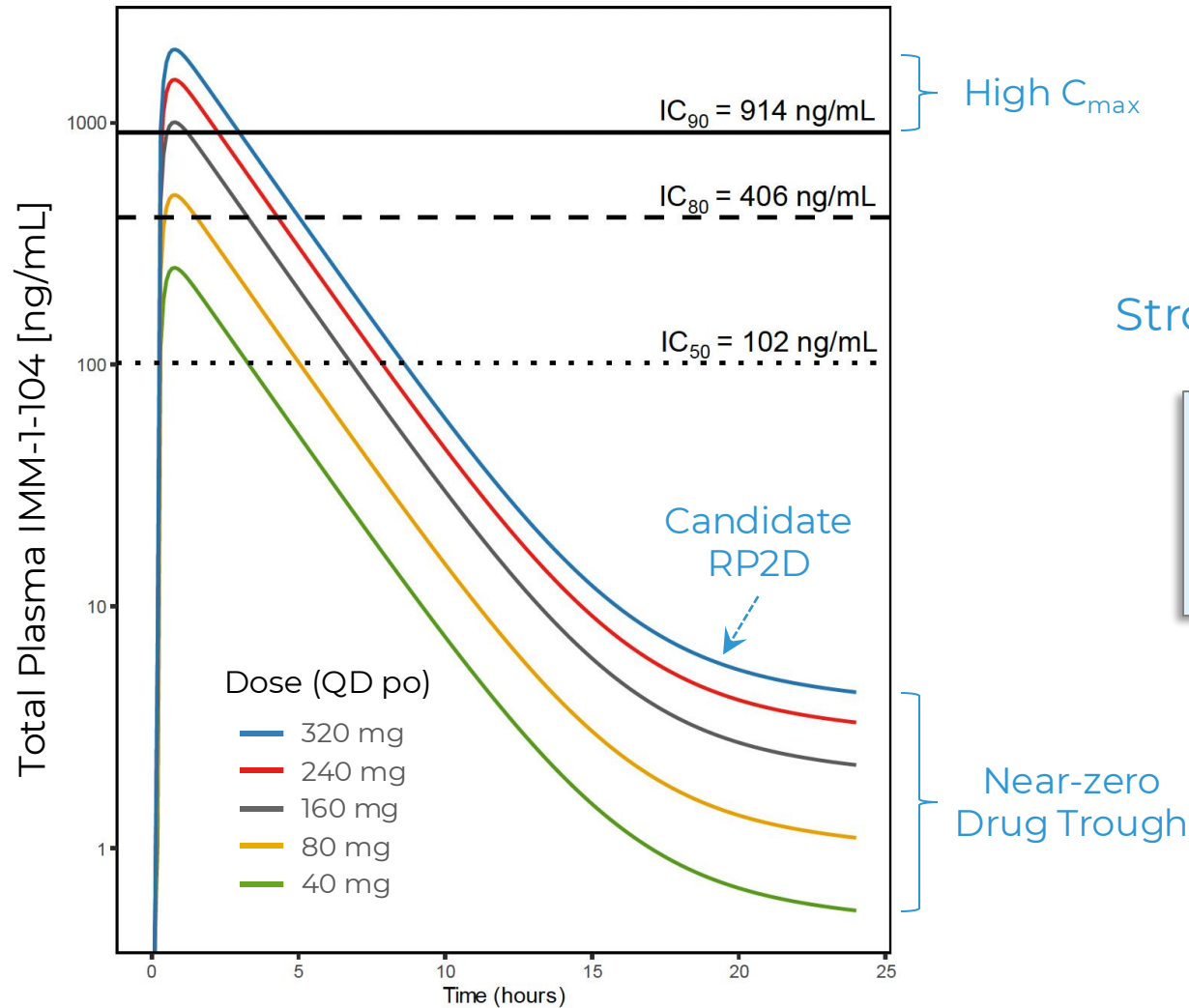


* On Treatment > 6 months



IMM-1-104 Inhibited the MAPK Pathway at pERK > 90%

Topline PK/PD Data for IMM-1-104



Deep Cyclic Inhibition (DCI) Profile
Strongest for 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

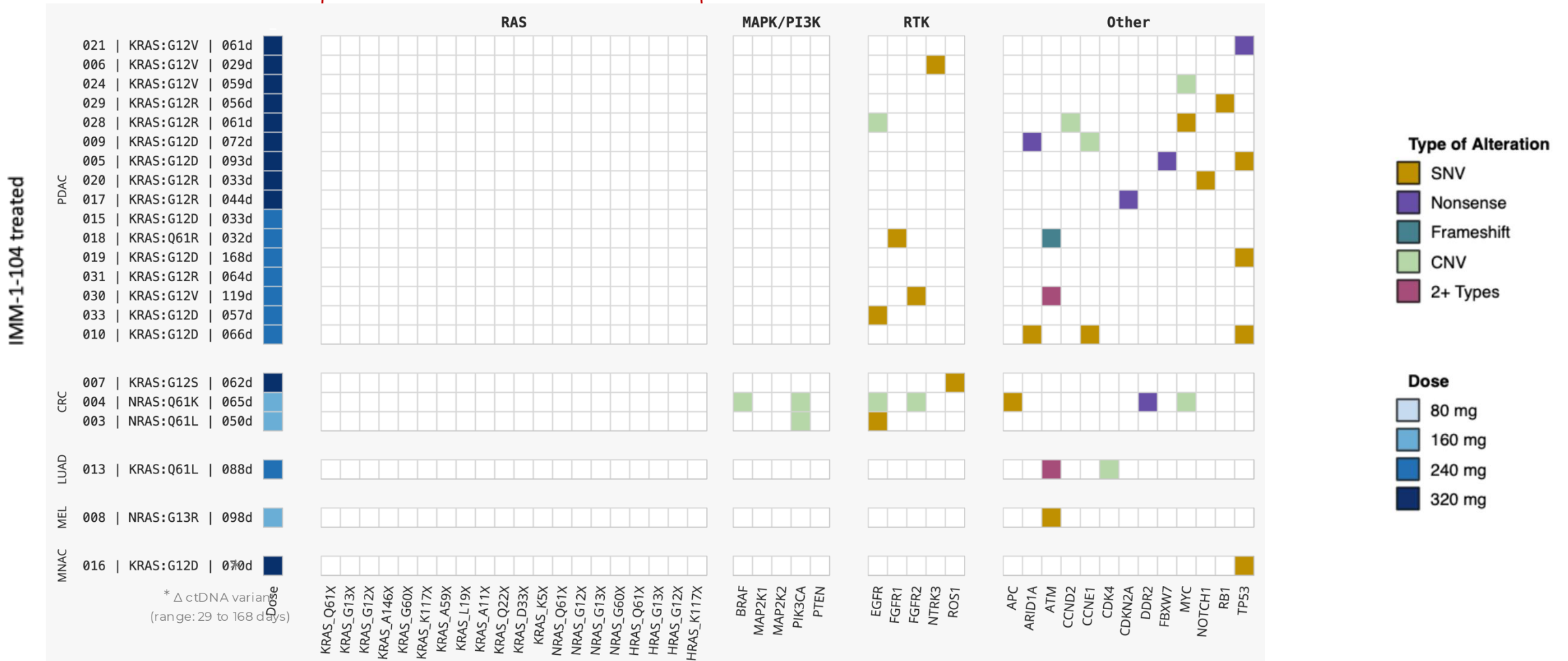
Modeled typical profiles based on 19 patients of IMM-1-104 plasma concentrations (ng/mL) versus time (h) on a semilogarithmic scale for different dose groups. Direct measure of time above PD IC_{90} does not consider k_{off} PD shadow. Approximately dose linear from 40 to 320 mg PO QD; no drug accumulation. Tight relationship observed between plasma concentrations and phosphorylated ERK (p-ERK) to total ERK (t-ERK) ratios; Longer time above pMEK IC_{90} at 320 mg (4.0 hr) vs. 240 mg (3.3 hr)

IMM-1-104 Demonstrates No Acquired Alterations in RAS

Means fewer resistance mutations

IMM-1-104 Phase 1 Clinical Data

Acquired Alterations: **No new RAS alterations observed**



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

Emergent IMM-1-104 Monotherapy and Combinations

Monotherapy

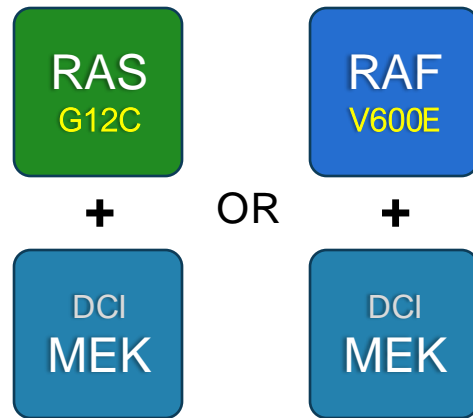
Pulsatile
MAPK Pathway
Inhibition



Ideal: In patients with broad MAPK pathway addiction

Vertical Combinations

Selective
Vertical Drug
Combinations



Goal: Greater Depth & Durability of Response

Immune Modifying Combinations

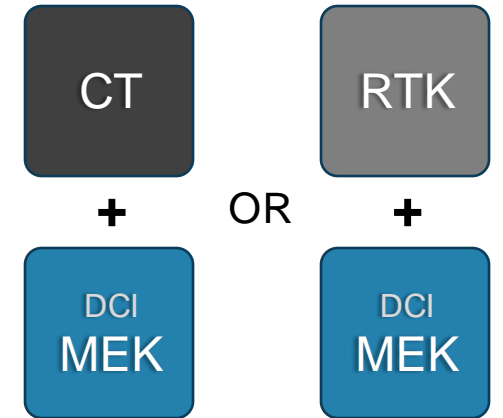
Dual-targeting of
Tumor & Immune
System



Goal: Break MAPK Addiction; Enhance Antitumor Immunity

Orthogonal MoA Combinations

Non-overlapping
Mechanism of Action
Combinations



Goal: Expand & Improve Overall Antitumor Response

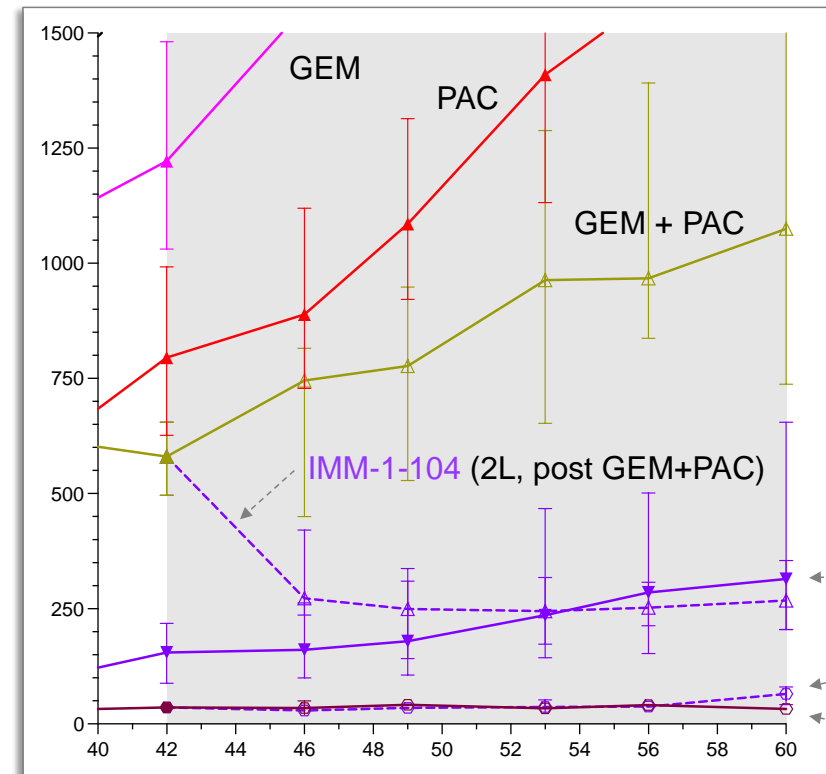
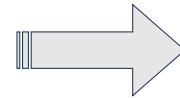
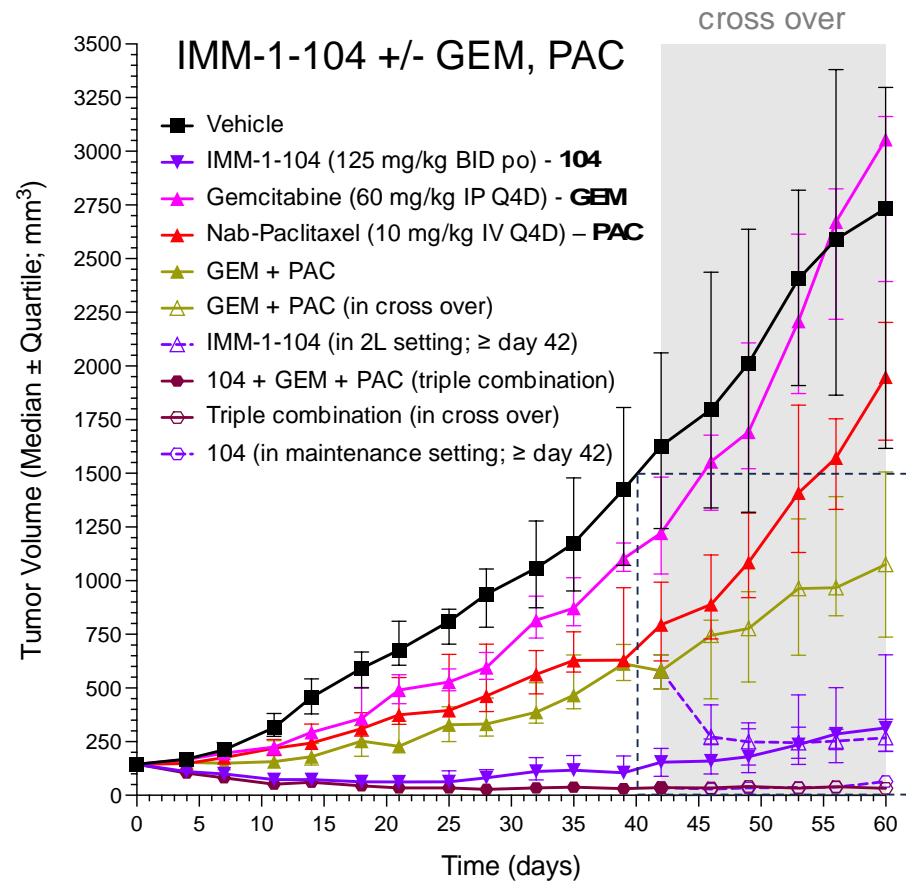
IMM-1-104 combinations yielded deeper and more durable activity than either gemcitabine or paclitaxel alone

