Building a Universal-RAS Franchise

Immuneering

Nasdaq: IMRX

MARCH 2023

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These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, without limitation: our ability to successfully complete our Phase 1/2a clinical trial, or any planned clinical trials and for those trials to produce positive results, our estimates of the number of patients who suffer from the diseases we are targeting and benefit from the medicines we are developing, and the number of patients that may enroll in our clinical trials; our ability to file INDs in the future; the commercializing of our product candidates, if approved; 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 trial; our ability to advance additional product candidates into, and successfully complete, preclinical studies and clinical trials with those additional product candidates; the timing or likelihood of regulatory filings and approvals; our product development and marketing strategy; the negative impacts of the COVID-19 pandemic; our ability and the potential to successfully manufacture and supply our product candidates for clinical trials and for commercial use, if approved; future strategic arrangements and/or collaborations and the potential benefits of such arrangements; our estimates regarding expenses, future revenue, capital requirements and needs for financing and our ability to obtain capital; the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements; our ability to retain the continued service of our key personnel and to identify, hire and retain additional qualified professionals; the implementation of our business model, strategic plans for our business and product candidates; our compliance with laws, the scope of protection we are able to establish and maintain for intellectual property rights, product candidates and our pipeline; our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; the pricing, coverage and reimbursement of our product candidates, if approved; and developments relating to our competitors and our industry, including competing product candidates and therapies.

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Investment Summary

"Our approach is different."

- Targeting **large Universal-RAS** patient population (1.5M) versus more limited approaches.
- **Monotherapy** vs combination therapy potential
- **Deep cyclic inhibition** achieved briefly but forcefully, due to combination of:
  - **Manyfold higher C_{MAX}**
  - and **short half life**
- Approach designed to **spare healthy cells** and potential to **limit adaptive resistance**.

"IMM-1-104 demonstrates Universal-RAS potential."

- **Robust preclinical activity** observed in:
  - Pancreatic Cancer ($KRAS^{G12C\ \&\ G12V}$)
  - NSCLC ($KRAS^{G12S}$)
  - CRC ($KRAS^{G12D}$)
  - Melanoma ($NRAS^{Q61R}$)
  - And others
- Hypothesis for IMM-1-104 from **proprietary model**.
- **Validated using** proprietary **bioinformatics & 3D tumor growth assays**

"2023 is shaping up to be our breakout year."

- **First patient dosed** in Phase 1/2a trial of lead asset IMM-1-104 in November 2022.
- **Patient enrollment ongoing**; investigator enthusiasm high.
- Broad inclusion **criteria facilitates** rapid trial enrollment.
- **Upcoming data readouts, beginning mid-2023**
- **Cash runway projected into Q4 2024**

IMM-1-104's Potential …

Universal-RAS

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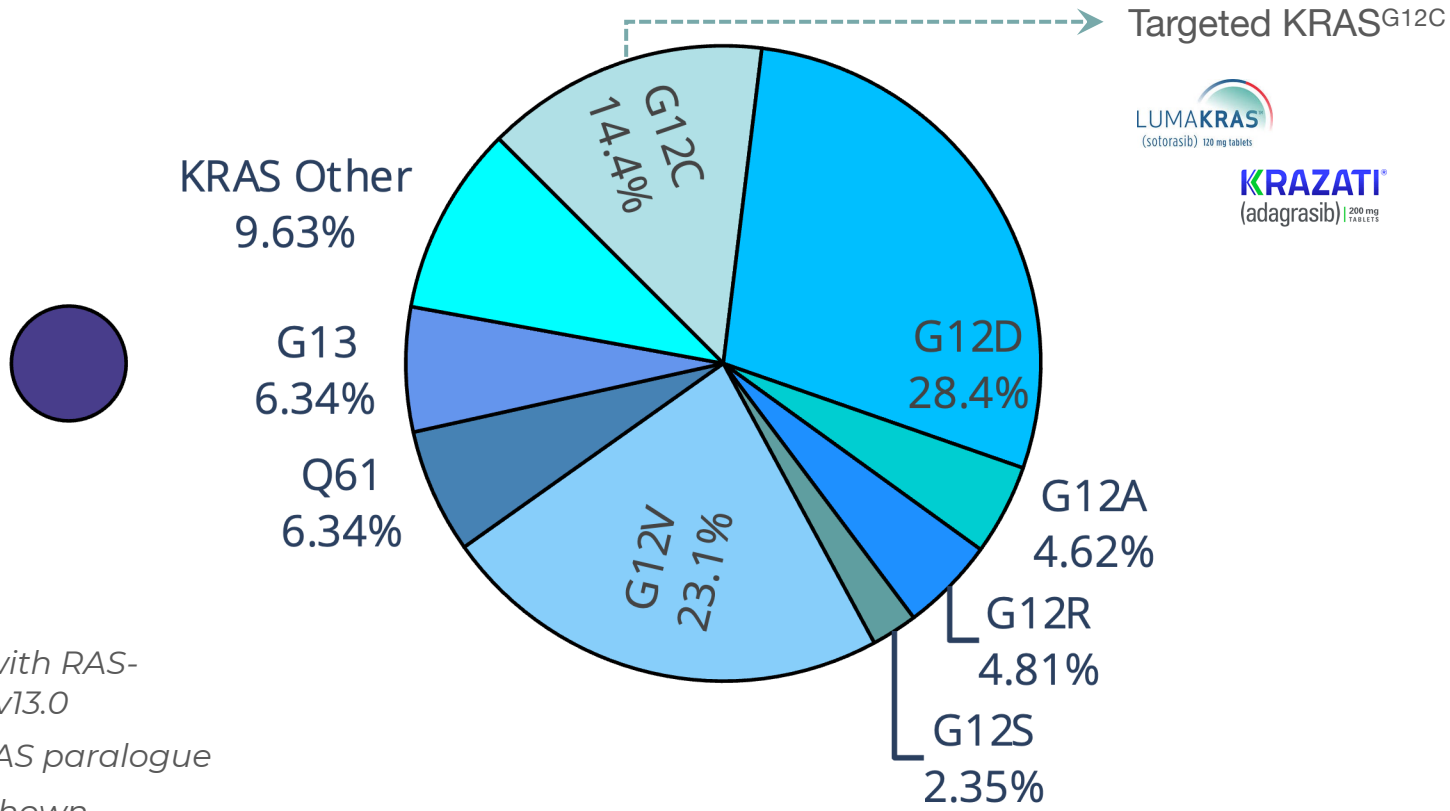
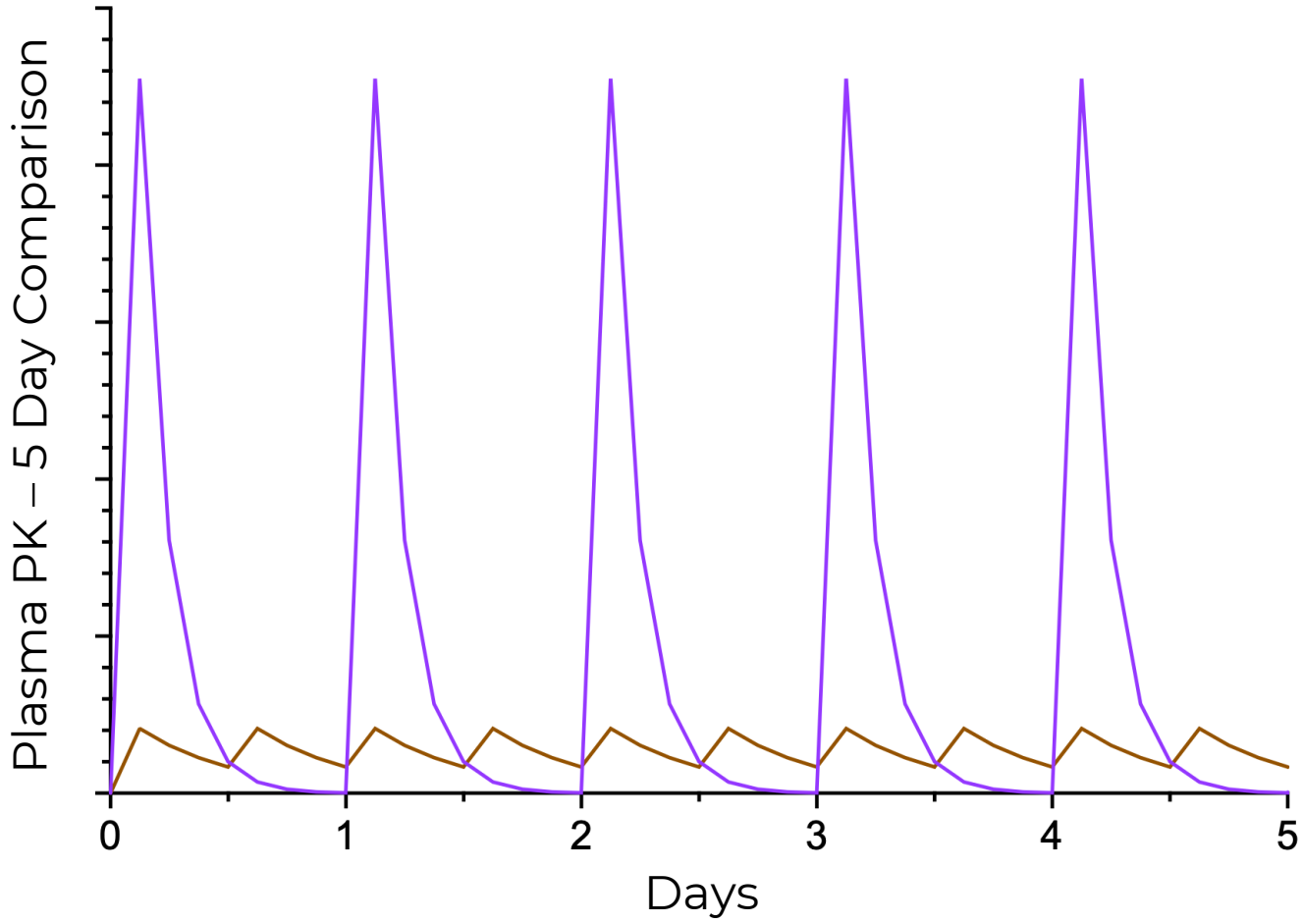
NRAS	HRAS	KRAS
(14.12%)	(2.78%)	(83.10%)



- *Based on 27,461 out of 148,268 (18.5%) patients with RAS-mutated tumors in the AACR GENIE database, v13.0*
- *Percentage of overall mutation shown under RAS paralogue*
- *Select mutation percentages within KRAS are shown*

Deep, Cyclic Inhibition



Conceptual illustration of deep cyclic inhibition

1. **Dramatic PK C_{MAX} Pulse**

   Many fold higher drug free fraction C_{MAX} than other MEK inhibitors

   GOAL: Break Tumor Addiction

2. **Near-Zero Drug Trough**

   Short plasma half-life

   GOAL: Improve tolerability and limit adaptive resistance:
   every day is a drug holiday

3. **MoA Target Engagement**

   Prevent MAPK-pathway bypass events

   GOAL: Expanded activity into RAS mutant setting

Development Pipeline

Wholly Owned Product Portfolio Differentiated by Indication and Half-life

PROGRAM	INDICATION	DISCOVERY	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	MILESTONE
IMM-1-104	**Universal-RAS**	**Once Daily (QD)**					**Phase 1/2a Trial Enrolling; initial PK and safety data expected mid-2023**
IMM-6-415	**Universal-MAPK**	**Twice Daily (BID)**					**IND filing in Q4 2023**
Multiple additional programs in discovery phase							

Cash, cash equivalents and marketable securities of $105.5M as of December 31, 2022 expected to fund operations into Q4 2024

IMM-1-104

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IMM-1-104

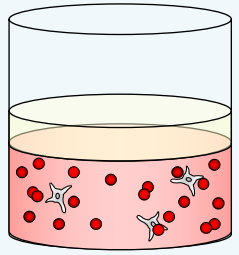
- **Potential for Universal-RAS Activity**
- **Deep Cyclic Inhibition; Once-Daily Oral Dosing**
- **Short plasma half-life to minimize drug trough**
- **Initially being developed as Monotherapy**
- **Designed to Resist CRAF-bypass in RAS mutant tumors**

- Phase 1 recruiting all-comer RAS solid tumors: NCT05585320
- First patient dosed November 2022
- Robust pre-clinical activity observed in 6 different animal models; well-tolerated (median body weight loss of less than 3-6% at top doses)

IMM-1-104 Demonstrates Universal-RAS Potential

132 Tumor Models

75 = RAS Mutant



Humanized 3D-TGA

Kolitz, et al. 2023
AACR: Targeting RAS
Philadelphia, PA

Tissue	Response #	Non-Response #
Pancreatic †	**17**	**2**
Melanoma †	**22**	**0**
Lung †	**19**	**6**
CRC	**20**	**5**
Thyroid	6	1
Soft Tissue	2	1
Breast	2	6
Gastric	4	2
Ovary	3	2
Prostate	1	2
Fibrosarcoma	1	0
Liver	4	2
Neuroblastoma	1	1
Total	**102** (77.3%)	**30** (22.7%)

RAS, RAF mutation	Response #	Non-Response #
NRAS G12	2	0
NRAS G13	1	0
NRAS Q61	17	2
KRAS A146	1	0
KRAS G12	36	8
KRAS G13 ^	3	1
KRAS Q61	3	0
HRAS G13 *	1	0
BRAF (Class I or II)	21	4
Total	**85** (85.0%)	**15** (15.0%)

RAS, RAF mutation	Response #	Non-Response #
Not Present	17	15
Total	**17** (53.1%)	**15** (46.9%)

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

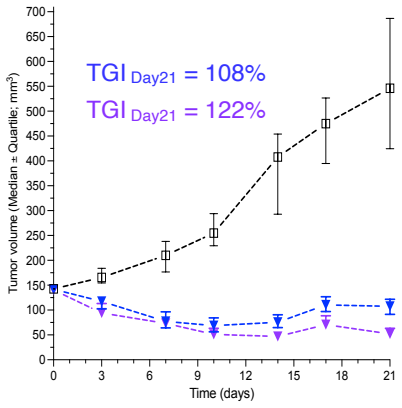
Response to IMM-1-104 based on 3D-TGA and other preclinical modeling. Parallel translational efforts are focused on projecting patient-aligned molecular profiles or 'Targetability'.

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)

IMM-1-104 Demonstrates Universal-RAS Potential

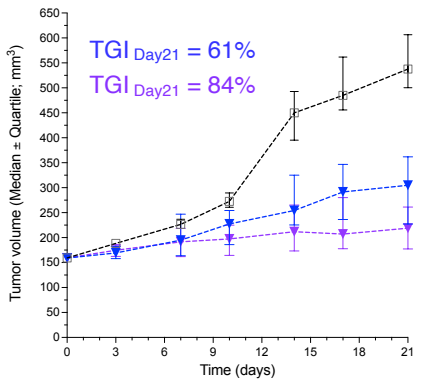
KRAS^{G12C} PANC — MIA PaCa-2



N=12

- **MEDIAN** Vehicle 0 mg/kg BID po
- **MEDIAN** 100 mg/kg IMM-01-00104 BID po
- **MEDIAN** 150 mg/kg IMM-01-00104 BID po

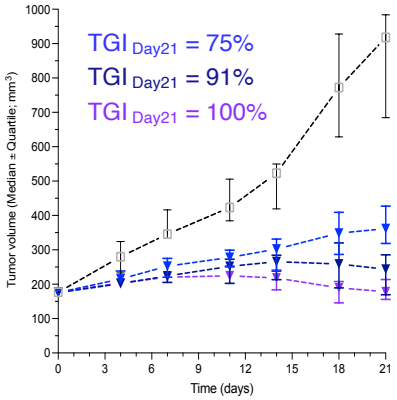
KRAS^{G12V} PANC — Capan-2



N=12

- **MEDIAN** Vehicle 0 mg/kg BID po
- **MEDIAN** 100 mg/kg IMM-01-00104 BID po
- **MEDIAN** 150 mg/kg IMM-01-00104 BID po

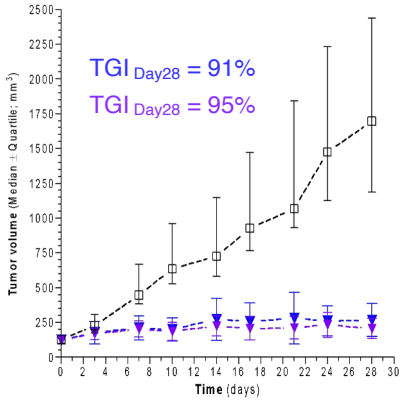
NRAS^{Q61R} MEL — SK-MEL-2



N=12

- **MEDIAN:** 0 mg/kg Vehicle BID po
- **MEDIAN:** 100 mg/kg IMM-1-104 BID po
- **MEDIAN:** 125 mg/kg IMM-1-104 BID po
- **MEDIAN:** 150 mg/kg IMM-1-104 BID po

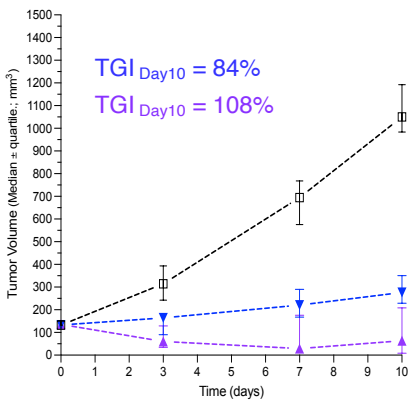
KRAS^{G12S} NSCLC — A-549



N=12

- **MEDIAN** Vehicle 0 mg/kg BID po
- **MEDIAN** 100 mg/kg IMM-01-00104 BID po
- **MEDIAN** 150 mg/kg IMM-01-00104 BID po

KRAS^{G12D} CRC — Colon-26



N=8

- **MEDIAN** Vehicle 0 mg/kg BID po
- **MEDIAN** 100 mg/kg IMM-01-00104 BID po
- **MEDIAN** 150 mg/kg IMM-01-00104 BID po

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

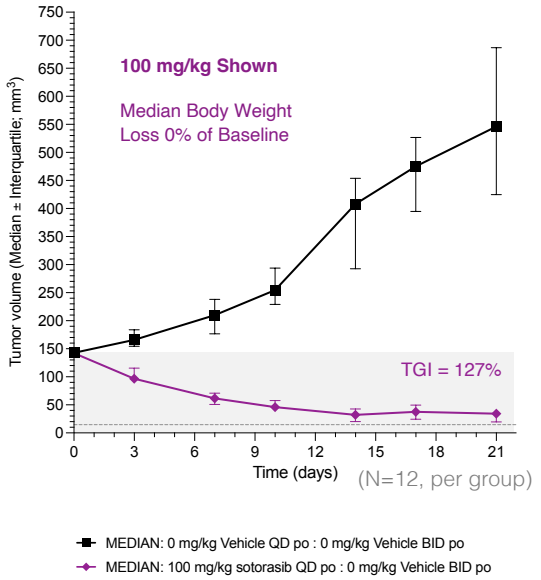
Tumor Growth Inhibition (TGI) % = [1 – (Ti – T0)/(Ci – C0)]x100 ; T = treatment groups ; C = control groups
*Well-tolerated at top doses with no more than 3-6% median body weight loss (BWL)
**Capan-2 PANC model, as reported at ASCO 2022 (0% TGI for sotorasib and adagrasib at top doses)

Pancreatic: Head-to-Head Comparison of IMM-1-104 +/- Sotorasib in a KRAS-G12C Pancreatic Tumor Model

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

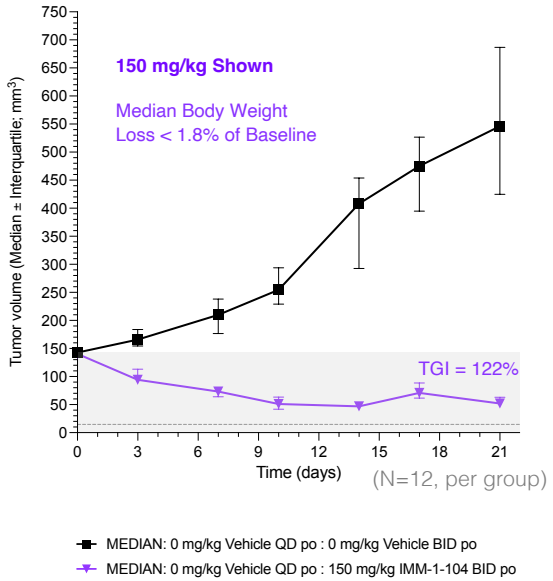
Sotorasib

10-30-100 mg/kg QD p.o.)



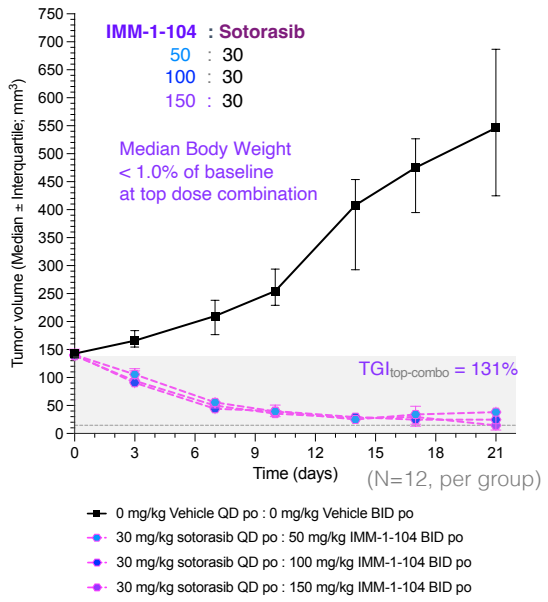
IMM-1-104

(50-100-150 mg/kg BID p.o.)



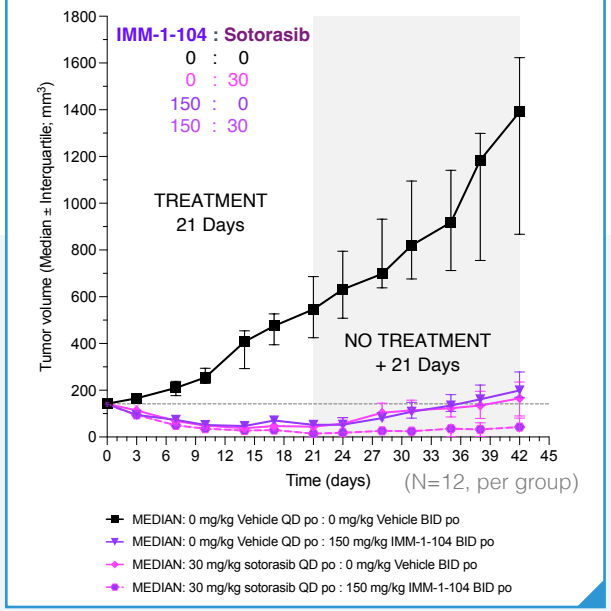
IMM-1-104 + Sotorasib

(50-100-150 mg/kg BID + 30 mg/kg QD)



IMM-1-104 + Sotorasib

(150 mg/kg BID + 30 mg/kg QD)



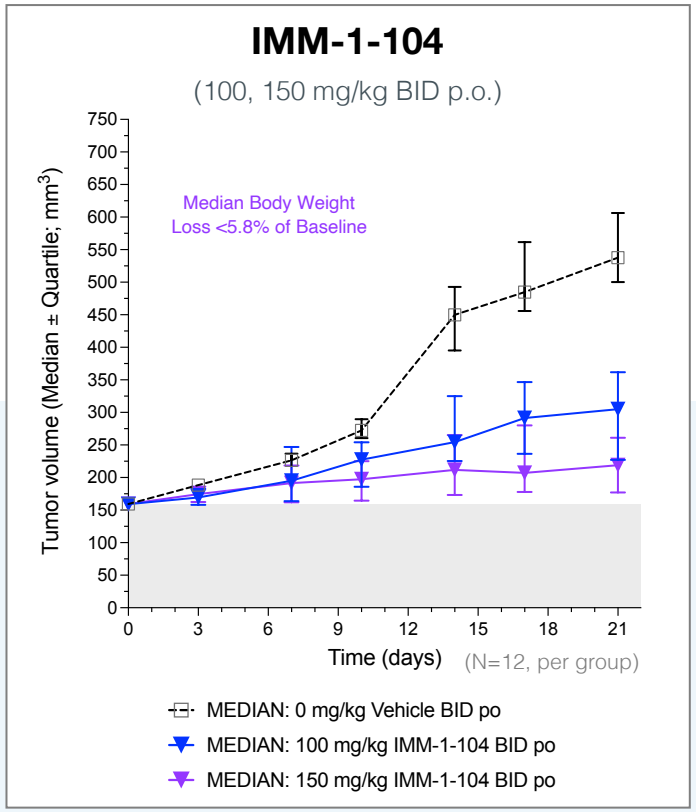
› MIA PaCa-2 ($KRAS^{G12C}$) Pancreatic Xenograft Tumor Model in Athymic Nude Mice