Currently evaluating IMM-104 + modified gemcitabine plus nab-paclitaxel in Phase 2a pancreatic cancer

IMM-1-104 +/- chemotherapy in MIA PaCa-2 pancreatic xenograft model

MIA PaCa-2 Tumor Xenograft

Magnified Inset (days 40 to 60)



IMM-6-415



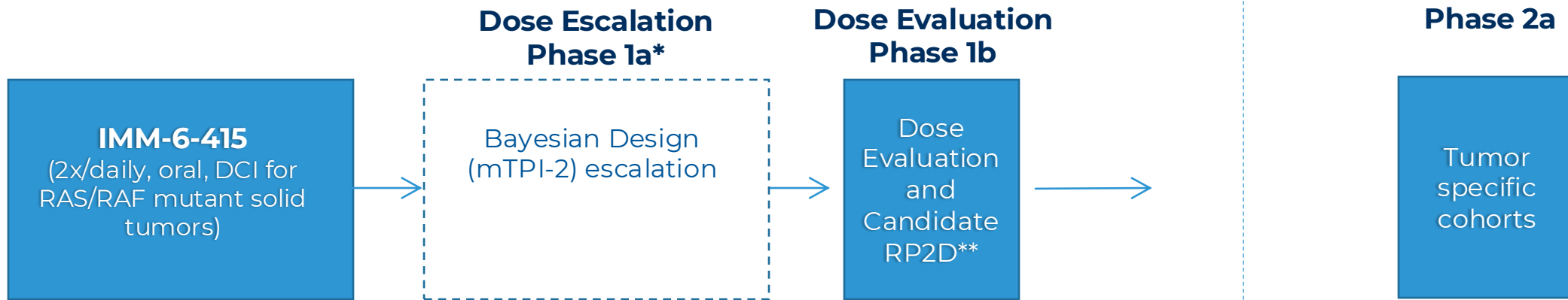
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IMM-6-415: Phase 1/2 Clinical Trial Plan

First Time in Humans

Phase 1: Dose Escalation & Evaluation



First patient dosed
March 2024

Phase 1 endpoints: safety, tolerability, PK & PD

* Solid tumor, all comer with evidence of RAF, KRAS, NRAS or HRAS mutation.

**RP2D = Recommended Phase 2 Dose

IMM-6-415: Monotherapy Activity in RAF and RAS Mutant Tumors

NRAS^{Q61R}
MEL

BRAF^{V600E}
MEL

BRAF^{V600E}
MEL

SK-MEL-2

A-375

SK-MEL-28

KRAS^{G12S}
NSCLC

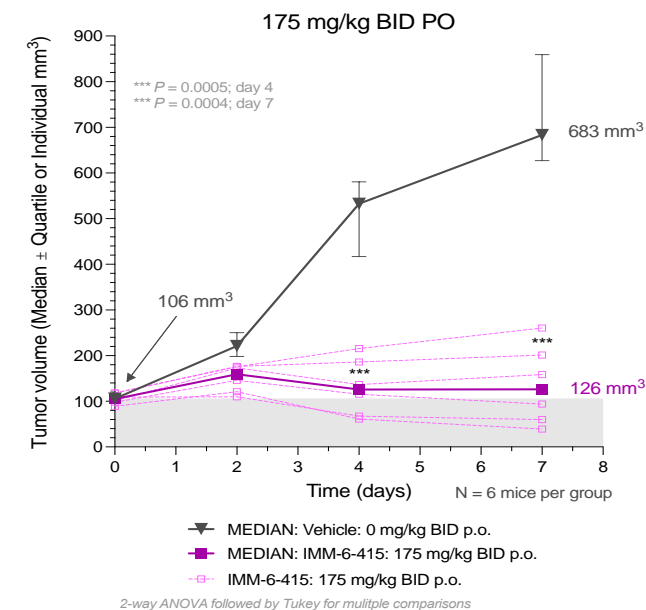
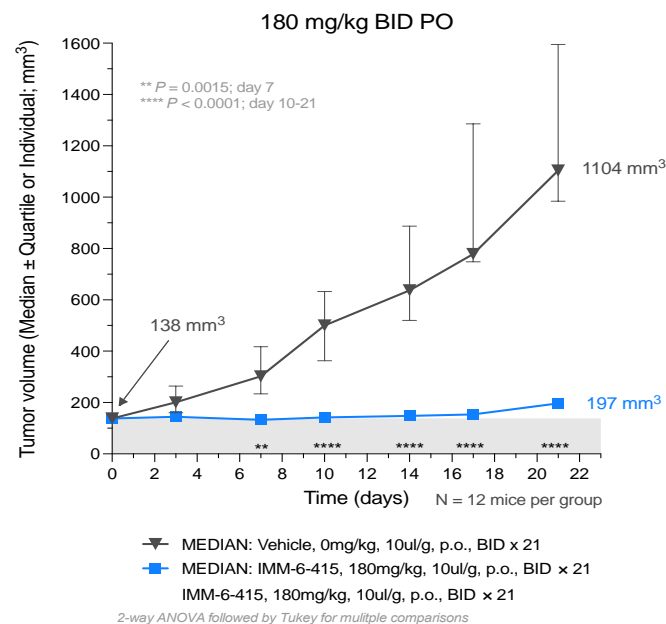
A-549

KRAS^{G12D}
CRC

Colon-26

Model	HRAS	NRAS	BRAF	NF1	3D-TGA
SK-MEL-2		p.Q61R			
MM127		p.G13R	p.G464E		n.t.
MM415		p.Q61L			n.t.
MEL-JUSO	p.G13D	p.Q61L			n.t.
SK-MEL-30		p.Q61K			n.t.
Hs852T		p.G12V			n.t.
MeWo				LoF	n.t.
A375			p.V600E		
SK-MEL-28			p.V600E		

3D-Tumor Growth Assay (3D-TGA) sensitivity (green)



Well Tolerated up to Maximum Monotherapy Effective Dose Range of 150 to 180 mg/kg

SITC 2022 Presentation: Maximum Effective Dose Range in Mice (plasma $t_{1/2}$ = 0.3 to 0.4 hours): 150-180 mg/kg BID

CRC = colorectal cancer; NSCLC = non-small cell lung cancer; MEL = melanoma

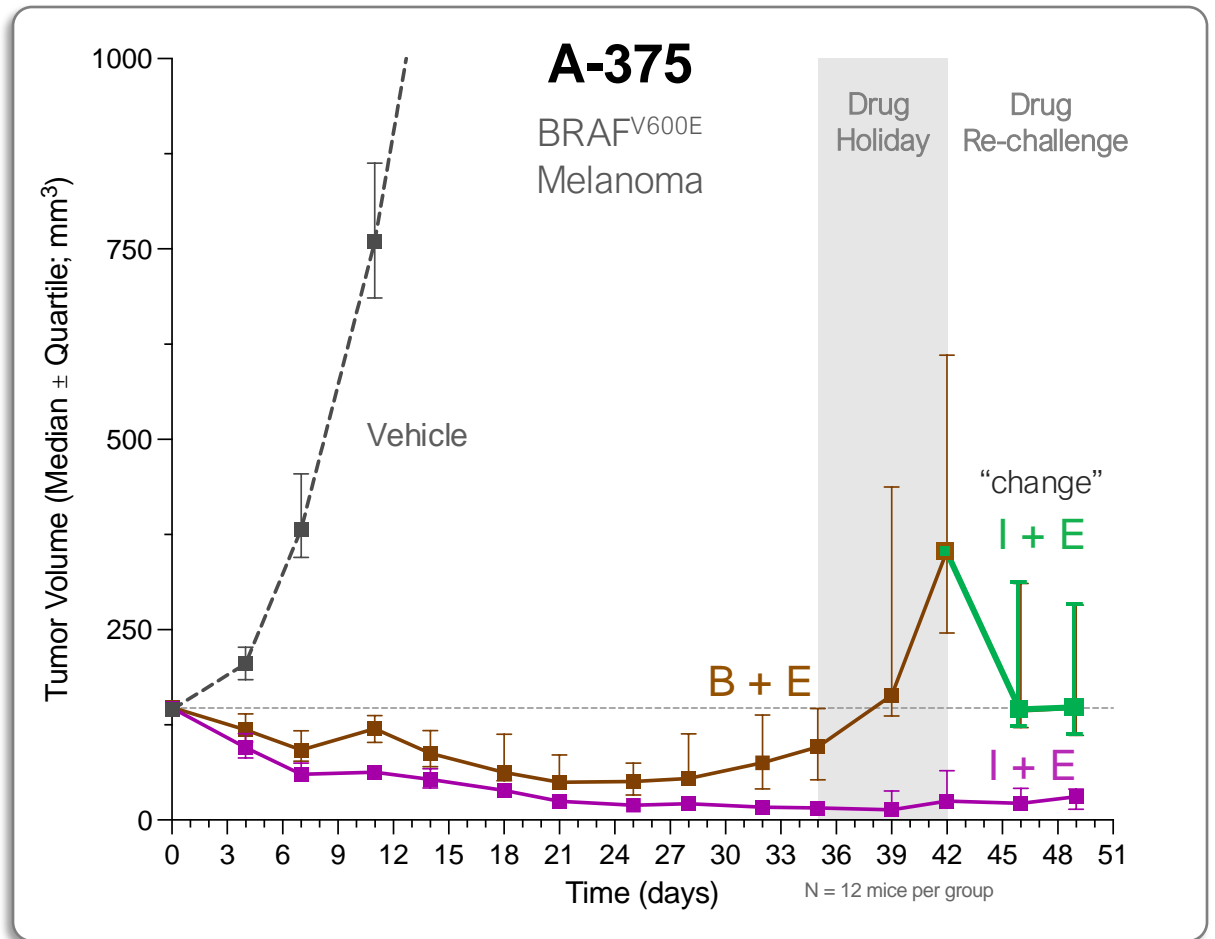
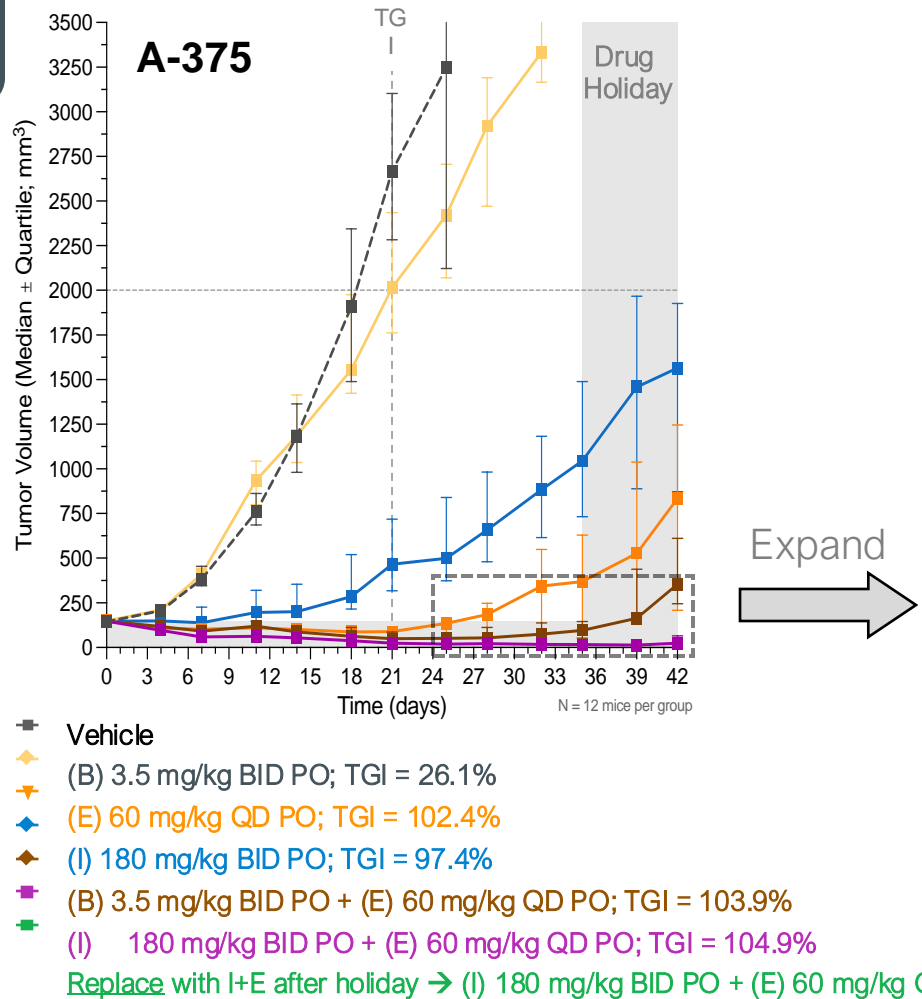
IMM-6-415 (I) ± Encorafenib (E) vs Binimetinib (B) ± Encorafenib in A-375

**BRAF^{V600E}
MEL**

**RAF
V600E**

+

**DCI
MEK**



A-375 Melanoma BRAF^{V600E} xenograft tumor models in athymic nude mice. Binimetinib (MEK inhibitor) and encorafenib (BRAF inhibitor) were commercially purchased. Tumor Growth Inhibition (TGI) % = $[1 - (Ti - To) / (Ci - Co)] \times 100\%$. No median body weight loss was noted.

Corporate



Immuneering



Milestones

Program	Milestone	Expected Timing
IMM-1-104	Phase 1 topline data (tolerability, candidate RP2D, PK/PD, ctDNA and initial clinical activity)	COMPLETE
IMM-1-104	First Patient Dosed in Phase 2a	COMPLETE
IMM-1-104	Initial Data from Multiple Arms of the Phase 2a	2024
IMM-6-415	First Patient Dosed in Phase 1/2a	COMPLETE
IMM-6-415	Initial Phase 1 PK/PD and safety data	2024

Differentiated Approach

- Targeting broad **Universal-RAS/RAF** patient population vs. single mutations
- Aim to **improve tolerability** and to **increase durability** vs. chronic inhibition
- **Deep Cyclic Inhibition:** a counterintuitive approach deeply rooted in data
- **IMM-1-104:** First Deep Cyclic Inhibitor of MAPK pathway. QD oral. Unique profile includes:
 - **Manyfold higher C_{MAX}**
 - **Shorter half-life**
- **IMM-6-415:** Deep Cyclic Inhibitor of MAPK pathway. BID oral.

IMM-1-104: Phase 1/2a Clinical Study In Progress

- **Positive initial Phase 2a data reported in combo with chemo in 1st line pancreatic cancer patients**
- **Phase 2a: monotherapy arms**
 - PDAC 1L or 2L
 - RASmut Melanoma 2L or 3L post-IO, or 1L*
 - RASmut NSCLC 2L-3L
- **Phase 1b/2a combination arms**
 - 1L PDAC IMM-1-104 + mFOLFIRINOX
 - 1L PDAC IMM-1-104 + mGem/nab-Pac

Future Directions

- **IMM-104 initial data from at least one additional Phase 2a arm expected in 2H 2024**
- **IMM-6-415: Initial PK/PD and safety data from Phase 1 portion of Phase 1/2a trial expected in 2024**
- **Active discovery pipeline**
- **Cash runway projected into 2H 2025**



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Appendix

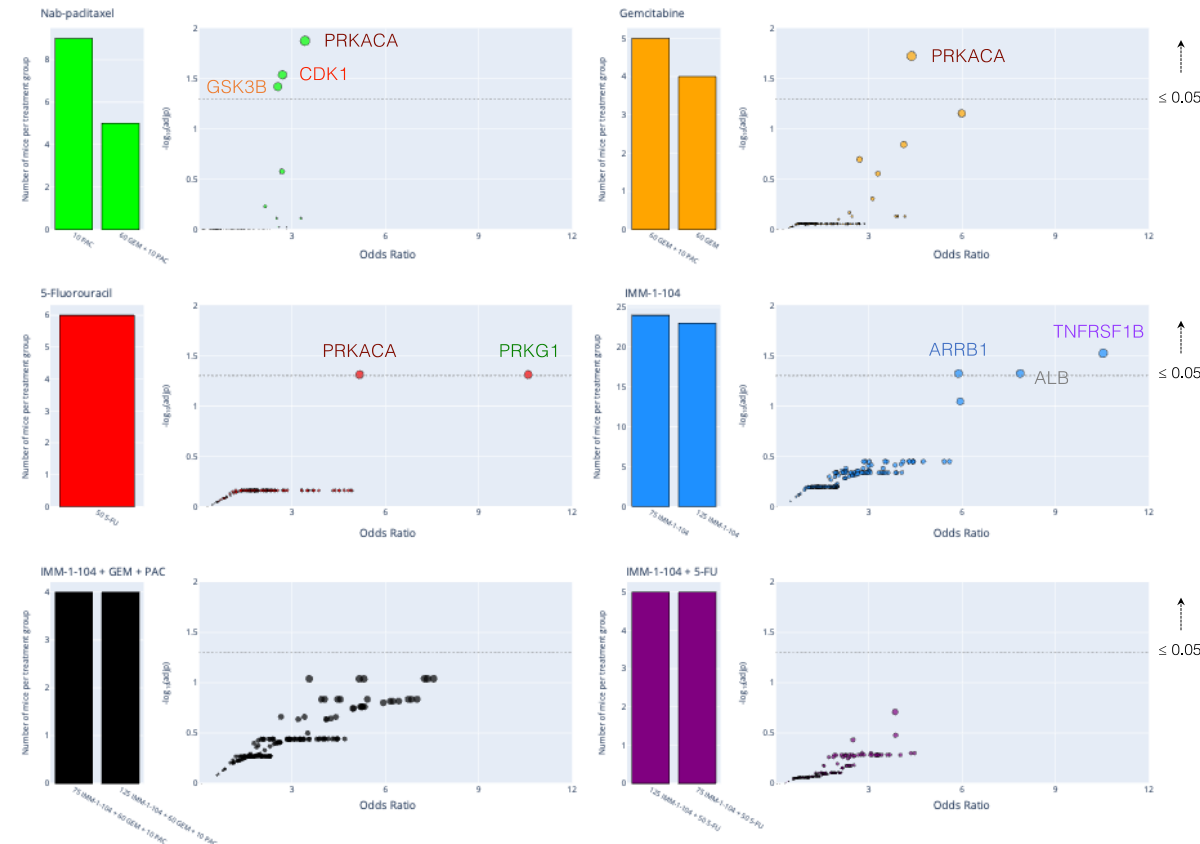


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Treatment-Acquired Mutations Show Distinct Mechanisms of Adaptation

Enrichment Analysis of Recurring-Mutated Genes Under Continuous Antitumor Treatment in Protein-Protein Interaction Hubs



PRKACA activates MAPK signaling via RAF; with 5-FU treatment or combination therapy using Nab-paclitaxel + Gemcitabine, tumors may exhibit increased reliance on MAPK for survival and proliferation. Notably, this enrichment is absent in IMM-1-104 monotherapy or combinations. **CDK1** mediates paclitaxel resistance⁵, while **GSK3B** acts as a compensatory mechanism in paclitaxel treatment; co-treatment with a GSK3 inhibitor enhances paclitaxel efficacy⁶. **PRKG1** gene set itself is likely not a driver of resistance, but its component gene BRAF signals through MAPK. **TNFRSF1B** regulates PI3K-Akt, a MAPK-independent pro-survival pathway. **ARRB1** facilitates ERK auto-phosphorylation in the absence of MEK.⁷

≥ 3 Line PDAC: No benchmarks, increased lesion-to-lesion heterogeneity

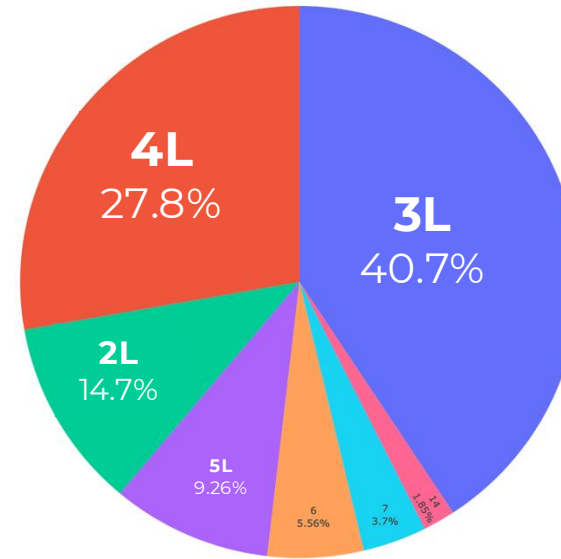
Pancreatic Cancer Benchmarks

Trial	Treatment	Line of Treatment	ORR
^a Phase III MPACT	Gemcitabine	1 st Line	7%
^a Phase III MPACT	Gemcitabine + nab-paclitaxel	1 st Line	23%
^b Phase III PRODIGE/ACCORD 11	FOLFIRINOX	1 st Line	32%
^c Phase III NAPOLI-3	NALIRIFOX	1 st Line	42%
^d Phase III NAPOLI-1	nal-IRI + FU/LV	2 nd Line	17%
^e Phase III MPACA-3	mFOLFIRINOX	2 nd Line	15%

^a Phase III MPACT trial ([link](#))
^c Phase III NAPOLI-3 trial ([link](#))
^e Phase III MPACA-3 trial ([link](#))

^b Phase III PRODIGE/ACCORD 11 trial ([link](#))
^d Phase III NAPOLI-1 trial ([link](#))

Phase 1 Patients IMM-1-104 treatment line



Topline EDC snapshot as of August 19, 2024 (IMM-1-104) 54 patients with prior treatment history

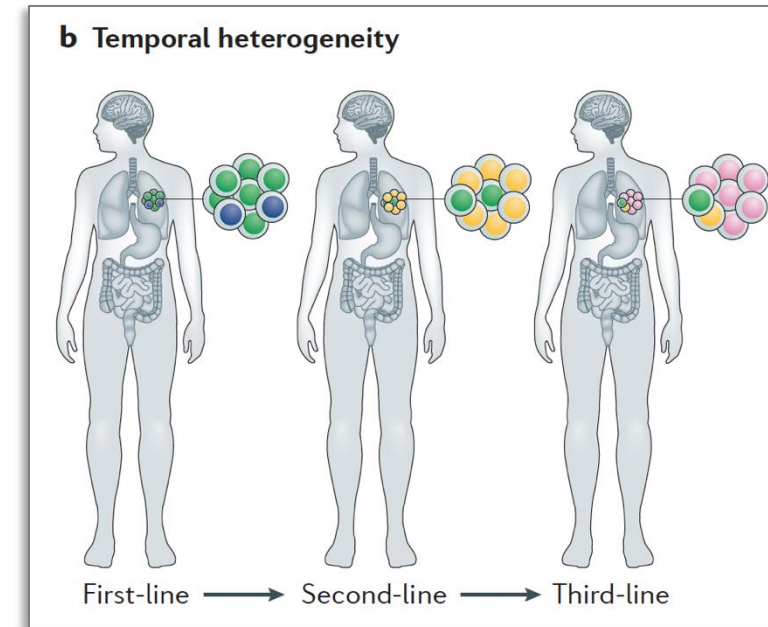
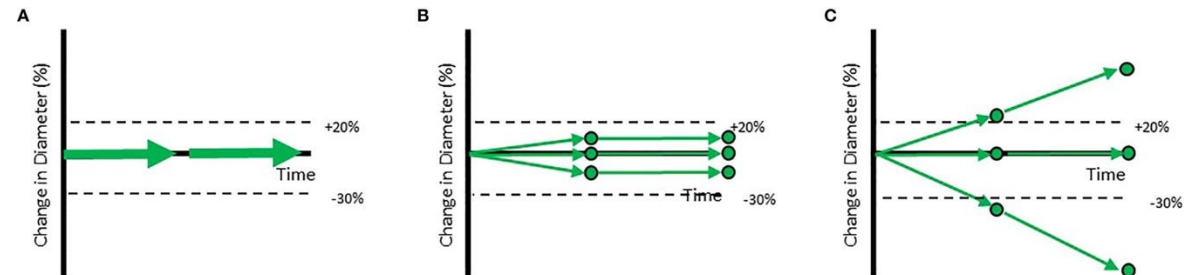


Figure from: 2018 Nat. Rev. Clin. Onc. 15:81



“...patient response evaluation with an appreciation of lesion-to-lesion heterogeneity can potentially improve decision-making at the early stage of oncology drug development...” [Kumar, et al. 2023]

Figure from: <https://doi.org/10.3389/fimmu.2023.1173546>

Patient Status Summary for IMM-1-104 (as reported at AACR April 2023)

#	Patient	RAS Mutation	Dose Level	Dose	C1D1 (t _{1/2})	C1D15 (t _{1/2})	Mean (t _{1/2})	DLT Window
1.	PANCREATIC	KRAS-G12D	I	40 mg QD p.o.	1.82 hours	2.10 hours	1.96 hours	Cleared
2.	COLORECTAL	KRAS-G12V	II	80 mg QD p.o.	1.41 hours	1.43 hours	1.42 hours	Cleared
3.	COLORECTAL	NRAS-Q61L	III	160 mg QD p.o.	2.04 hours	1.83 hours	1.94 hours	Cleared
4.	COLORECTAL	NRAS-Q61K	III	160 mg QD p.o.	1.91 hours	1.97 hours	1.94 hours	Cleared
5.	PANCREATIC	KRAS-G12D	IV	320 mg QD p.o.	2.31 hours	2.46 hours	2.38 hours	Cleared
6.	PANCREATIC	KRAS-G12V	IV	320 mg QD p.o.	2.04 hours	2.27 hours	2.16 hours	Cleared
7.	COLORECTAL	KRAS-G12S	IV	320 mg QD p.o.	1.45 hours	2.27 hours	1.86 hours	Cleared

BLUE = Clinical data timeline reported through April 10th, 2023 (i.e., ~20 weeks since first patient dosed)

GRAY = Data subsequent to AACR that are part of phase 1a dose escalation and have cleared the DLT window

Represents a variety of tumor types, RAS mutations and covers four dose levels

Additional patient enrolled at 160 mg QD p.o. (NRAS-G13R Melanoma); independent of DLT dose escalation

IMM-1-104 Demonstrated Universal-RAS Potential

193 Tumor Models

114 = RAS Mutant

33 = RAF Mutant



Humanized
3D-TGA

Nair, et al. 2023
AACR EORTC
Boston, MA

Tissue	Response #	Non-Response #
Pancreatic †	18	2
Melanoma †	24	0
Lung †	25	11
CRC	25	5
Thyroid	9	2
Cholangiocarcinoma	7	0
AML	9	0
Uveal Melanoma	4	1
Multiple Myeloma	4	4
Soft Tissue	4	2
Breast	2	6
Gastric	4	2
Ovary	2	3
Prostate	1	2
Fibrosarcoma	1	0
Liver	4	2
Neuroblastoma	1	1
Other (BLA, UTE, ESO, HNSQ)	5	1
Total	149 (77.2%)	44 (22.8%)

RAS, RAF mutation	Response #	Non-Response #
NRAS G12	5	0
NRAS G13	1	0
NRAS Q61	23	3
KRAS A146	2	1
KRAS G12	54	10
KRAS G13 ^	4	1
KRAS Q61	5	3
HRAS G12	1	0
HRAS G13 *	1	0
HRAS Q61	2	0
BRAF (Class I or II)	29	5
Total	126 (84.7%)	23 (15.3%)

RAS, RAF mutation	Response #	Non-Response #
Not Present	25	19
Total	25 (56.8%)	19 (43.18%)

^ 1 model also bearing KRAS Q61 /// * 1 model also bearing NRAS Q61

Response to IMM-1-104 based on 3D-TGA and other preclinical modeling. Parallel translational efforts are focused on projecting patient-aligned molecular profiles or 'Targetability'.