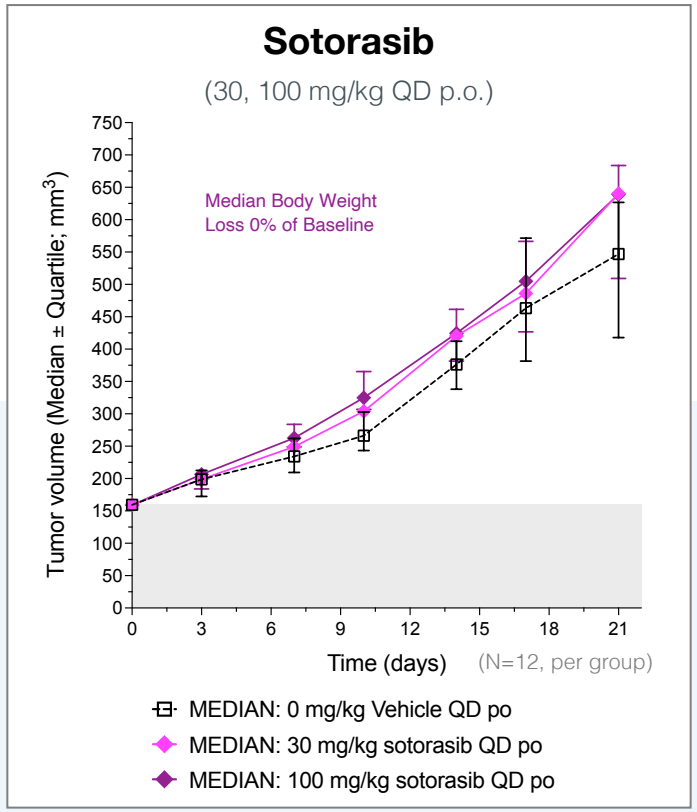
› *Sotorasib was commercially purchased*

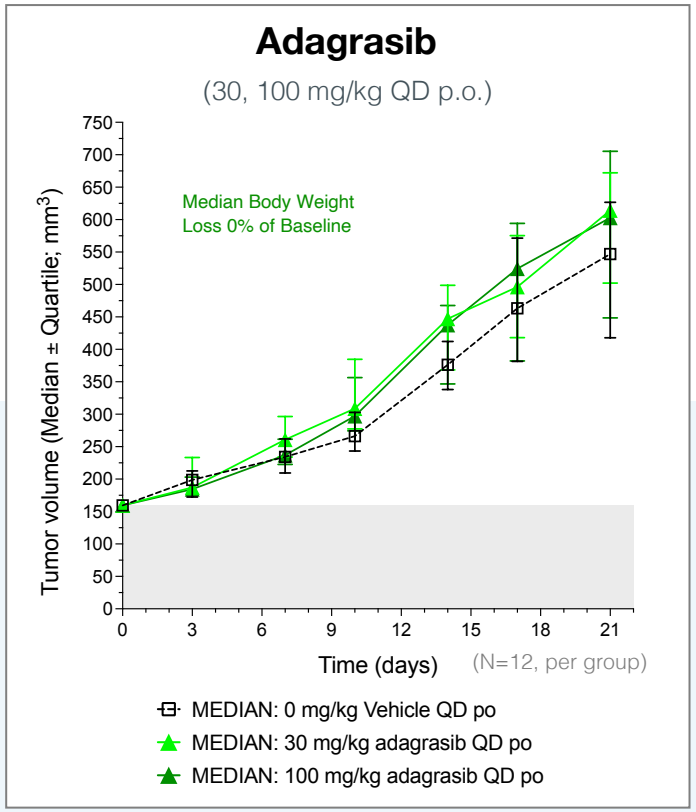
Tumor Growth Inhibition (TGI) % = $[1 - (T_i - T_0)/(C_i - C_0)]x100\%$; Expanded TGI formula vs. previous 1-[T/C]x100% method

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 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) % = $[1 – (T_i – T_0)/(C_i – C_0)]x100\%$; Expanded TGI formula vs. previous 1-[T/C]x100% method

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

Summary of phase 3 data from the NEMO study as reported in Lancet (c.2017)

	Progression Free Survival	Overall Survival
Binimetinib	2.8 months	11.0 months
Hazard Ratio	0.62	1.00
Dacarbazine	1.5 months	10.1 months

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%)

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

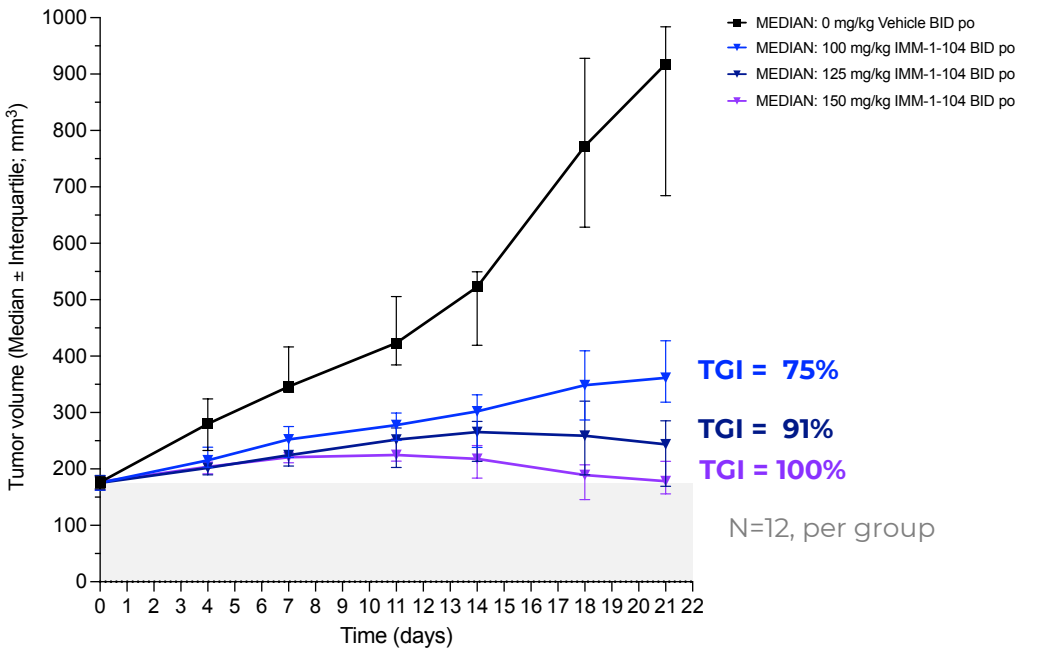
Dummer, et al 2017 Lancet S1470-2045 (17) 30180-8

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)

IMM-1-104

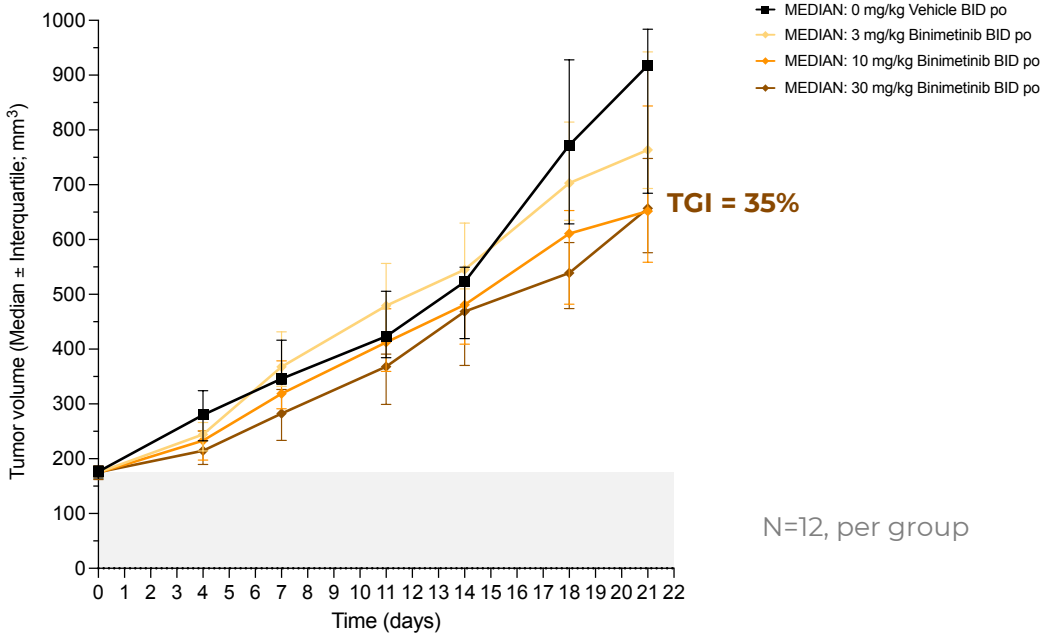
(100-125-150 mg/kg BID p.o.)



N=12, per group

Binimetinib

(3-10-30 mg/kg BID p.o.)



N=12, per group

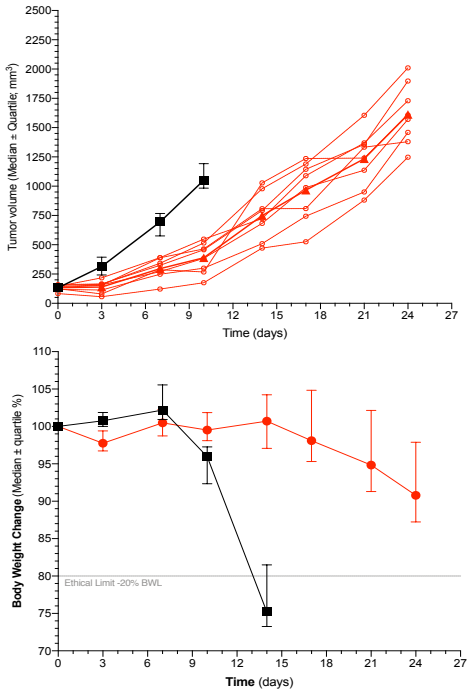
SK-MEL-2 (NRAS-Q61R) Melanoma Xenograft Tumor Model in Athymic Nude Mice

Binimetinib was commercially purchased

CRC: Head-to-Head Comparison of IMM-1-104 Against Selumetinib and Binimetinib in a KRAS-G12D CRC Syngeneic Mouse Tumor Model

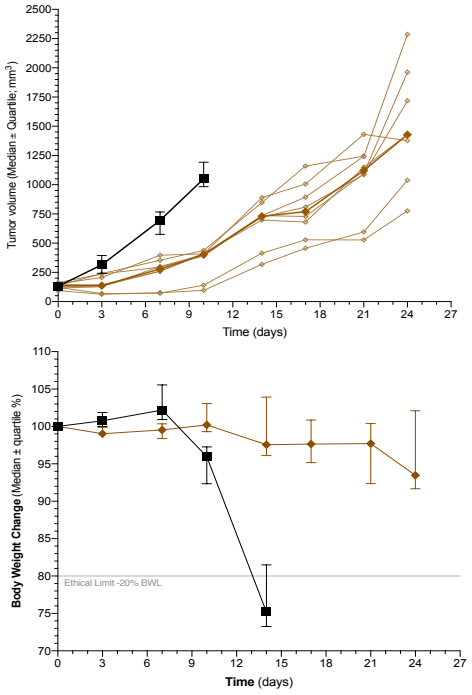
IMM-1-104 demonstrated greater tumor growth inhibition (TGI), lower body weight loss (BWL) and greater durability via reductions in tumor volume (TV)

Selumetinib
(FDA approved)



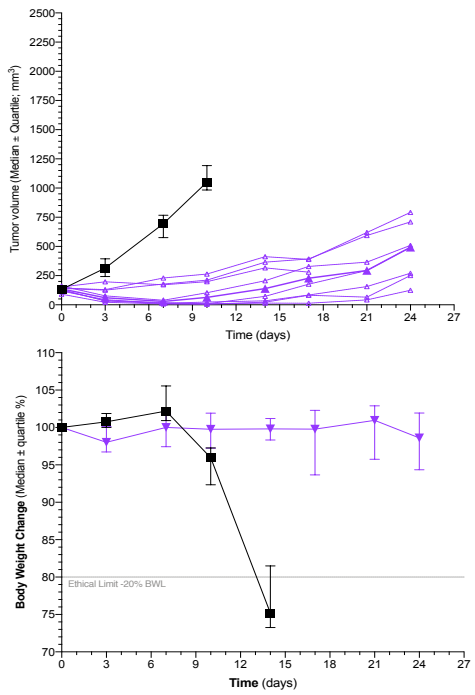
N=8, per group

Binimetinib
(FDA approved)



N=8, per group

IMM-1-104
(Clinical)



N=8, per group

Colon-26 (KRAS-G12D) Syngeneic Colorectal Tumor Model in Balb/c Mice

Selumetinib and binimetinib were commercially purchased
Tumor Growth Inhibition (TGI) % = [1 – (Ti – T0)/(Ci – C0)]x100%; Expanded TGI formula vs. previous 1-[T/C]x100% method

IMM-1-104: Phase 1/2 Clinical Trial Plan

Study 1 First Time in Humans

Dose Escalation - Phase 1a*

IMM-1-104
(Dual MEK inhibitor)

Bayesian Design (mTPI-2) escalation and dose evaluation in select solid tumor types[1]

May expand tolerated dose cohorts for a max of 42 patients treated in Phase 1

RP2D

IND cleared; First patient dosed on Nov 21, 2022

Dose Expansion - Phase 2a**

Expansion 1:

- **RAS mutated Melanoma** (~40 pts)

Expansion 2:

- **RAS Mutated Pancreatic (PAAD)** (~40 pts)

Expansion 3 & 4: *biomarker stratification*

- **RAS Mutated NSCLC-Adeno** (~40 pts)
- **RAS Mutated, APC *wt* CRC** (~40 pts)

* Solid tumor, all comer with evidence of RAS mutation
** Simon 2-Stage Design. Proposed tumor types may change based upon preclinical PGx studies and clinical function review

- MTD = Maximum Tolerated Dose;
- RP2D = Recommended Phase 2 Dose;
- PGx = Pharmacogenomics

Phase 1 Sites

A Phase 1/2a Study of IMM-1-104 in Participants With Previously Treated, RAS-Mutant, Advanced or Metastatic Solid Tumors

ClinicalTrials.gov Identifier: NCT05585320

United States, California	City of Hope › Duarte, California, United States, 91010 › Principal Investigator: Vincent Chung, MD
United States, New York	MD Weill Cornell Medicine › New York, New York, United States, 10021 › Principal Investigator: Anna Pavlick, DO
United States, Texas	MD Anderson Cancer Center › Houston, Texas, United States, 77030 › Principal Investigator: Shubham Pant, MD NEXT Oncology › San Antonio, Texas, United States. 78229 › Principal Investigator: David Sommerhalder, MD
United States, Virginia	NEXT Oncology › Fairfax, Virginia, United States, 22031 › Principal Investigator: Alex Spira, MD, PhD

Upcoming Potential Milestones

Program	Milestone	Expected Timing
IMM-1-104	Initial Phase 1 pharmacokinetic (PK) and safety data	Mid-2023
IMM-1-104	Initial Phase 1 pharmacodynamic (PD) modeling data and additional PK and safety data	2H 2023
IMM-1-104	RP2D and Safety data	Mid-2024
IMM-1-104	Additional trial updates	On a periodic basis
IMM-6-415	IND filing	4Q 2023

IMM-6-415

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

$NRAS^{Q61R}$ MEL — SK-MEL-2

$BRAF^{V600E}$ MEL — A-375

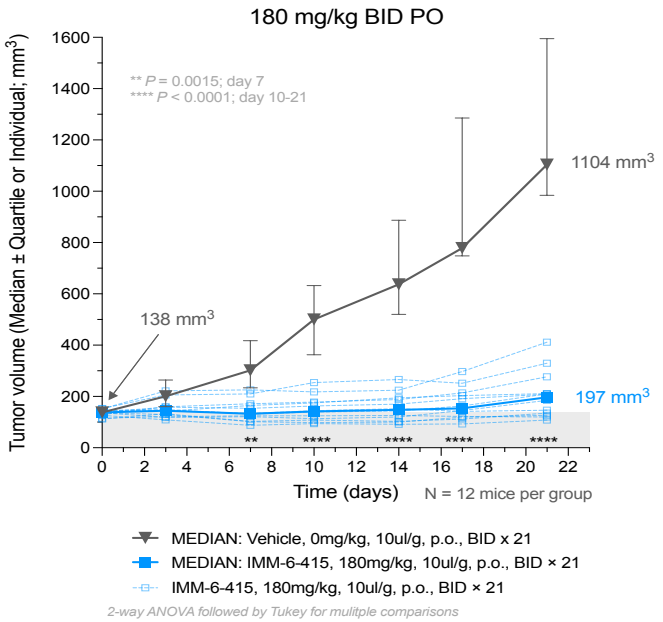
$BRAF^{V600E}$ MEL — SK-MEL-28

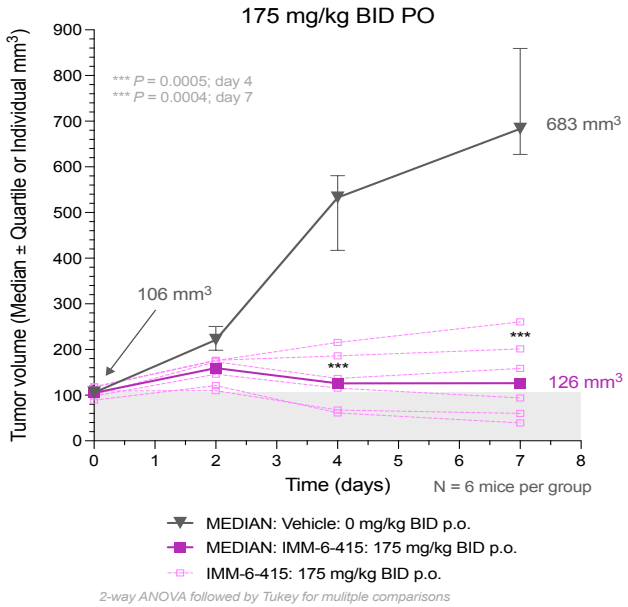
$KRAS^{G12S}$ NSCLC — A-549

$KRAS^{G12D}$ 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

Accelerated Cadence of IMM-6-415 Enhances Activity of Checkpoint Inhibitors

KRAS^{G12D} CRC

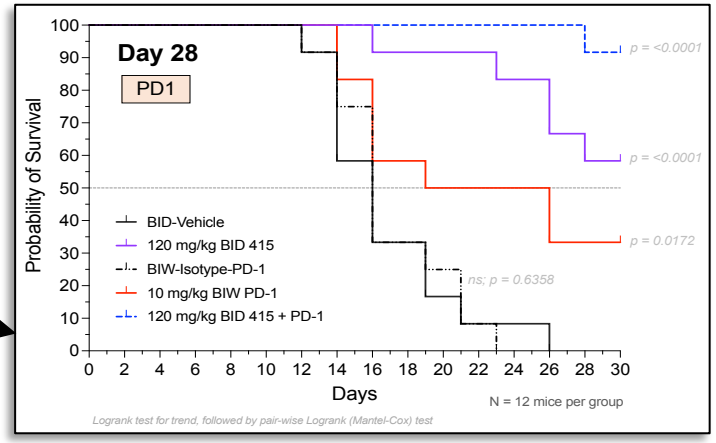
Syngeneic CT-26 Model

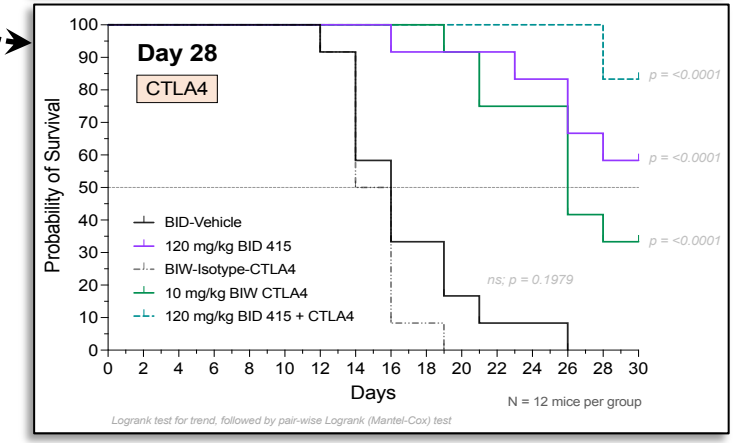
Schedule	Dose (mg/kg)	Veh	αPD-1 (BIW)	αCTLA-4 (BIW)	IMM-6-415	IMM-6-415 + PD-1	IMM-6-415 + CTLA-4
BID	120	**0/12**			**7/12**	**11/12**	**10/12**
BID	60	**0/12**			**0/12**	**8/12**	**8/12**
BID	30	**0/12**			**0/12**	**5/12**	**5/12**
QD	120	**0/12**			**0/12**	**7/12**	**7/12**
QD	60	**0/12**			**1/12**	**4/12**	**8/12**
QD	30	**0/12**			**0/12**	**6/12**	**7/12**
BIW	10	**0/12**	**4/12**				
BIW	10	**0/12**		**4/12**			

- Number of BALB/c mice (out of 12) with tumors through Day 28 with volumes lower than 2,000 mm^3

Monotherapy Treated Alive at Day 28

Combination ≥ 3 Advantage





Cyclic disruption of MEK improves overall survival with check point inhibitors (SITC 2022)

Presented at SITC (Nov. 2022): RAS wild type MC38 IO model ≥3 advantage only observed in IMM-6-415 (120 p.o. BID) + anti-PD-1

Corporate

Immuneering

Finance & Intellectual Property

Finance

- Cash, cash equivalents and marketable securities as of December 31, 2022: **$105.5M**
- **Cash runway into Q4 2024** supports:
  - IMM-1-104:
  - Multiple data readouts from Phase 1/2a trial
  - IMM-6-415:
    - Anticipate IND filing in Q4 2023
  - Research in additional oncology programs

Intellectual Property

Patents issued/pending:

- Pending U.S. and ex-U.S. applications relating to IMM-1-104
- Pending U.S. provisional and PCT applications relating to IMM-6-415
- Issued U.S. patent and pending application relating to DCT
- Pending U.S. applications to Fluency

Expected patent expiration:
(excluding patent term adjustments, etc.)

- IMM-1-104 = 2041
- IMM-6-415 = 2043
- DCT = 2039
- Fluency = 2039

Immuneering

Investment Summary

"Our approach is different."

- Targeting **large Universal-RAS** patient population (1.5M) versus more limited approaches.
- **Monotherapy** vs combination therapy potential
- **Deep cyclic inhibition** achieved briefly but forcefully, due to combination of:
  - **Manyfold higher C_{MAX}** and
  - **short half life**
- Approach designed to **spare healthy cells** and potential to **limit adaptive resistance**.

"IMM-1-104 demonstrates Universal-RAS potential."

- **Robust preclinical activity** observed in:
  - Pancreatic Cancer ($KRAS^{G12C}$)
  - NSCLC ($KRAS^{G12S}$)
  - CRC ($KRAS^{G12D}$)
  - Melanoma ($NRAS^{Q61R}$)
  - And others
- Hypothesis for IMM-1-104 from **proprietary model**.
- **Validated using** proprietary **bioinformatics & 3D tumor growth assays**

"2023 is shaping up to be our breakout year."

- **First patient dosed** in Phase 1/2a trial of lead asset IMM-1-104 in November 2022.
- **Patient enrollment ongoing**; investigator enthusiasm high.
- Broad inclusion **criteria facilitates** rapid trial enrollment.
- **Upcoming data readouts, beginning mid-2023**
- **Cash runway projected into Q4 2024**

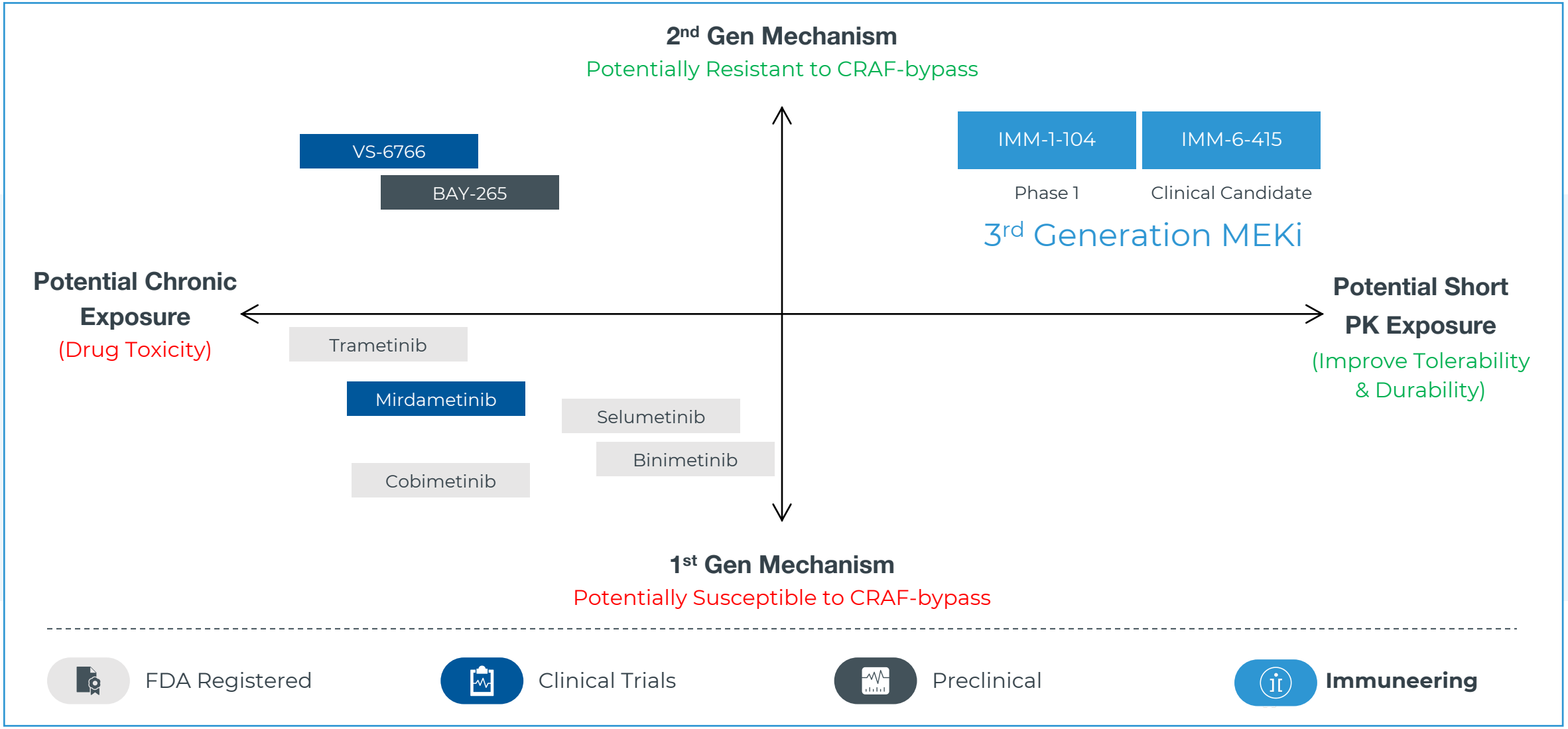
Appendix

Immuneering

Nasdaq: IMRX

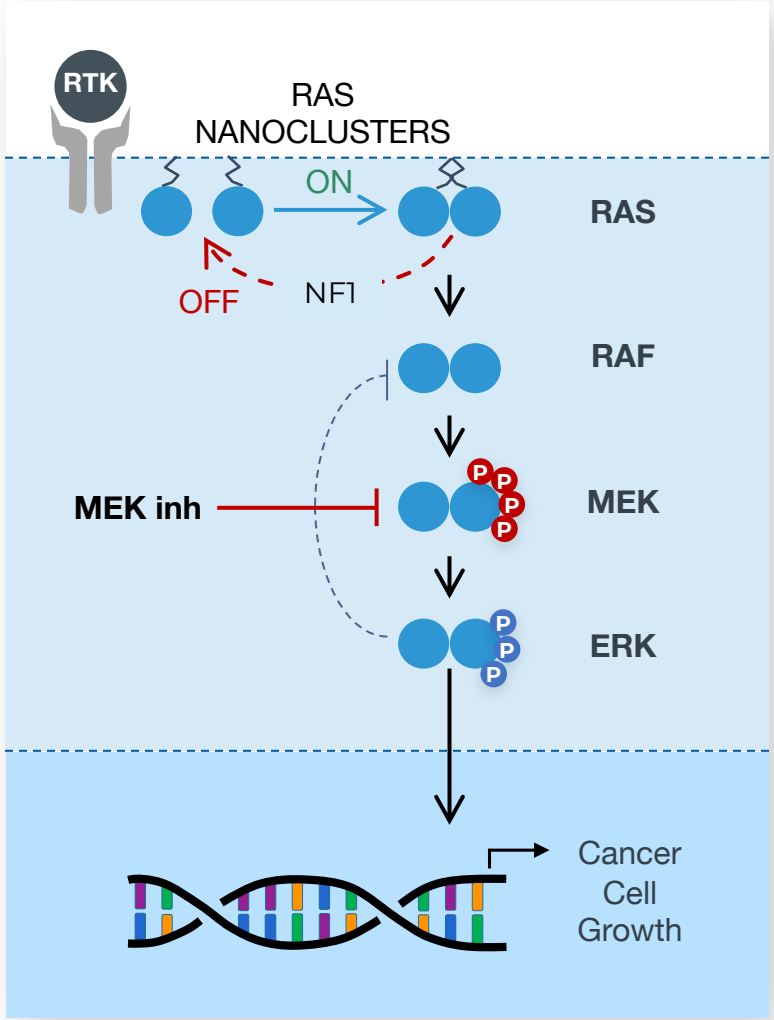
March 2023

Differentiation Versus Other MEK Inhibitors

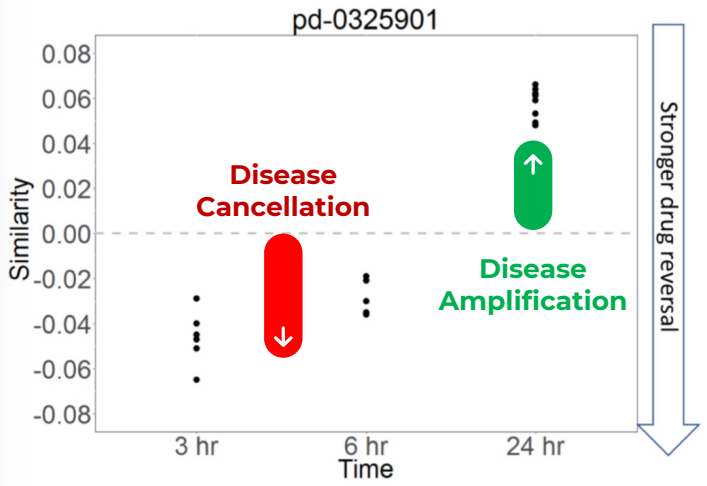


Our Platform Converts Gene Expression to Counterintuitive Insights

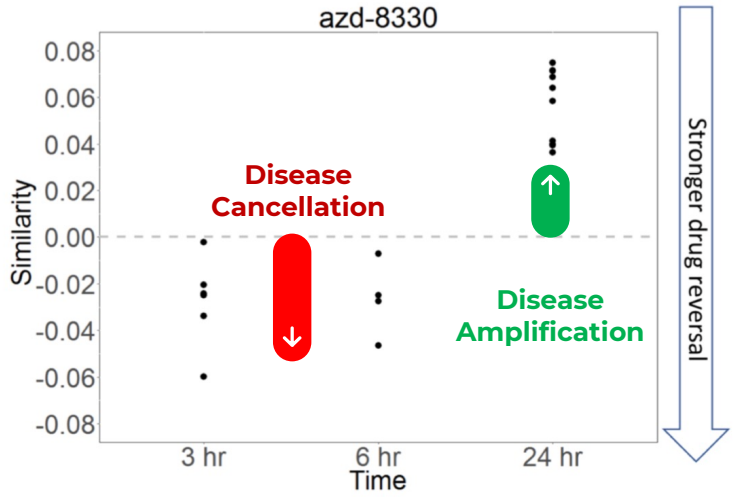
Goal: achieve **broader activity** and **better tolerability** in RAS and beyond mutant disease



1st generation MEKi



1st generation MEKi



Note: dots are representative of various concentrations

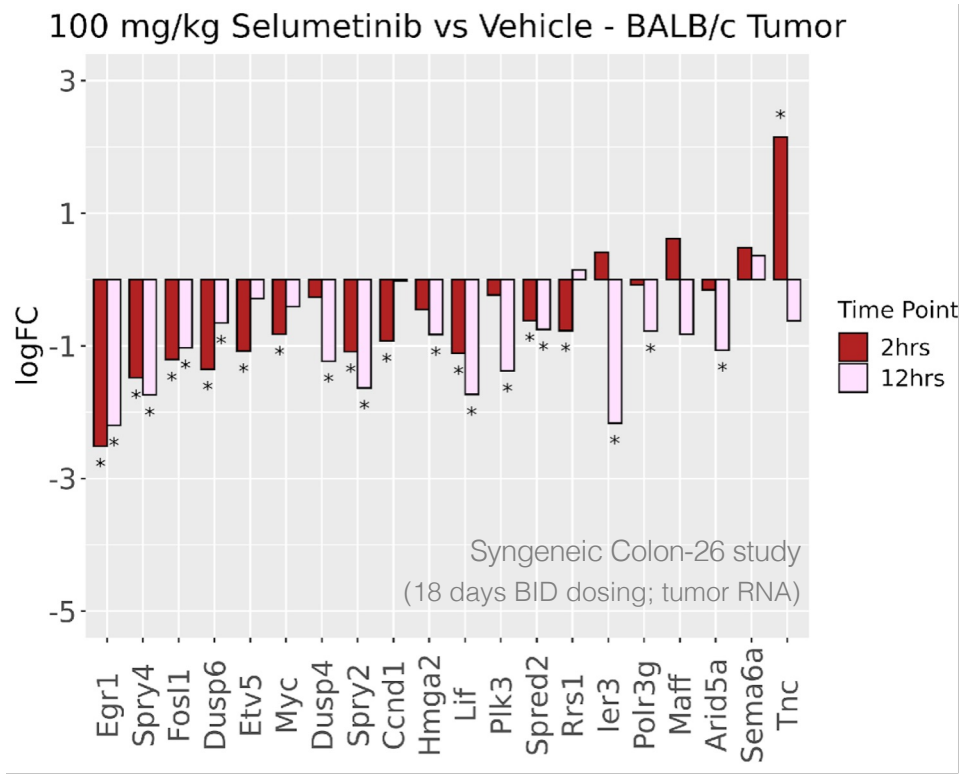
› *IMRX Disease Cancelling Technology - US Patent 11,043,305*

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

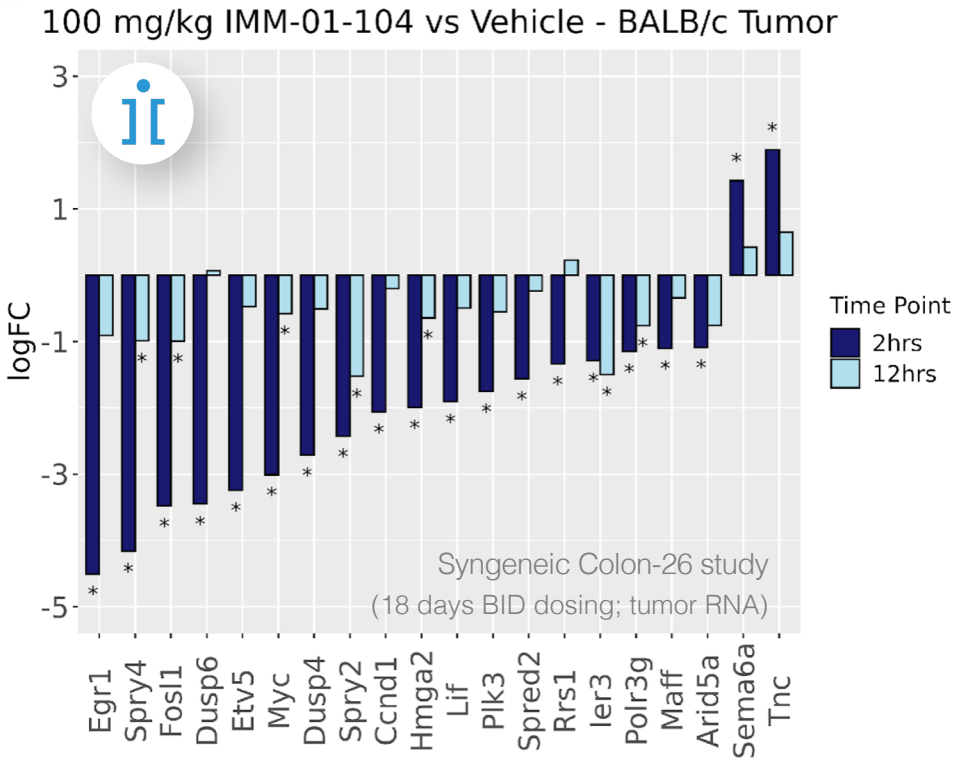
Deep Cyclic Inhibition Confirmed Using Transcriptomics

Traditional Approach



Chronic Suppression → TOXICITY

Signaling Dynamics



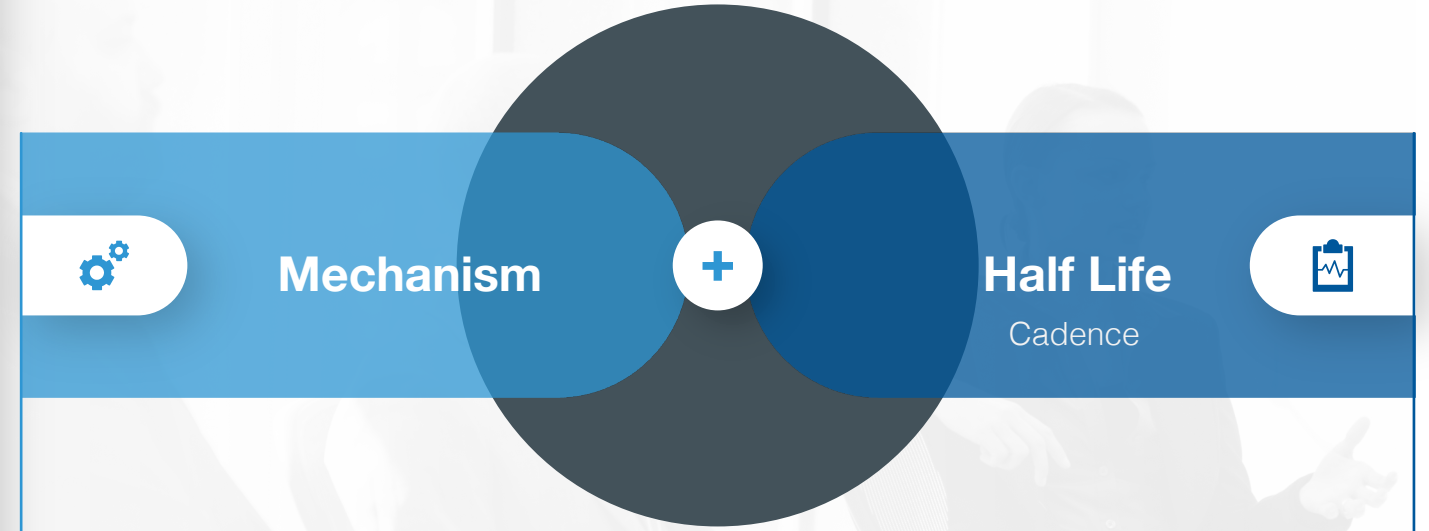
Cyclic Disruption → TOLERABILITY

IMM-1-104 is a Dual-MEK Inhibitor

Goal

deep, cyclic inhibition with ability to prevent MEK-reactivation (improve tolerability and activity)