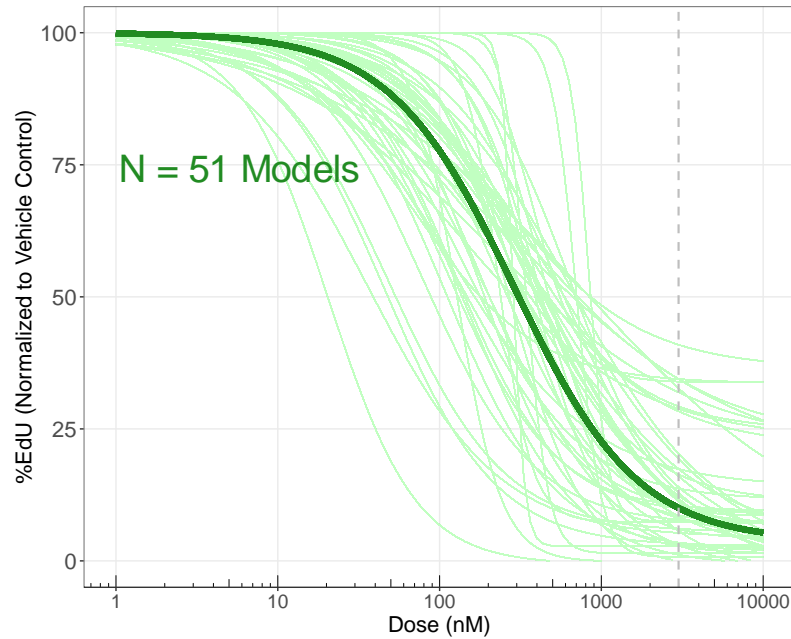
Models tested in 3D-TGA were assigned responsive if dose response IC50 < 1uM (sensitive) or IC50 ≥ 1 with >25% reduction at 10uM (intermediate), and non-responsive otherwise (resistant)

† Select 3D-TGA models: (1.) Pancreatic MIA PaCa-2 (sensitive/responsive), (2.) Pancreatic Capan-2 (intermediate/responsive), (3.) Melanoma SK-MEL-2 (sensitive/responsive), (4.) Lung A549 (intermediate/responsive)

3D-TGA IMM-1-104 Dose Responses (N = 193 Models; > 20 Tumor Types)

Attaining Clinical Free Fraction C_{max} of ~1-3 μ M; Aligns with 3D-TGA Response Categorization

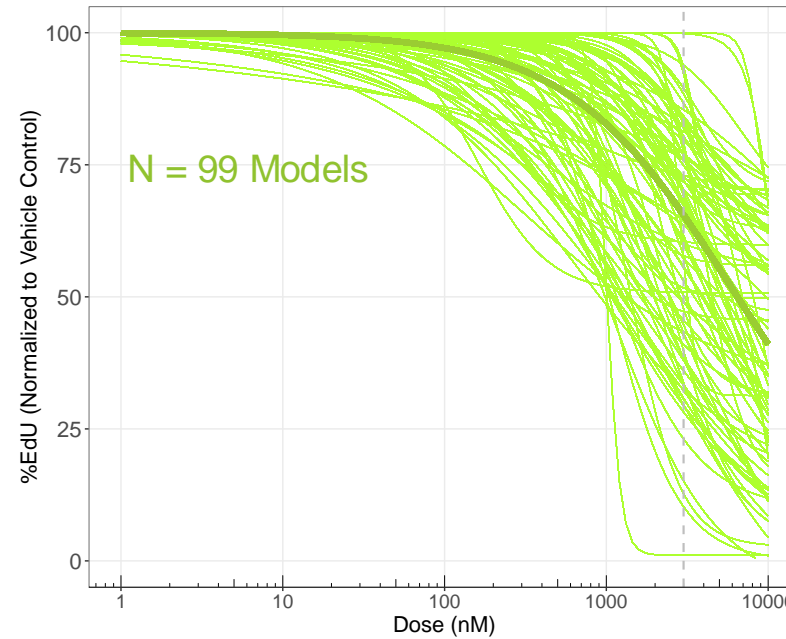
3D-TGA: Sensitive Tumor Models



Subset of **Sensitive** Models:

- MEL: 62.5% (15/24)
- PANC: 35.0% (7/20)
- LUNG: 16.7% (6/36)
- CRC: 6.7% (2/30)

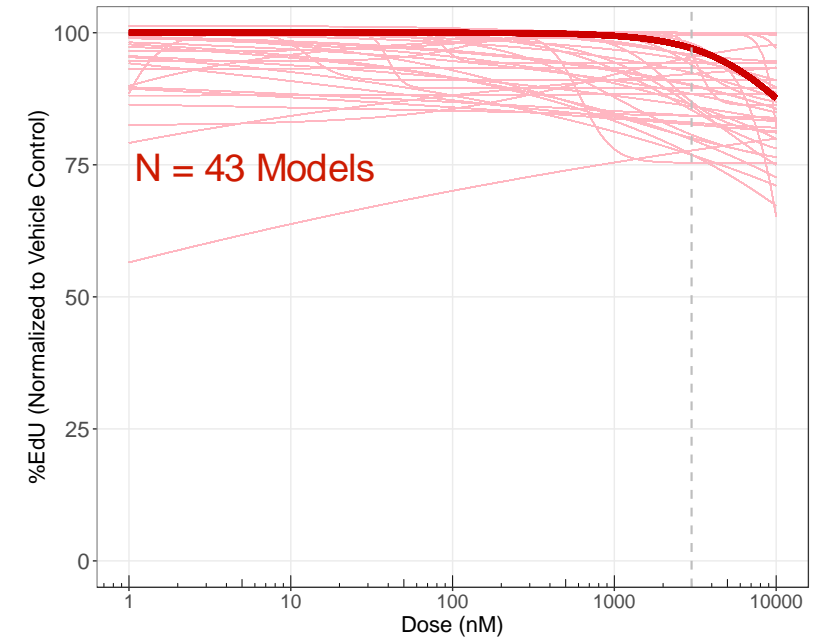
3D-TGA: Intermediate Tumor Models



Subset of **Intermediate** Models:

- MEL: 37.5% (9/24)
- PANC: 55.0% (11/20)
- LUNG: 52.8% (19/36)
- CRC: 76.7% (23/30)

3D-TGA: Resistant Tumor Models



Subset of **Resistant** Models:

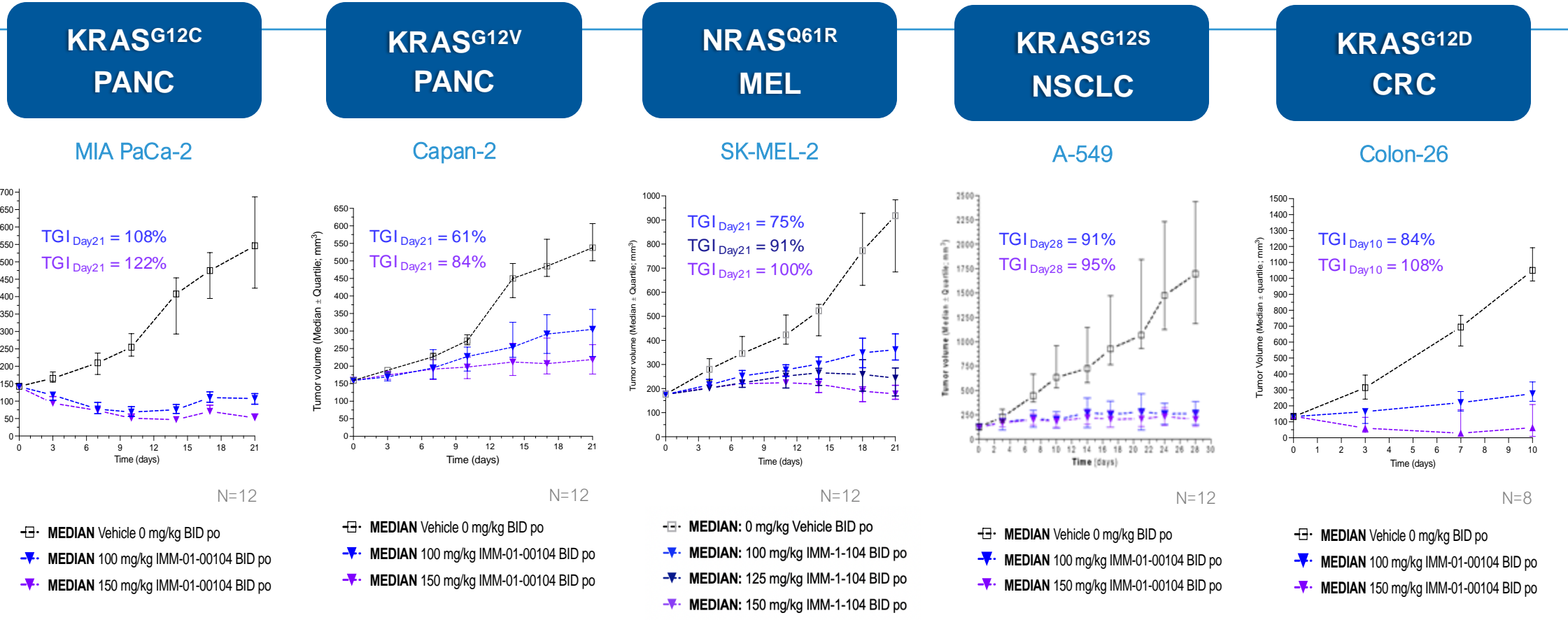
- MEL: 0.0% (0/24)
- PANC: 10.0% (2/20)
- LUNG: 30.6% (11/36)
- CRC: 16.7% (5/30)

- Cell lines tested in 3D-TGA (N=193) were assigned response of sensitive ($IC_{50} < 1\mu$ M), intermediate ($IC_{50} \geq 1$ and >25% reduction at 10 μ M), and resistant otherwise
- The dark line on each plot represents the median of the individual curves; Dotted vertical line matches C_{max} IMM-1-104 drug free-fraction levels achieved at 320 mg QD p.o.
- Major tumor types with activation mutation in the MAPK pathway upstream of MEK (Biomarker Positive): MEL (23/24), PANC (19/20), LUNG (33/36), CRC (28/30)

IMM-1-104 Demonstrated Universal-RAS Potential

IMM-1-104 demonstrated significant and consistent Tumor Growth Inhibition (TGI)

DCI
MEK



Well Tolerated: Median Body Weight Loss ≤ 3-6%* of baseline at top doses

Maximum Effective Dose Range in Mice (plasma t_{1/2} = 1.3 hours) is 100 mg/kg to 150 mg/kg BID po

CRC = colorectal cancer; NSCLC = non-small cell lung cancer; MEL = melanoma; PANC = pancreatic cancer

Tumor Growth Inhibition (TGI) % = $[1 - (T_i - T_0)/(C_i - C_0)] \times 100$; T = treatment groups; C = control groups

*Well-tolerated at top doses with no more than 3-6% median body weight loss (BWL)

**Capan-2 PANC model, as reported at ASCO 2022 (0% TGI for sotorasib and adagrasib at top doses)

Head-to-Head Comparison of IMM-1-104 +/- Sotorasib in KRAS^{G12C} PANC

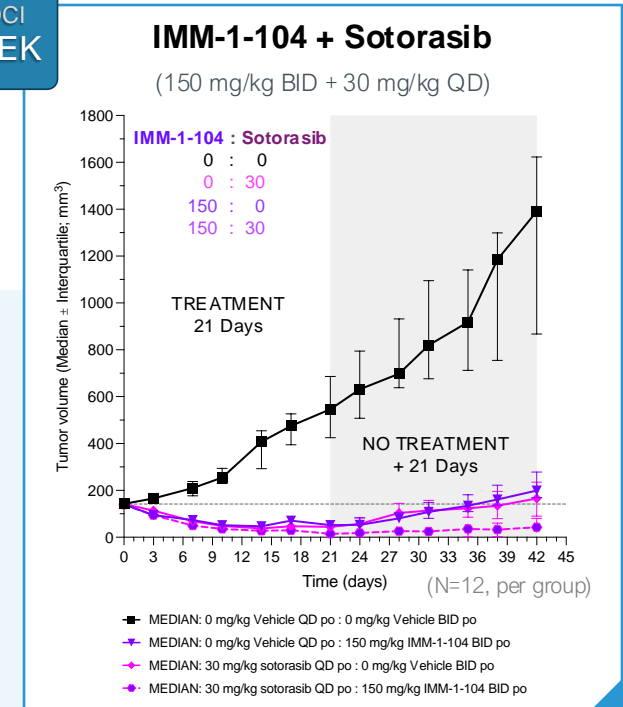
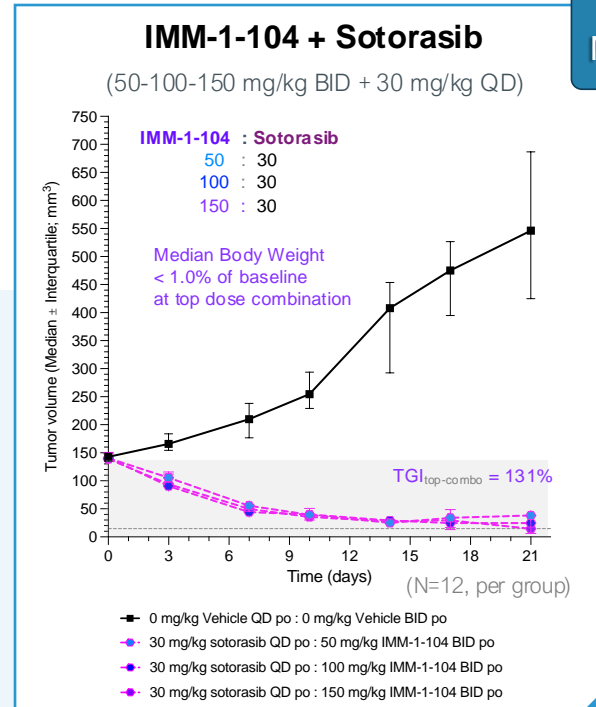
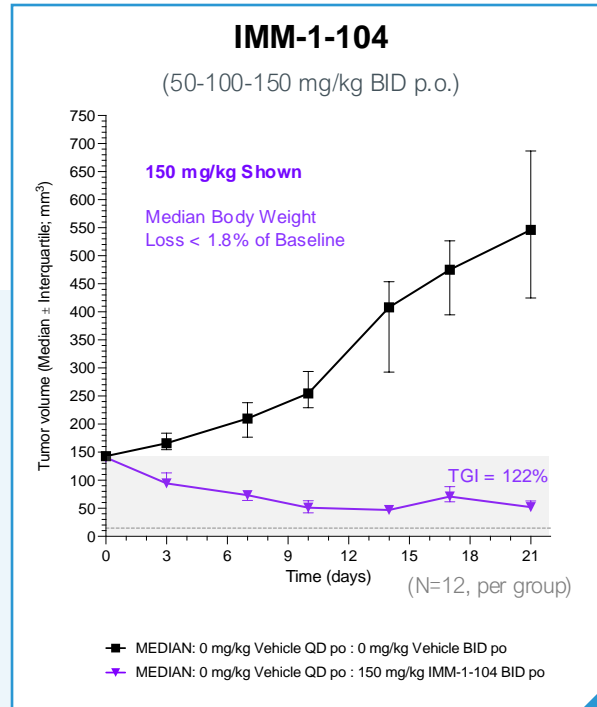
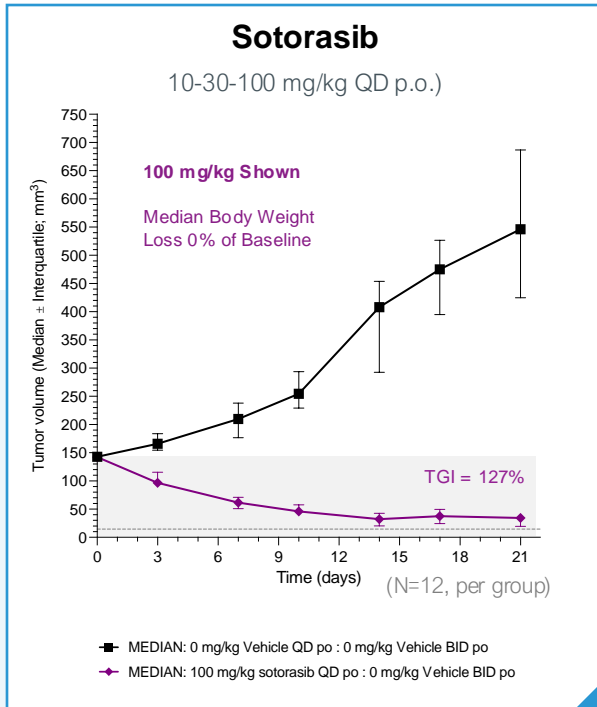
IMM-1-104 as compared to sotorasib demonstrated tumor regression, both with insignificant BWL