IMM-1-104

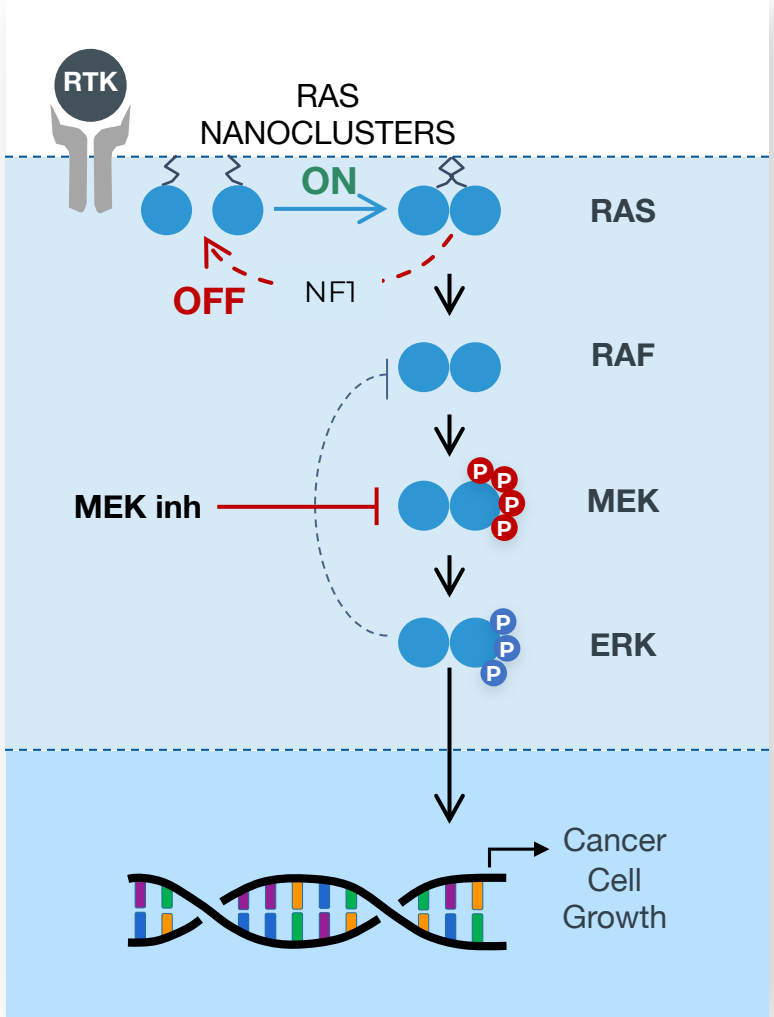


Resists CRAF-bypass in RAS mutant tumors
(↓ pERK and pMEK)

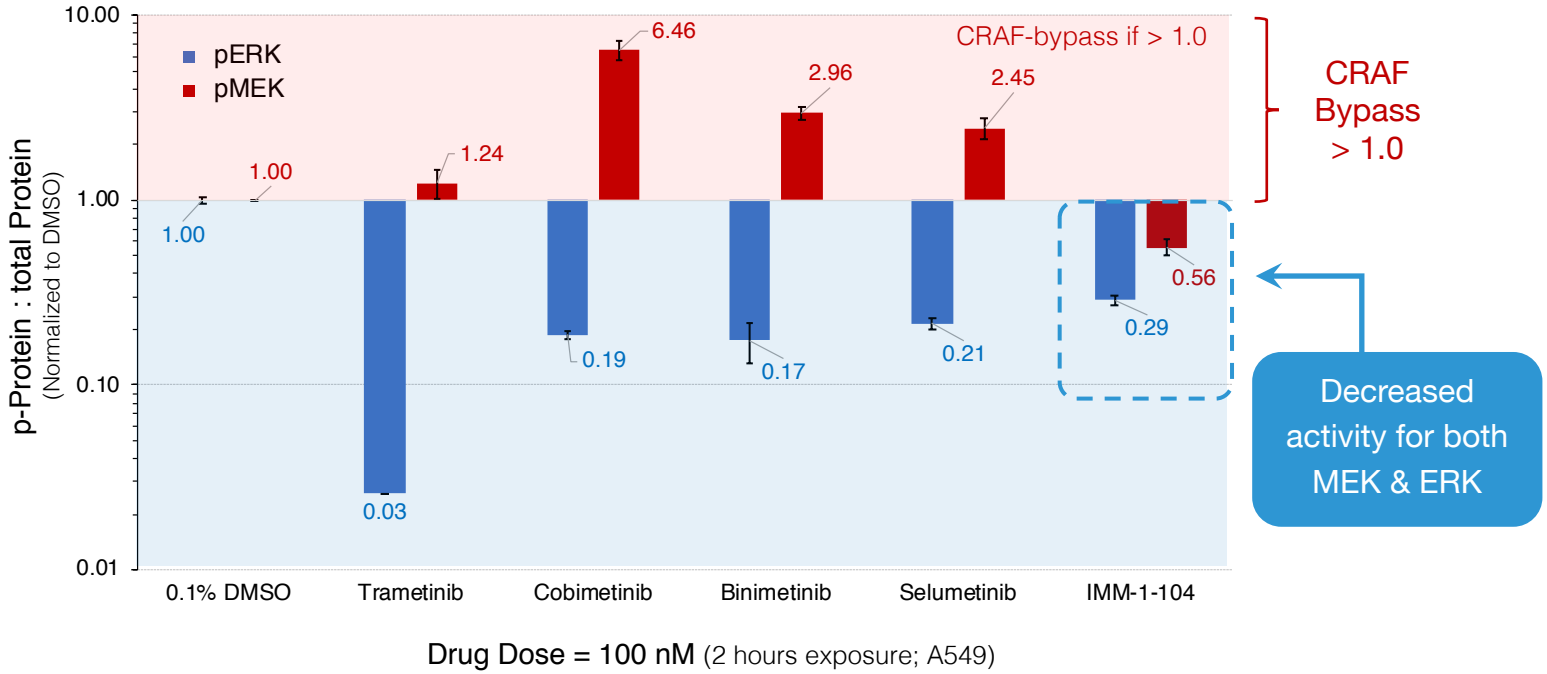
Short plasma half life to minimize drug trough
(~ 1 to 2 hours $t_{1/2}$)

Ideal Dosing Schedule: ≥ 7-8 half lives between doses
(BID for < 1.5 hr $t_{1/2}$; QD for 2 to 3 hr $t_{1/2}$)

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



A549KRAS-mut Lung Cancer: pERK and pMEK



Drug Dose = 100 nM (2 hours exposure; A549)

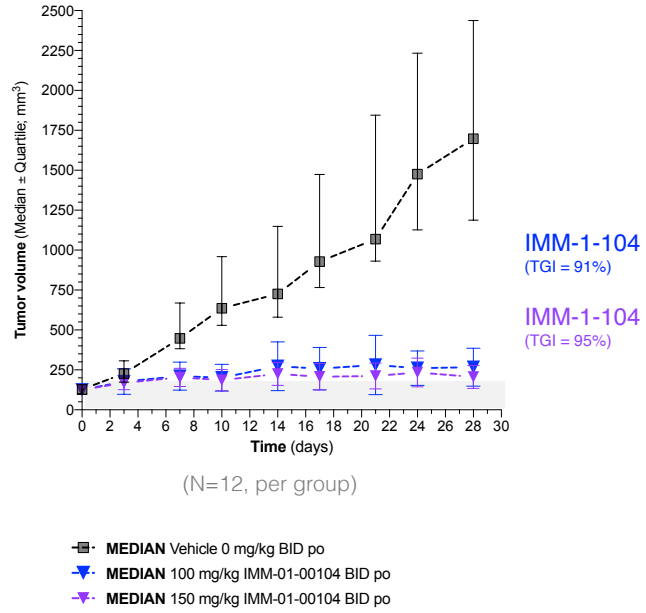
- ***FDA-Approved MEK inhibitors:*** *Trametinib, Cobimetinib, Binimetinib, Selumetinib commercially purchased*

Head-to-Head Comparison of IMM-1-104 Against Binimetinib +/- Encorafenib in KRAS-G12S NSCLC Tumor Model

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

IMM-1-104

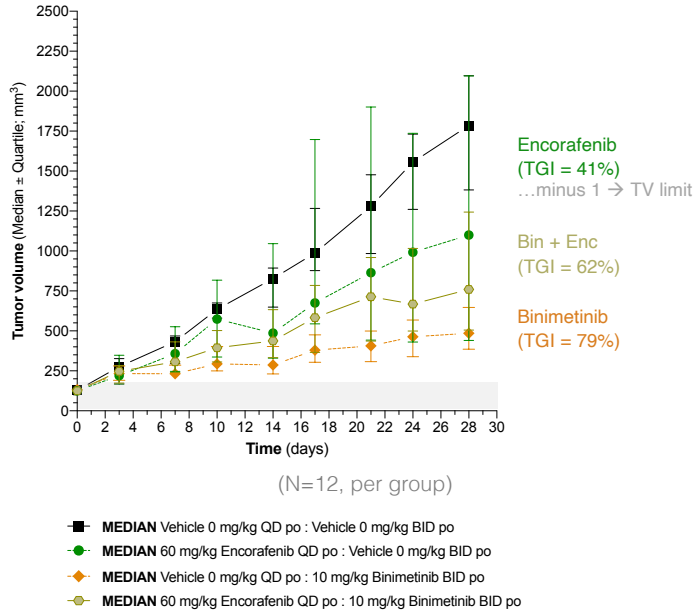
(150 mg/kg BID p.o.)



(N=12, per group)

Binimetinib + Encorafenib

(10 mg/kg BID + 60 mg/kg QD p.o.)



(N=12, per group)

- A549 ($KRAS^{G12S}$) NSCLC Xenograft Tumor Model in Athymic Nude Mice
- Binimetinib and encorafenib were commercially purchased

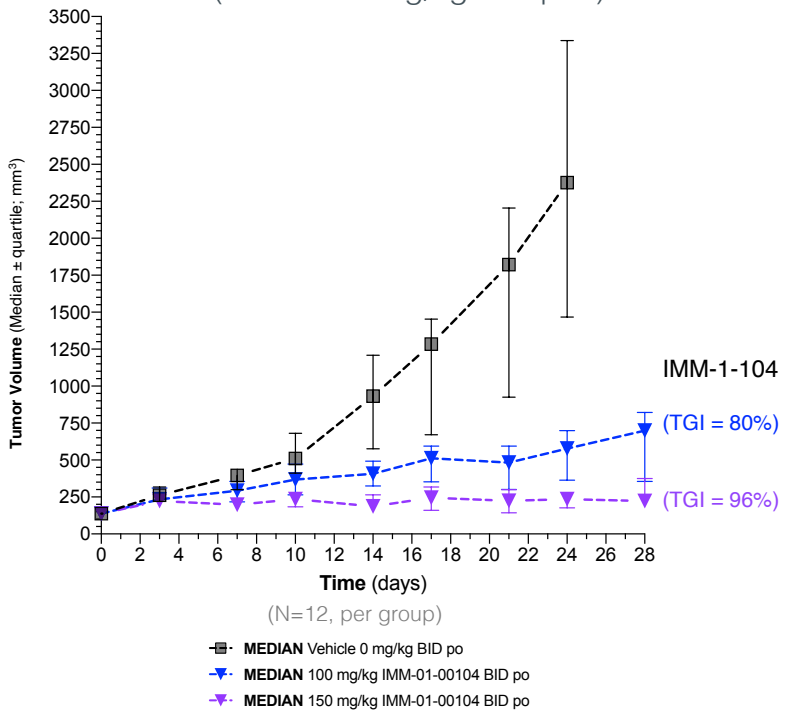
- *Tumor Growth Inhibition (TGI) % = $[1 – (T_i – T_0)/(C_i – C_0)]x100\%$; Expanded TGI formula vs. previous 1-[T/C]x100% method*
- *Human Dose Equivalent (HDE) binimetinib = 1-3 mg/kg BID*