**KRAS^{G12C}
PANC**

**RAS
G12C**

+

**DCI
MEK**



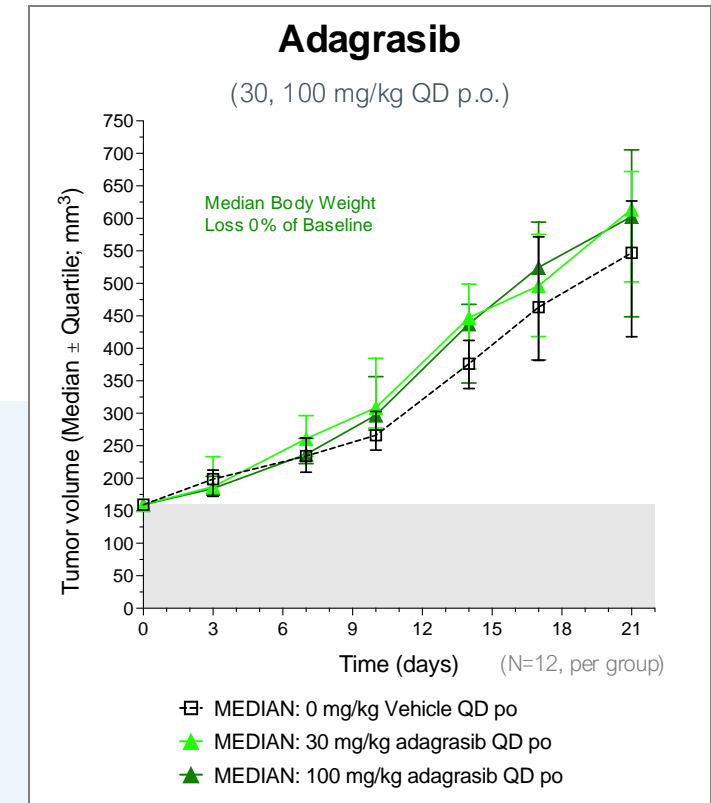
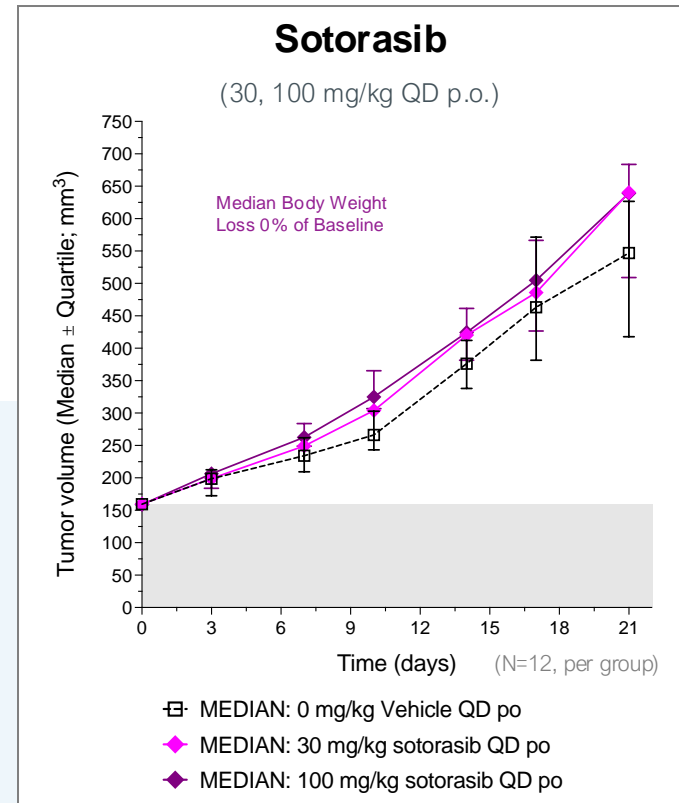
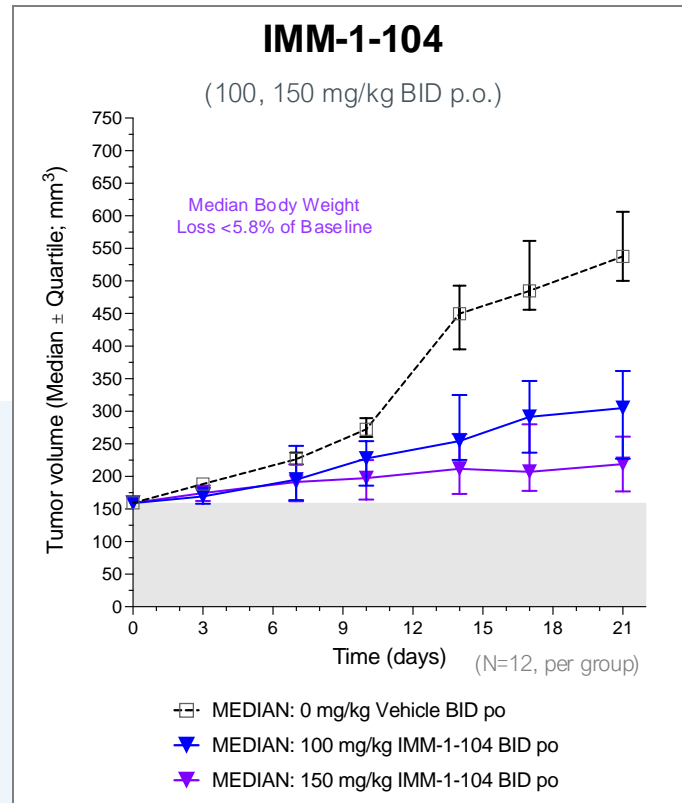
> MIA PaCa-2 (KRAS^{G12C}) Pancreatic Xenograft Tumor Model in Athymic Nude Mice

> Sotorasib was commercially purchased

Tumor Growth Inhibition (TGI) % = $[1 - (T_i - T_o) / (C_i - C_o)] \times 100\%$;
Expanded TGI formula vs. previous $1 - [T/C] \times 100\%$ method

Pancreatic: Head-to-Head Comparison of IMM-1-104 vs. Sotorasib and Adagrasib in a KRAS-G12V Pancreatic Tumor Model

IMM-1-104 demonstrated tumor regression as compared to no reduction with sotorasib or adagrasib, with insignificant BWL



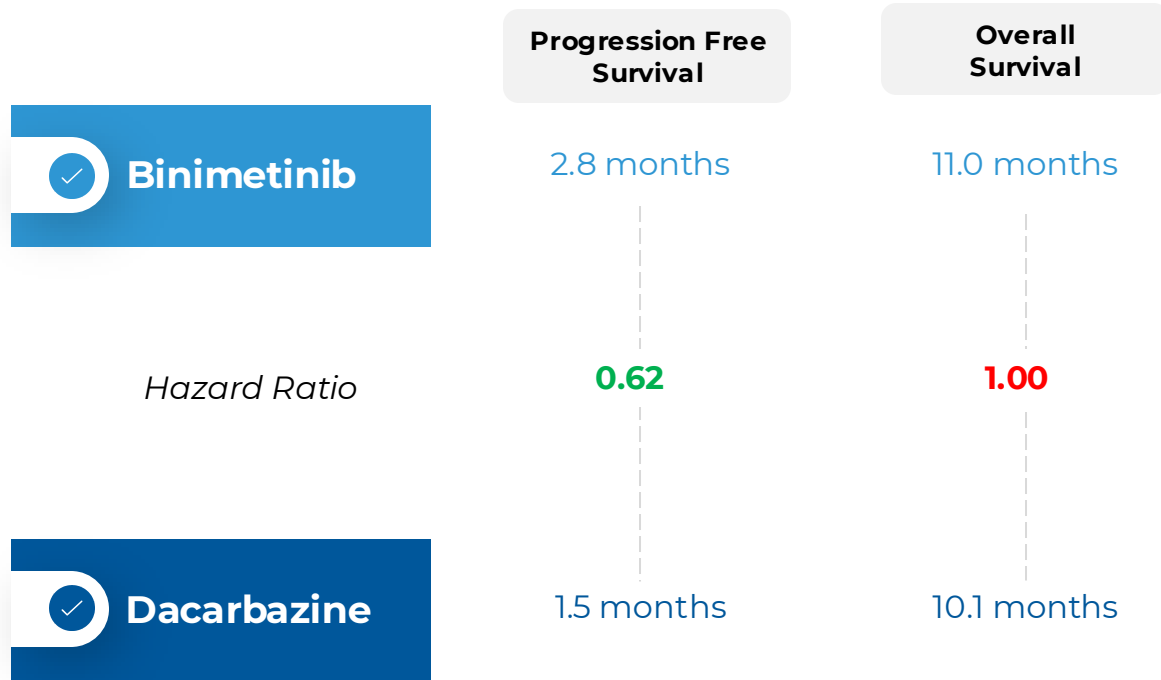
> Capan-2 (KRAS^{G12V}) Pancreatic Xenograft Tumor Model in Athymic Nude Mice

> Sotorasib and adagrasib were commercially purchased

Tumor Growth Inhibition (TGI) % = $[1 - (T_i - T_0)/(C_i - C_0)] \times 100\%$;
Expanded TGI formula vs. previous $1 - [T/C] \times 100\%$ method

Melanoma: Phase 3 NEMO Study: Binimetinib vs. Dacarbazine (NRAS^{mut} Melanoma)

Summary of Phase 3 NEMO study of Binimetinib as reported in Lancet (c.2017) - [a potential opportunity for IMM-1-104](#)