Head-to-Head Comparison of IMM-1-104 versus Binimetinib +/- Encorafenib in BRAF-V600E Melanoma Tumor Model

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

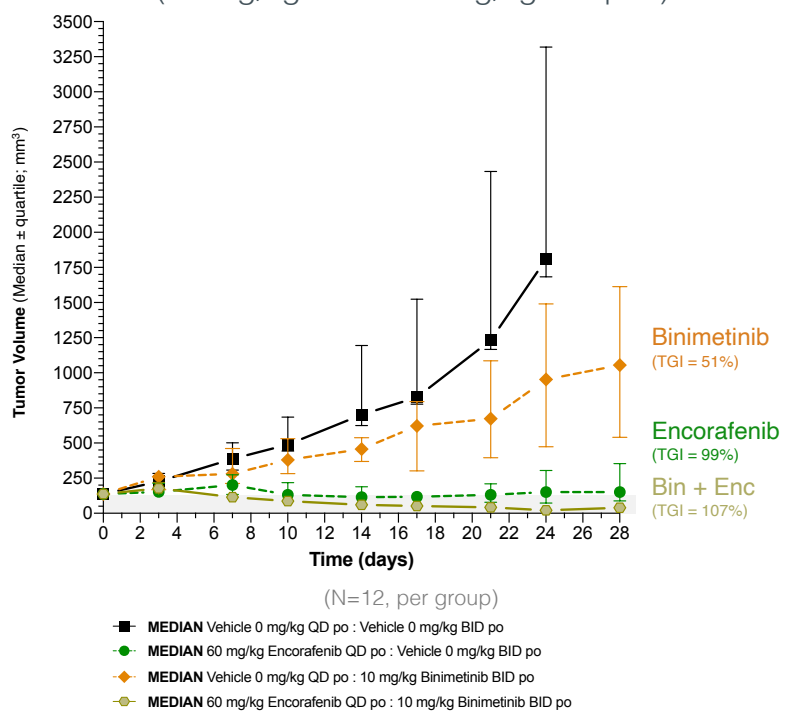
IMM-1-104

(100 & 150 mg/kg BID p.o.)



Binimetinib + Encorafenib

(10 mg/kg BID + 60 mg/kg QD p.o.)



- A375 ($BRAF^{V600E}$) Melanoma Xenograft Tumor Model in Athymic Nude Mice
- Binimetinib and encorafenib were commercially purchased

- *Tumor Growth Inhibition (TGI) % = $[1 - (T_i - T_0)/(C_i - C_0)]x100\%$; Expanded TGI formula vs. previous 1-[T/C]x100% method*
- *Human Dose Equivalent (HDE) binimetinib 1-3 mg/kg BID*

Conclusions (NRAS mutant Melanoma)

In the phase 3 NEMO study published in Lancet (c. 2017), binimetinib failed to substantially improve overall survival vs. dacarbazine (11.0 vs. 10.1 months) in NRAS mutant melanoma patients and led to a ~50% increase in serious adverse events (34% vs. 22%).

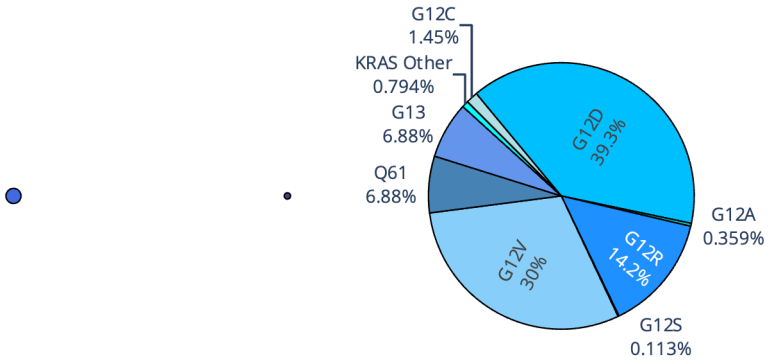
The most common NRAS mutation in the NEMO study was Q61R. We further compared binimetinib vs. IMM-1-104 in vivo using SK-MEL-2 (NRAS-Q61R).

Collectively, our data suggest that binimetinib may not effectively control MAPK pathway reactivation in RAS mutant tumors. In contrast, the deep cyclic inhibition combined with a dual-MEK mechanism of action of IMM-1-104 may offer a unique therapeutic advantage over first generation MEK inhibitors in RAS mutant tumors.

RAS Mutation Profiles Within Select Tumor Indications

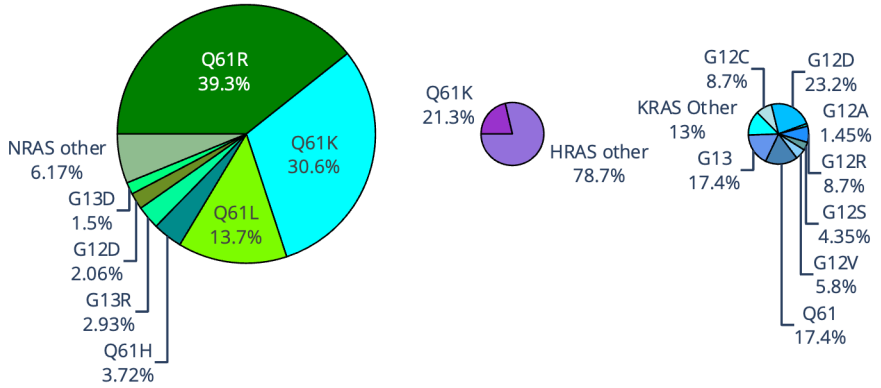
Pancreatic Cancer

NRAS = 0.34% HRAS = 0.06% KRAS = 99.60%



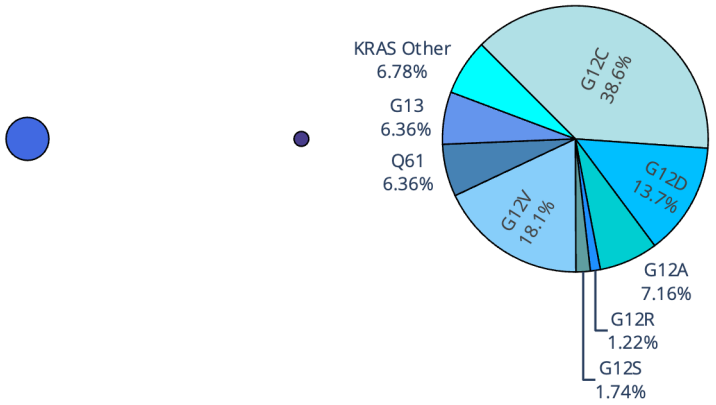
Melanoma

NRAS = 89.14% HRAS = 5.29% KRAS = 5.57%



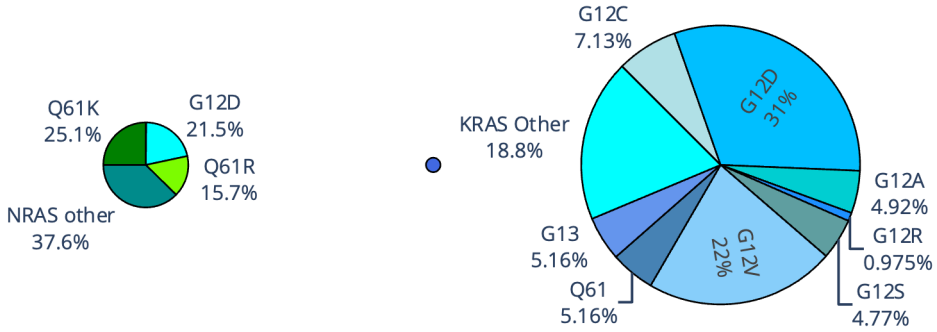
Lung Cancer

NRAS = 2.67% HRAS = 0.31% KRAS = 97.02%



Colorectal Cancer

NRAS = 8.25% HRAS = 0.24% KRAS = 91.51%



- *Based on given tumor type of patients with RAS-mutated tumors in the AACR GENIE database, v13.0*
- *Each RAS paralogue shown as percent overall RAS mutant tumors within each indication*
- *Presented at 2023 AACR: Targeting RAS. Kolitz, et al. (Philadelphia, PA)*

Immuneering

KRAS Mutant Pancreatic (PAAD): Translational Opportunity

Translational Step: Assess sensitivity of a panel of cell lines in the 3D-TGA; determine key mutations present in each

Bioinformatics Step: How many patients does each cell line represent, based on key mutations present in each

of 5,736

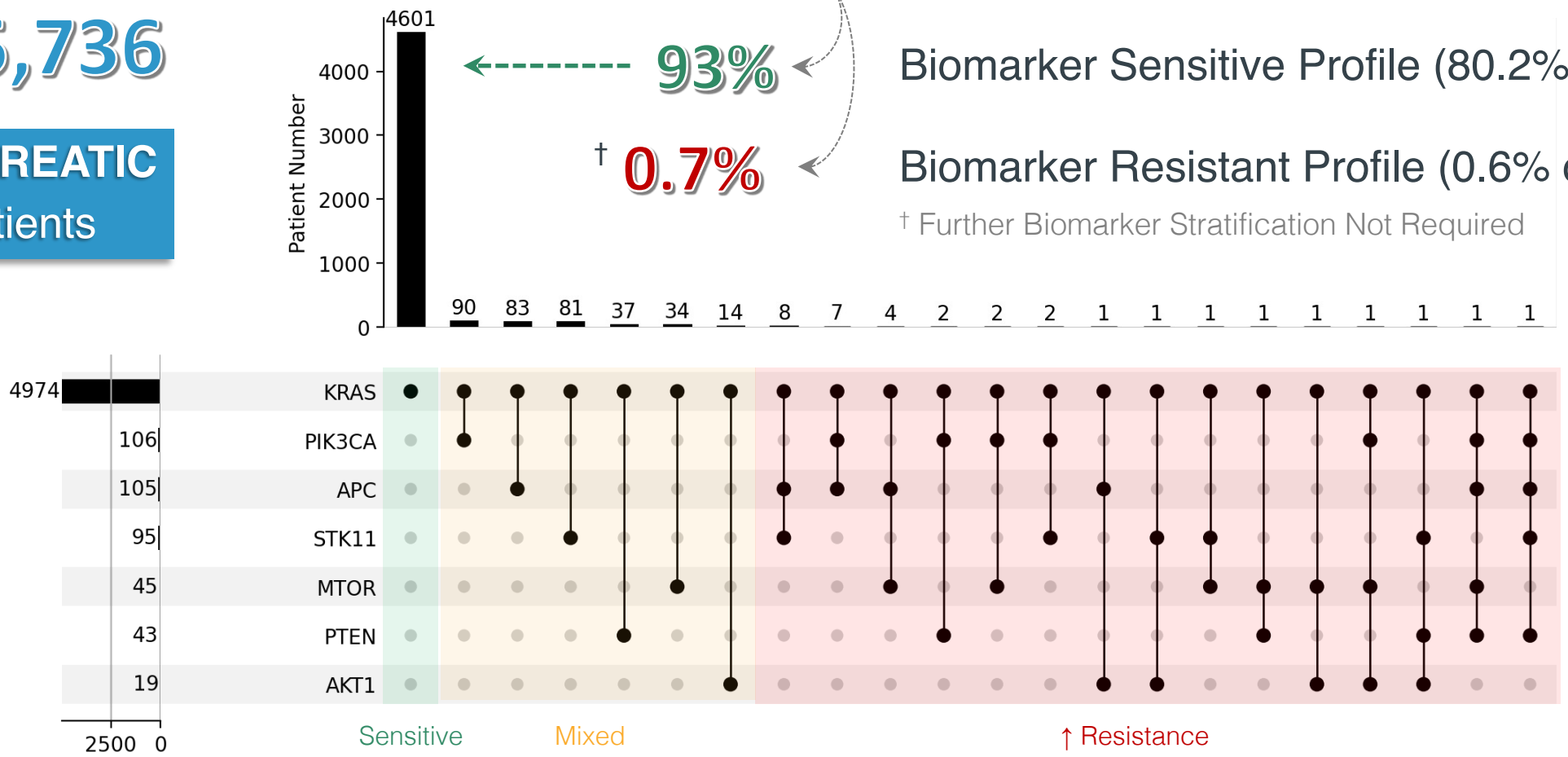
PANCREATIC Patients

87% Have Altered KRAS: Biomarker Positive

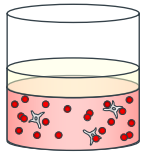
93% Biomarker Sensitive Profile (80.2% overall)

† 0.7% Biomarker Resistant Profile (0.6% overall)

† Further Biomarker Stratification Not Required



Patient mapping with 3D-TGA



GENIE cohort v13.0-public

The AACR Project GENIE Consortium. AACR Project GENIE: Powering Precision Medicine Through An International Consortium, Cancer Discov. 2017 Aug;7(8):818-831

NRAS Mutant Melanoma: Translational Opportunity

Translational Step: Assess sensitivity of a panel of cell lines in the 3D-TGA; determine key mutations present in each

Bioinformatics Step: How many patients does each cell line represent, based on key mutations present in each

of 5,194

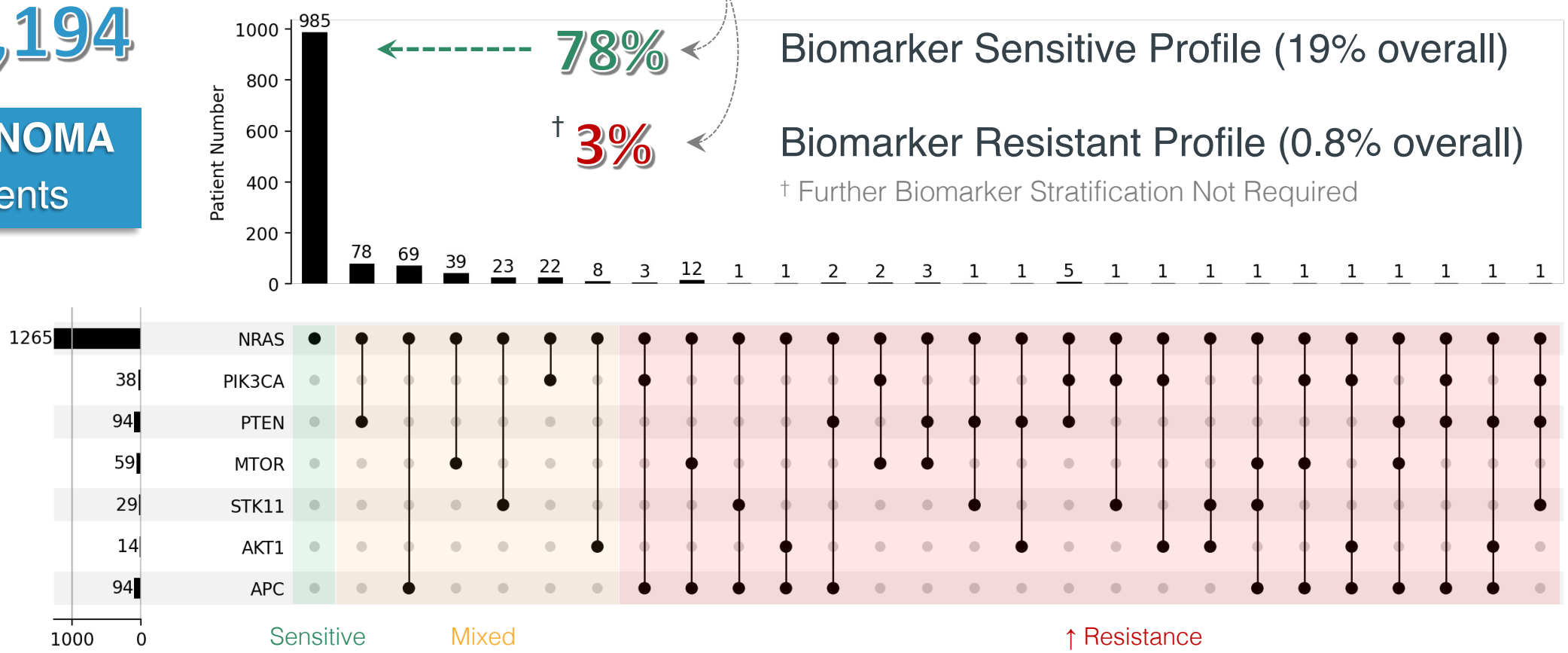
MELANOMA Patients

24% Have Altered NRAS: Biomarker Positive

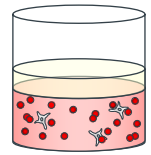
78% Biomarker Sensitive Profile (19% overall)

† 3% Biomarker Resistant Profile (0.8% overall)

† Further Biomarker Stratification Not Required



Patient mapping with 3D-TGA



GENIE cohort v13.0-public

The AACR Project GENIE Consortium. AACR Project GENIE: Powering Precision Medicine Through An International Consortium, Cancer Discov. 2017 Aug;7(8):818-831

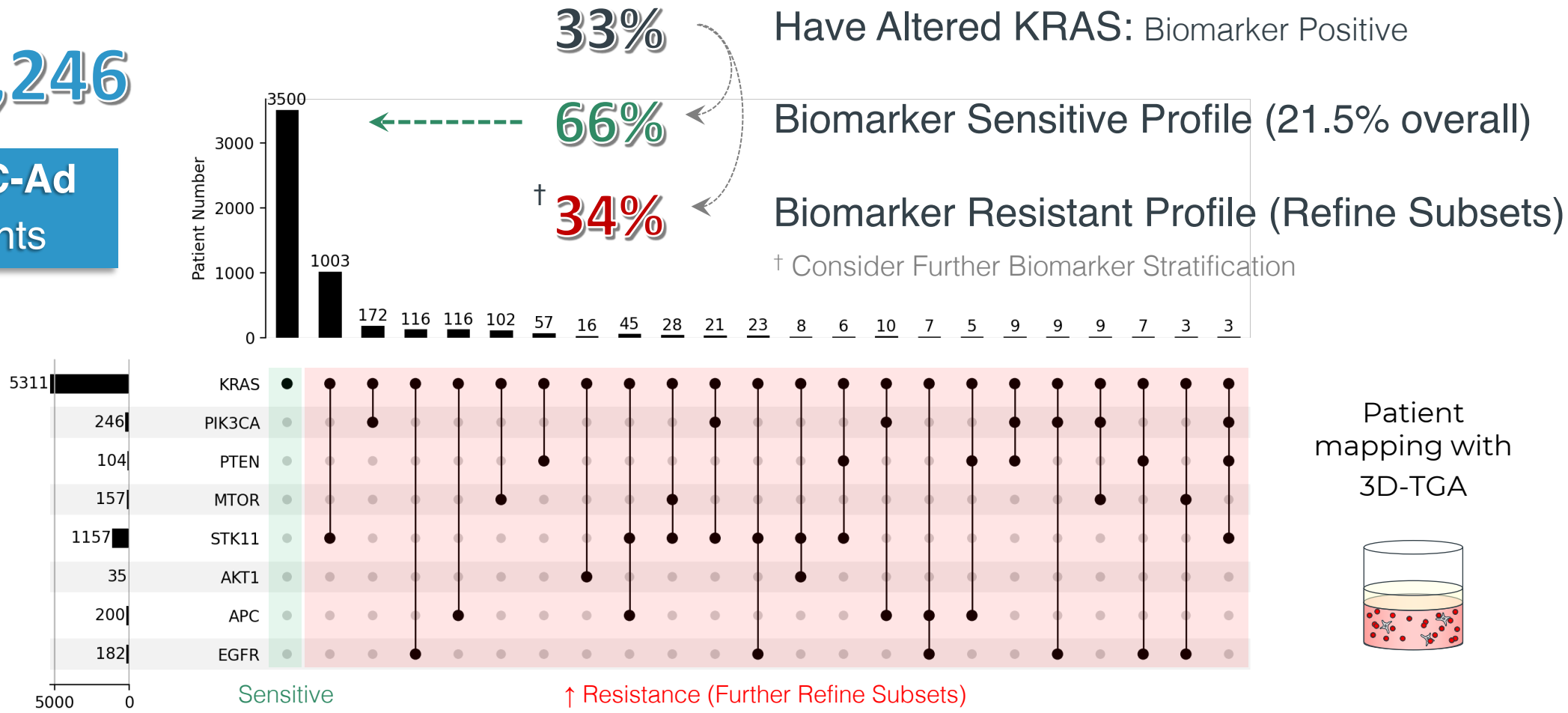
KRAS Mutant NSCLC (Adeno): Translational Opportunity

Translational Step: Assess sensitivity of a panel of cell lines in the 3D-TGA; determine key mutations present in each

Bioinformatics Step: How many patients does each cell line represent, based on key mutations present in each

of 16,246

NSCLC-Ad Patients



Patient mapping with 3D-TGA

GENIE cohort v13.0-public

The AACR Project GENIE Consortium. AACR Project GENIE: Powering Precision Medicine Through An International Consortium, Cancer Discov. 2017 Aug;7(8):818-831

KRAS Mutant CRC: Translational Opportunity

Translational Step: Assess sensitivity of a panel of cell lines in the 3D-TGA; determine key mutations present in each

Bioinformatics Step: How many patients does each cell line represent, based on key mutations present in each

of 14,356

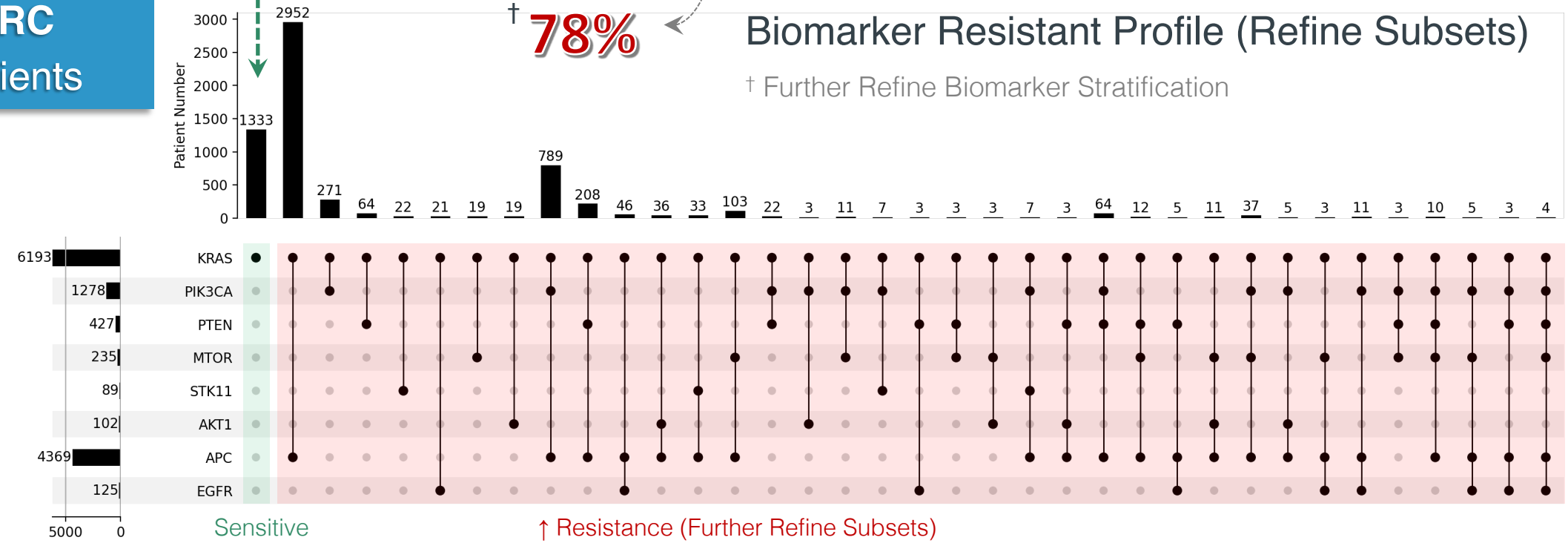
CRC Patients

43% Have Altered KRAS: Biomarker Positive

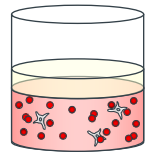
22% Biomarker Sensitive Profile (9.3% overall)

† **78%** Biomarker Resistant Profile (Refine Subsets)

† Further Refine Biomarker Stratification



Patient mapping with 3D-TGA



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The AACR Project GENIE Consortium. AACR Project GENIE: Powering Precision Medicine Through An International Consortium, Cancer Discov. 2017 Aug;7(8):818-831

Phase 1/2a Primary and Secondary Outcomes

Phase 1: Primary Outcomes

Safety

- Adverse Events (AEs)

Dose-limiting Toxicities

- Number of participants with dose limiting toxicities

Recommended Phase 2 Dose

- Selection of dose candidate

Phase 1/2a: Secondary Outcomes

C_{MAX}

- Maximum Observed Plasma Concentration

T_{MAX}

- Time to Reach Maximum Plasma Concentration

AUC

- Area Under Plasma Concentration Time Curve

Phase 2a: Primary Outcome

Overall Response Rate

- CR or PR based on RECIST 1.1

Phase 2a: Secondary Outcomes

Disease Control Rate

Progression Free Survival (PFS)

Duration of Response

Landmark 3-Month Survival

Landmark 6-Month Survival

Overall Survival (OS)