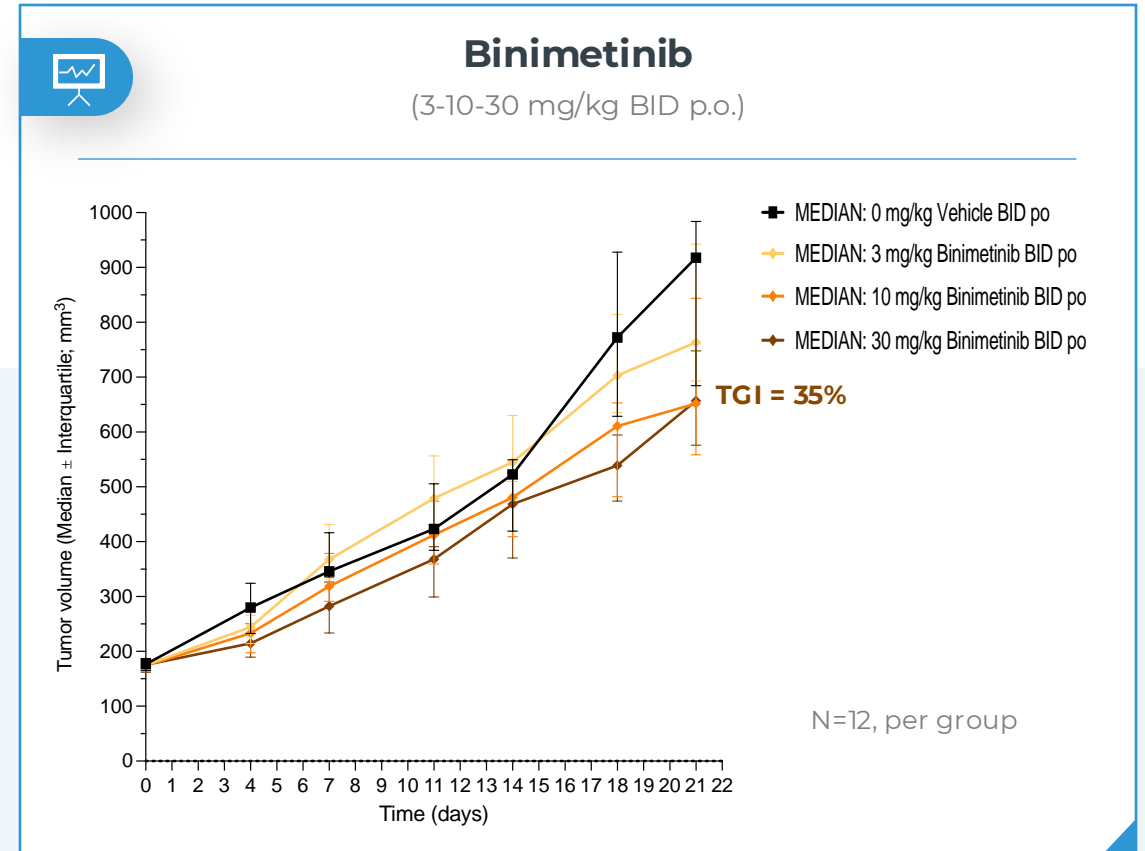
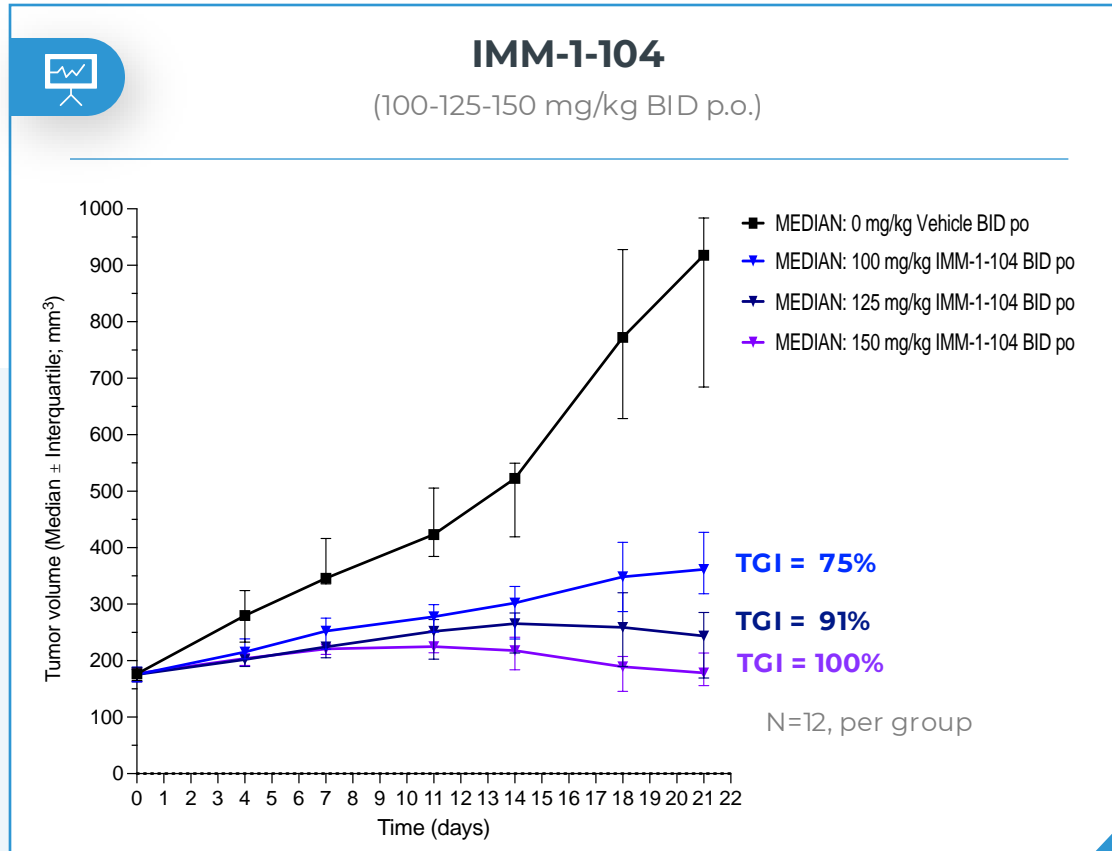


- > Serious Adverse Events (34% binimetinib vs. 22% dacarbazine)
- > Overall Response Rate (ORR: 15% binimetinib vs. 7% dacarbazine)

NRAS Status	Binimetinib 2:1	Dacarbazine
	N = 269	N = 133
Q61K	100 (37%)	51 (38%)
Q61L	32 (12%)	17 (13%)
Q61R	137 (51%)	64 (48%)
Wildtype	0	1 (1%)

Melanoma: Head-to-Head NRAS-Q61R Melanoma Xenograft Study: Binimetinib vs. IMM-1-104 in SK-MEL-2

IMM-1-104 as compared to binimetinib monotherapy demonstrated greater tumor growth inhibition (TGI)



SK-MEL-2 (NRAS-Q61R) Melanoma Xenograft Tumor Model in Athymic Nude Mice

Enhanced Antitumor Activity of IMM-1-104 with Gemcitabine and Paclitaxel

RAS^{mut}
PANC

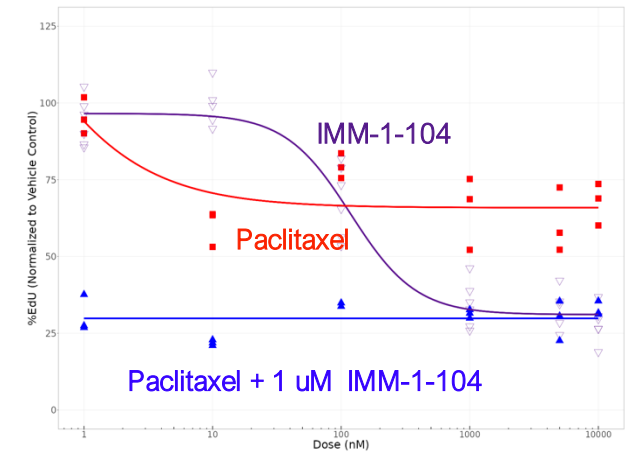
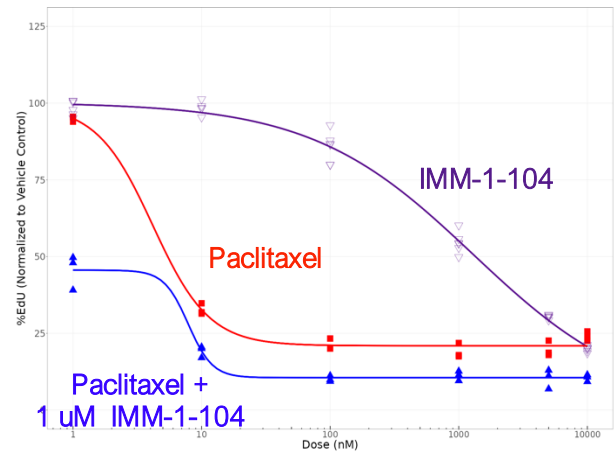
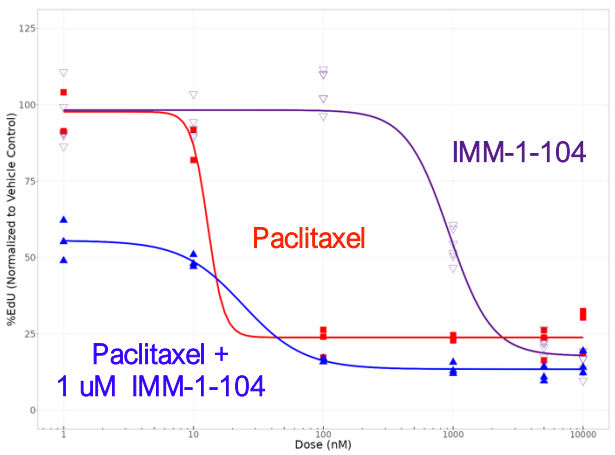
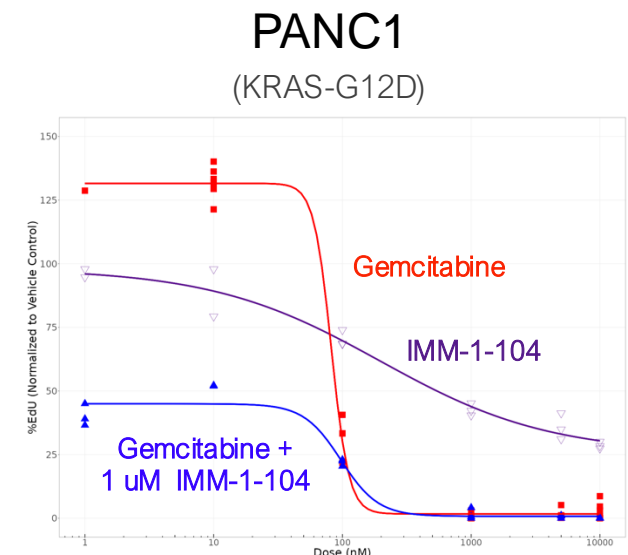
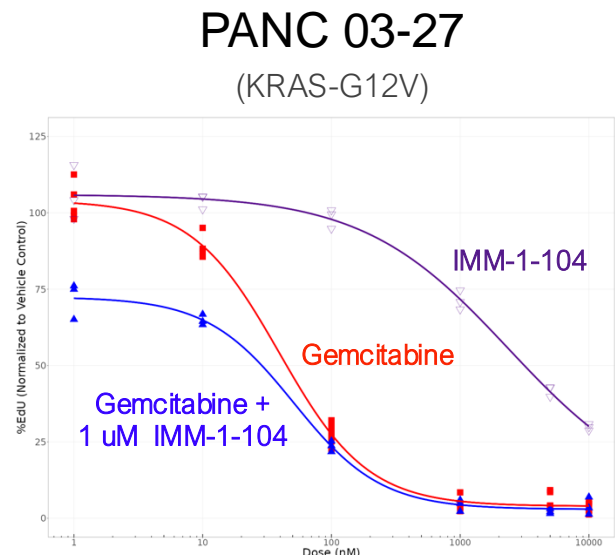
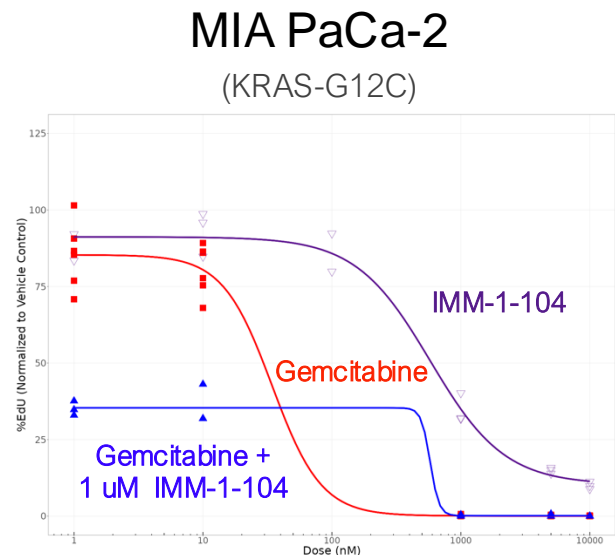
CT

+

DCI
MEK

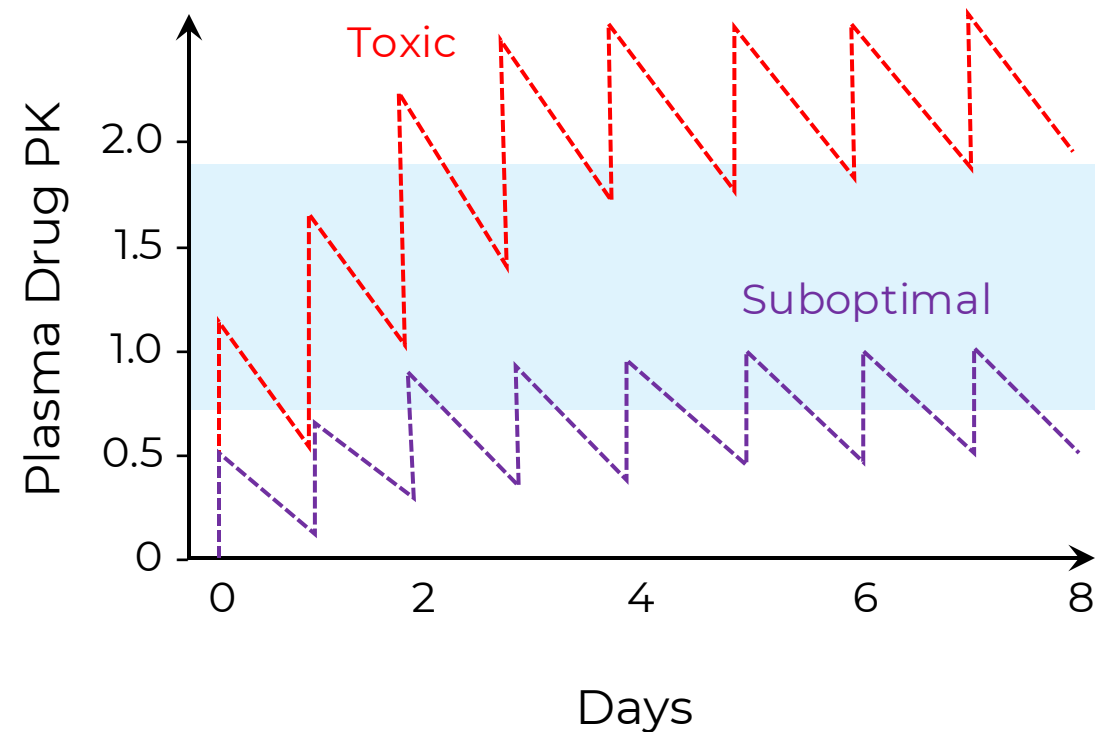
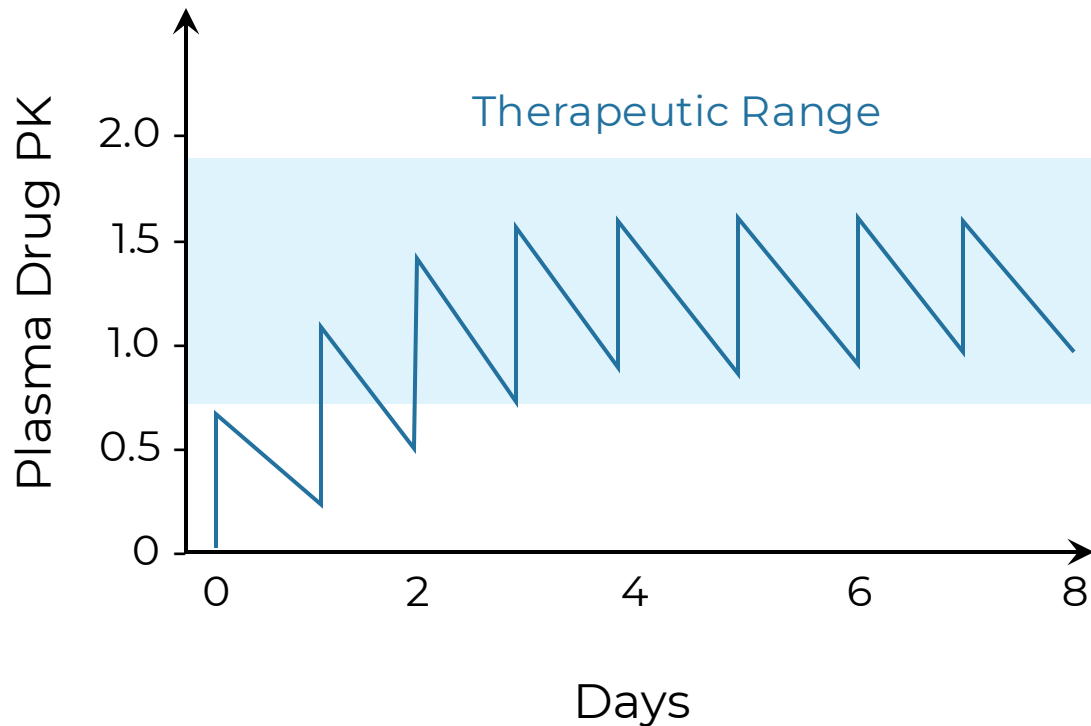
IMM-1-104 +/- Gemcitabine

IMM-1-104 +/- Paclitaxel



IMM-1-104 ± CT dose response curves in the humanized 3D Tumor Growth Assay (3D-TGA)^{2,3}. Three human pancreatic cancer cell models were selected based on patient alignment scores, where each model's mutational profile mapped to three distinct subsets of GENIE v13.1 patients categorized as pancreatic adenocarcinoma. Gemcitabine and paclitaxel (CT agents commonly used for treatment of pancreatic cancer) were commercially purchased.

Chronic Pathway Inhibition in Targeted Oncology



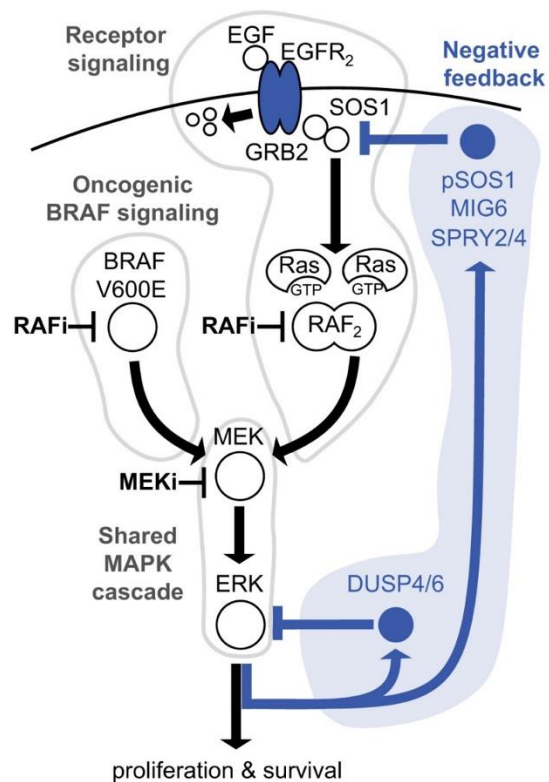
Common approach for therapeutic dosing (**chronic drug exposures**)

Challenges with Chronic Pathway Inhibition

Limited response, short durability, toxicity and limited clinical utility

Loss of Negative Regulators

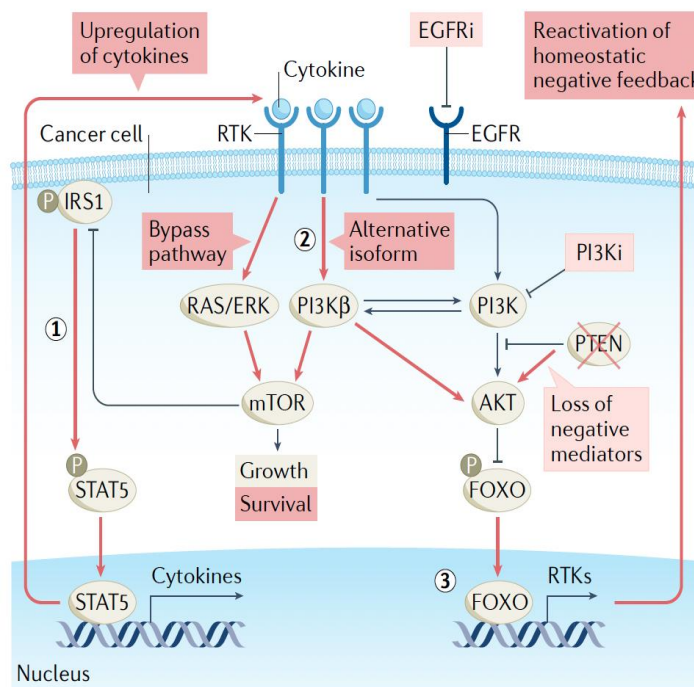
- Loss of MAPK Pathway Control -



Gerosa et al, Cell Systems, 2020

Increased Adaptive Resistance

- Gateway to acquired resistance -



2022 Nat Rev Can p.323

Increased Risk of MEK Toxicities

- Loss of key homeostatic pathway -

Clinical Scenario		V+C	D+T	E+B
Gastrointestinal disease	Diarrhea	Yellow	Green	Green
	Vomit	Yellow	Green	Green
	Anorexia	-	-	-
Liver disease	↑ AST	Red	Green	Yellow
	↑ ALT	Red	Green	Yellow
Cardiovascular disease	↓ Ejection fraction	Green	Green	-
	Hypertension	Yellow	Yellow	Yellow
Rheumatological disease	Arthralgia	Green	Green	Green
Dermatological disease	Skin rash	Yellow	Yellow	Yellow
Hematological disease	Anemia	Yellow	Yellow	Yellow

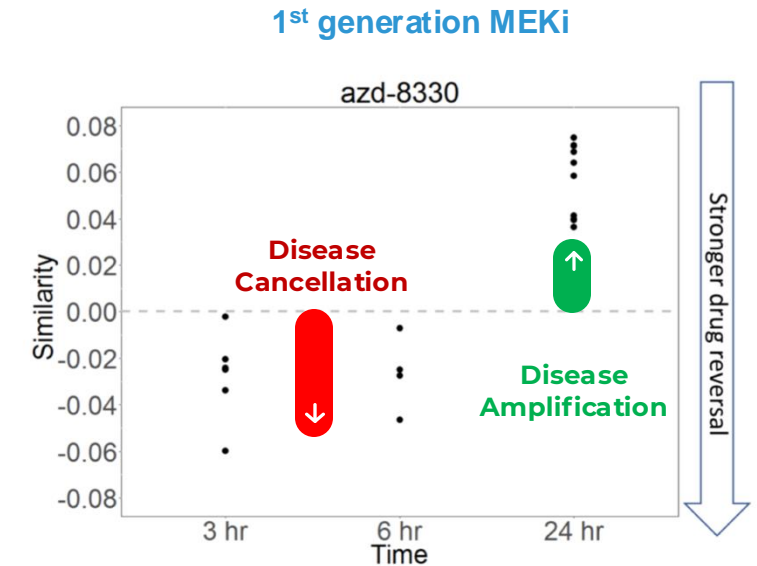
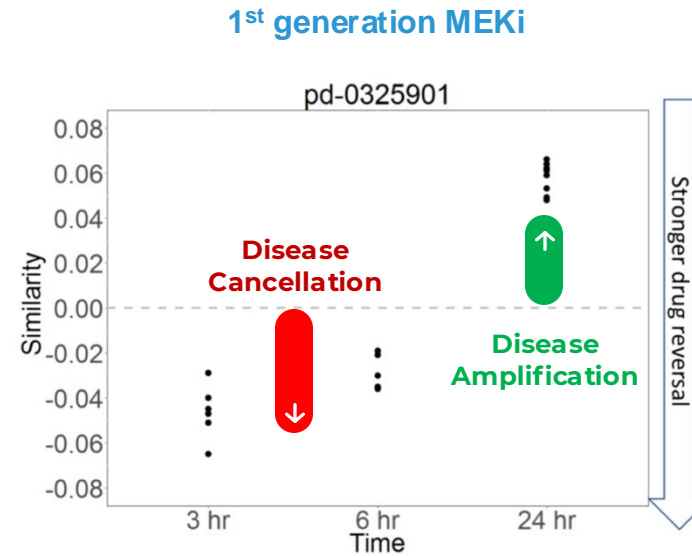
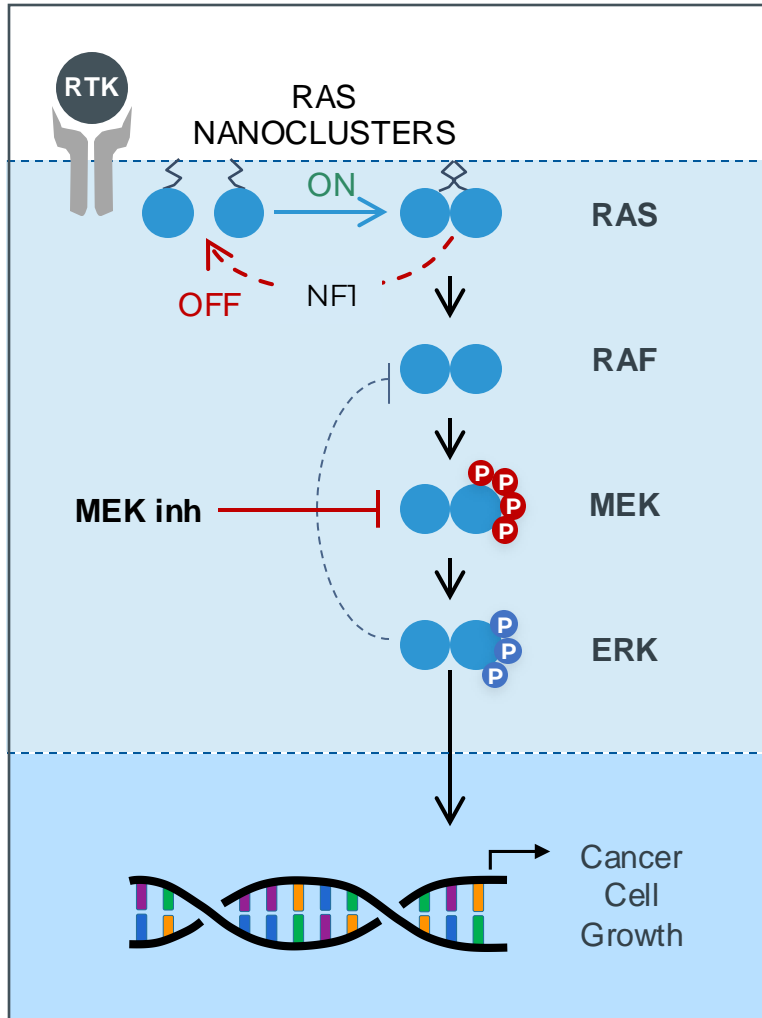
Grade 3, 4, 5 Events



2019 ESMO Open p.e000491
2023 Cancers 15:141

Our Platform Converts Gene Expression to Counterintuitive Insights

Goal: achieve broader activity and better tolerability in RAS and beyond mutant disease



Note: dots are representative of various concentrations

> IMRX Disease Cancelling Technology - US Patent 11,043,305



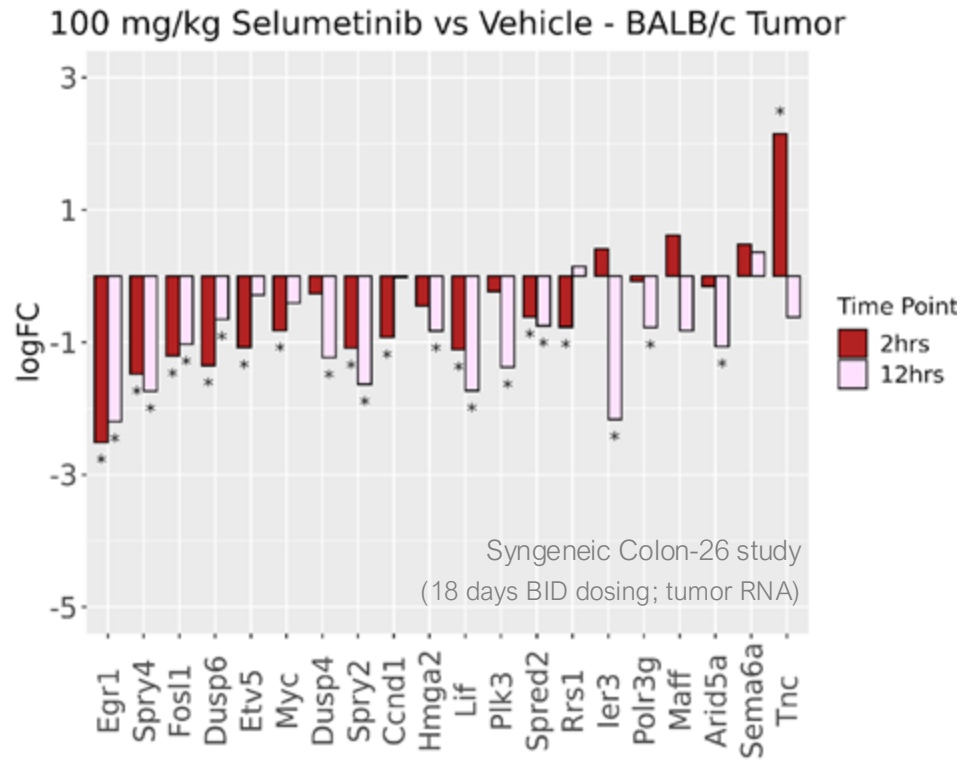
Unlike first generation MEK inhibitors, IMM-1-104 is designed to prevent RAF- and KSR-mediated activation of MEK (i.e., CRAF-bypass) and displays a short plasma half-life to potentially drive deep cyclic inhibition of the pathway.

Data-driven Identification and Optimization of New Medicines to Cancel Cancer Cachexia
Presented by Ben Zeskind at the 12th International Conference of Cachexia, Sarcopenia & Muscle Wasting (SCWD) in Berlin, Dec. 6-8, 2019

Deep Cyclic Inhibition Confirmed Using Transcriptomics



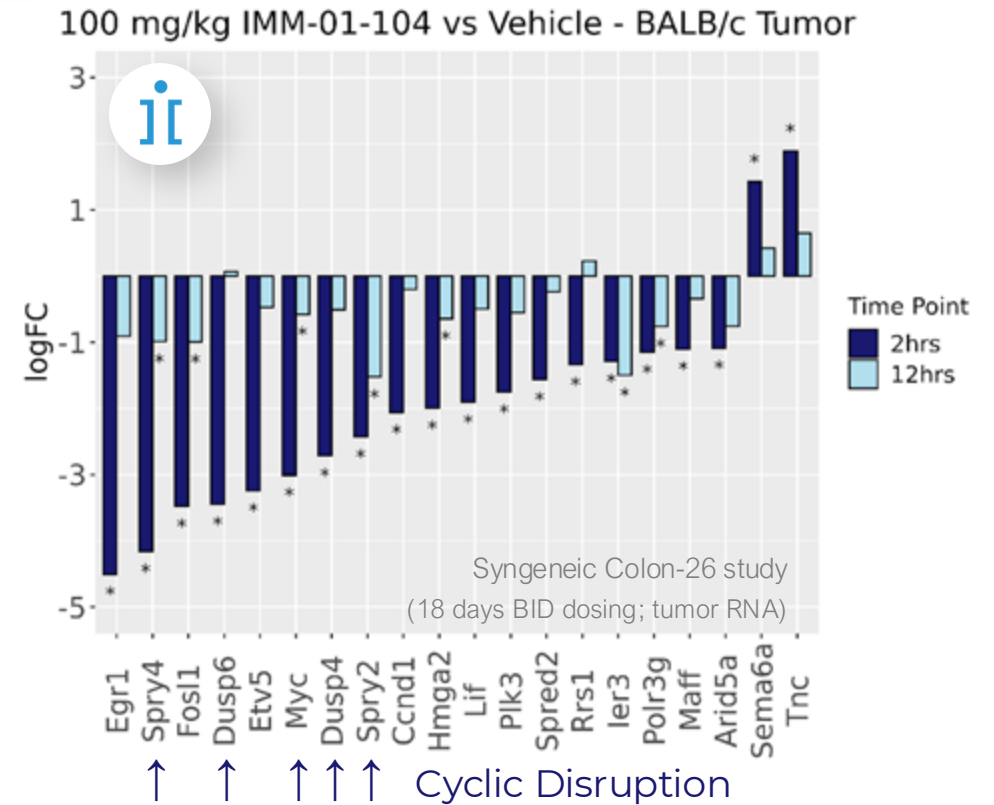
Traditional Approach



Chronic Suppression → TOXICITY



Signaling Dynamics



Cyclic Disruption → TOLERABILITY

Metastatic PDAC (mPDAC): Key Clinical Benchmarks

Trial	Treatment	Line of Treatment	PS	OS (months)	ORR	PFS (months)	CR (%)	PR (%)	SD (%)
^a No Treatment	None	-	-	< 6.0	-	-	-	-	-
^b Phase III MPACT	Gemcitabine	1st Line	0-1	6.7	7%	3.7	0	7.2	28.4
^b Phase III MPACT	nab-paclitaxel + Gemcitabine	1st Line	0-1	8.5	23%	5.5	0.2	22.7	27.4
^c Phase III PRODIGE/ACCORD 11	FOLFIRINOX	1st Line	0-1	11.1	32%	6.4	0.6	31.0	38.6
^d Phase III NAPOLI-3	NALIRIFOX	1st Line	0-1	11.1	42%	7.4	0.6	41.5	25.8
^e Phase III NAPOLI-1	nal-IRI + FU/LV	2nd Line	0-1	6.2	17%	3.1	0	17	32
^f Phase III MPACA-3	mFOLFIRINOX	2nd Line	0-1	9.2	15%	5.2	0	15	50

^a Metastatic PDAC clinical review reference ([link](#))

^b Phase III MPACT trial ([link](#))

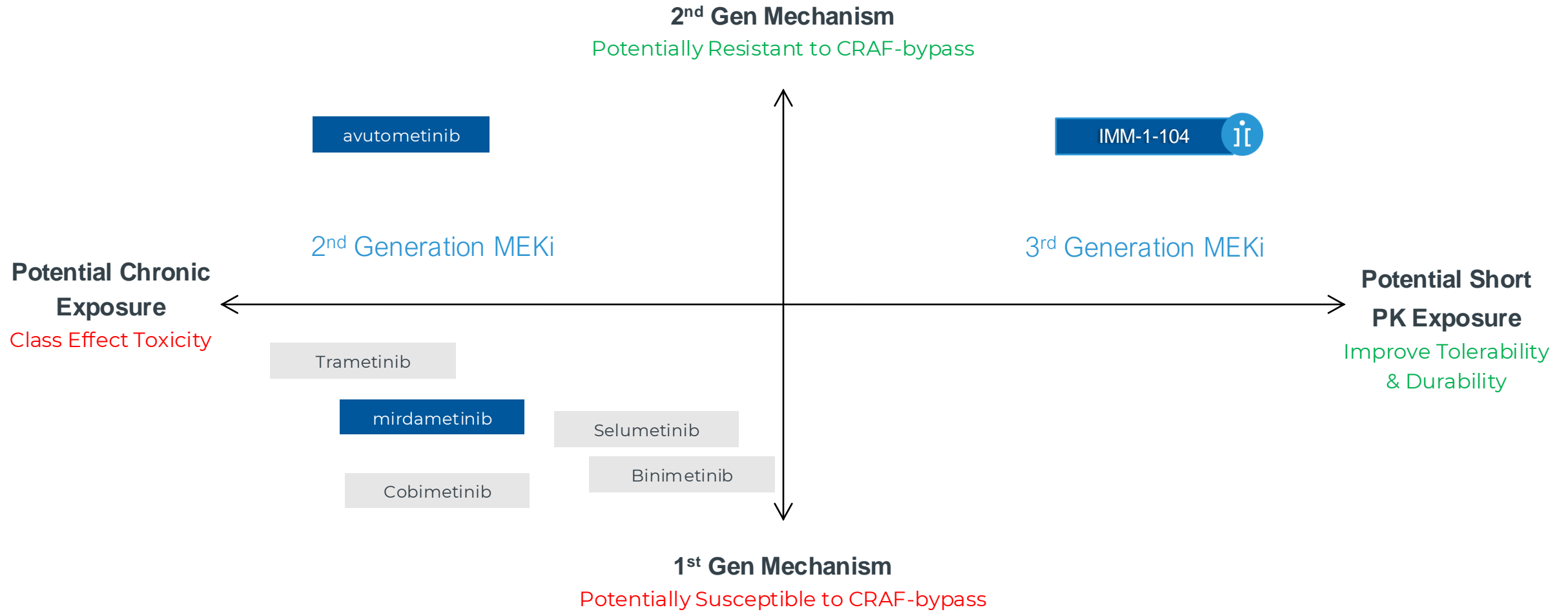
^c Phase III PRODIGE/ACCORD 11 trial ([link](#))

^d Phase III NAPOLI-3 trial ([link](#))

^e Phase III NAPOLI-1 trial ([link](#))

^f Phase III MPACA-3 trial ([link](#))

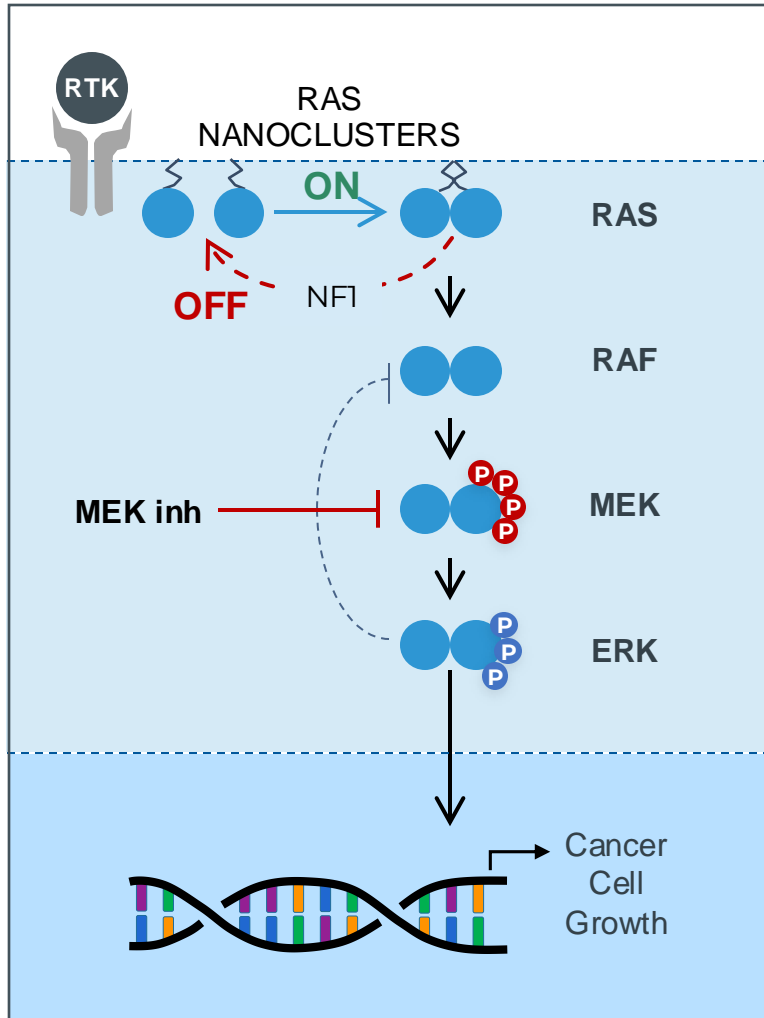
Clinical Stage MEK Inhibitors: Insights & Limitations



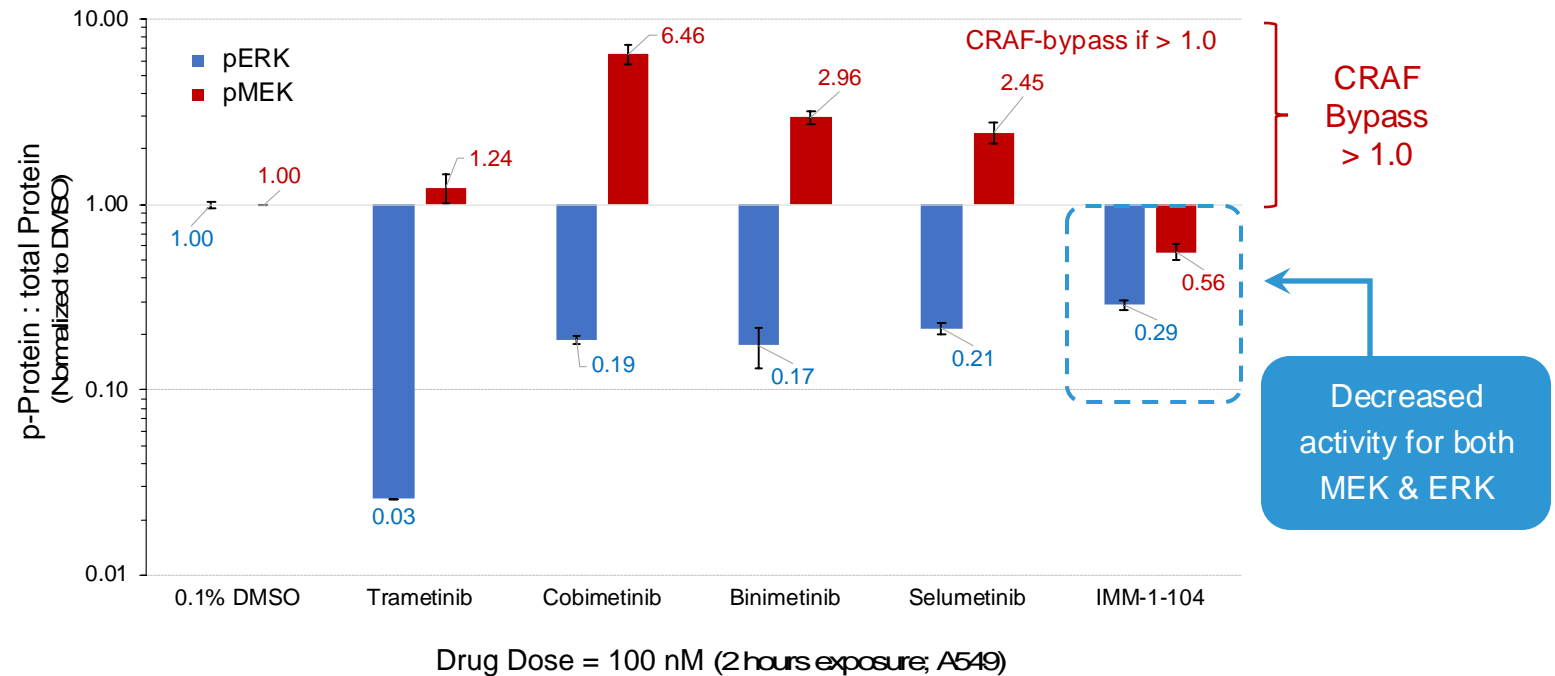
 FDA Registered

 Clinical Trials

Head-to-Head Comparison of IMM-1-104 Against FDA-Approved MEK Inhibitors: CRAF-Bypass Resistance



A549^{KRAS-mut} Lung Cancer: pERK and pMEK



> **FDA-Approved MEK inhibitors:** Trametinib, Cobimetinib, Binimetinib, Selumetinib commercially purchased

Decades of drug discovery and development experience

LEADERSHIP



Ben Zeskind
PhD, MBA
CEO, Co-founder
& Board Member



Michael Bookman
JD
Chief Legal Officer



E. B. Brakewood
Chief Business
Officer



Brett Hall
PhD
Chief Scientific
Officer



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pwc



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THERAPEUTICS



Daiichi-Sankyo



AstraZeneca



Johnson & Johnson



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LATHAM & WATKINS LLP



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science to medicine®



Intercept



Immuneering

