Initial Phase 1 PK, PD and Safety Data for IMM-1-104

Immuneering

Nasdaq: IMRX

AACR - APRIL 2023

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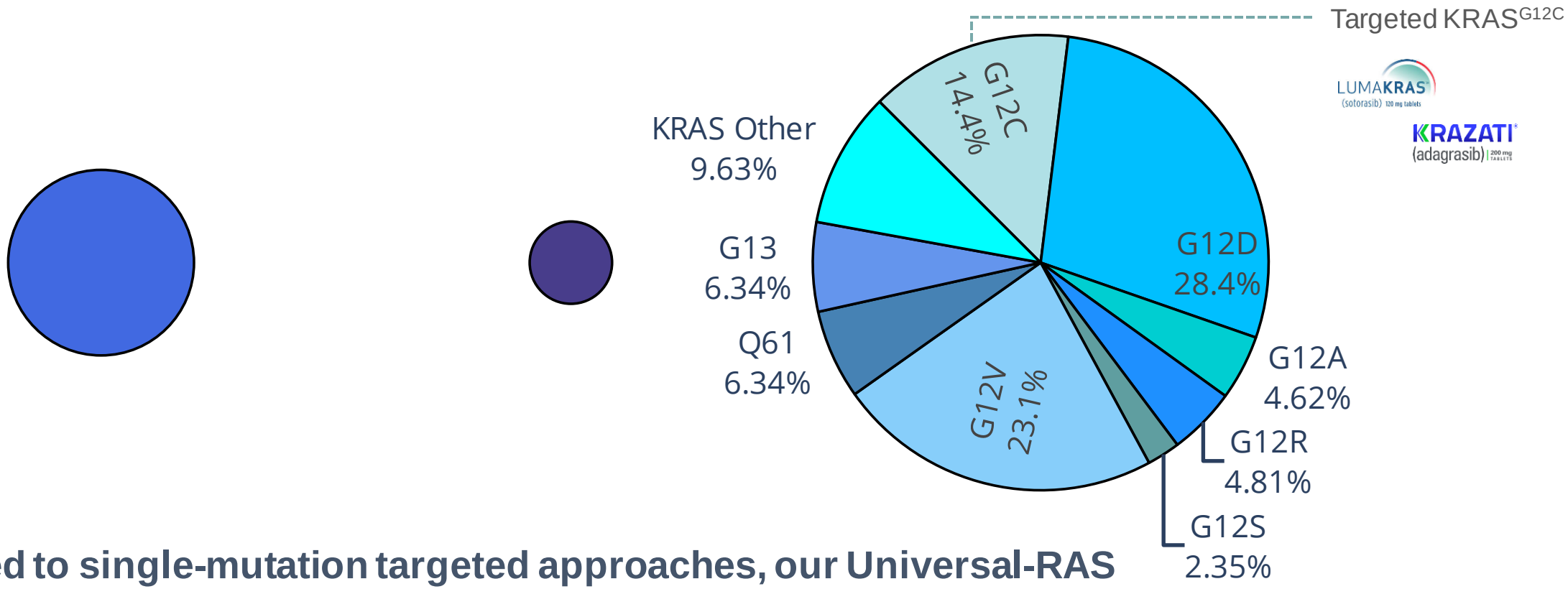
Data of trametinib, cobimetinib, binimetinib, selumetinib, encorafenib and AMG-510 (now known as sotorasib) as compared to IMM-1-104 presented in this presentation is based on head-to-head studies where these therapies have been purchased from commercial sources rather than the pharmaceutical company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

IMM-1-104's Potential: Universal-RAS

NRAS (14.12%)

HRAS (2.78%)

KRAS (83.10%)



Compared to single-mutation targeted approaches, our Universal-RAS approach potentially addresses a much larger patient population

- *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*

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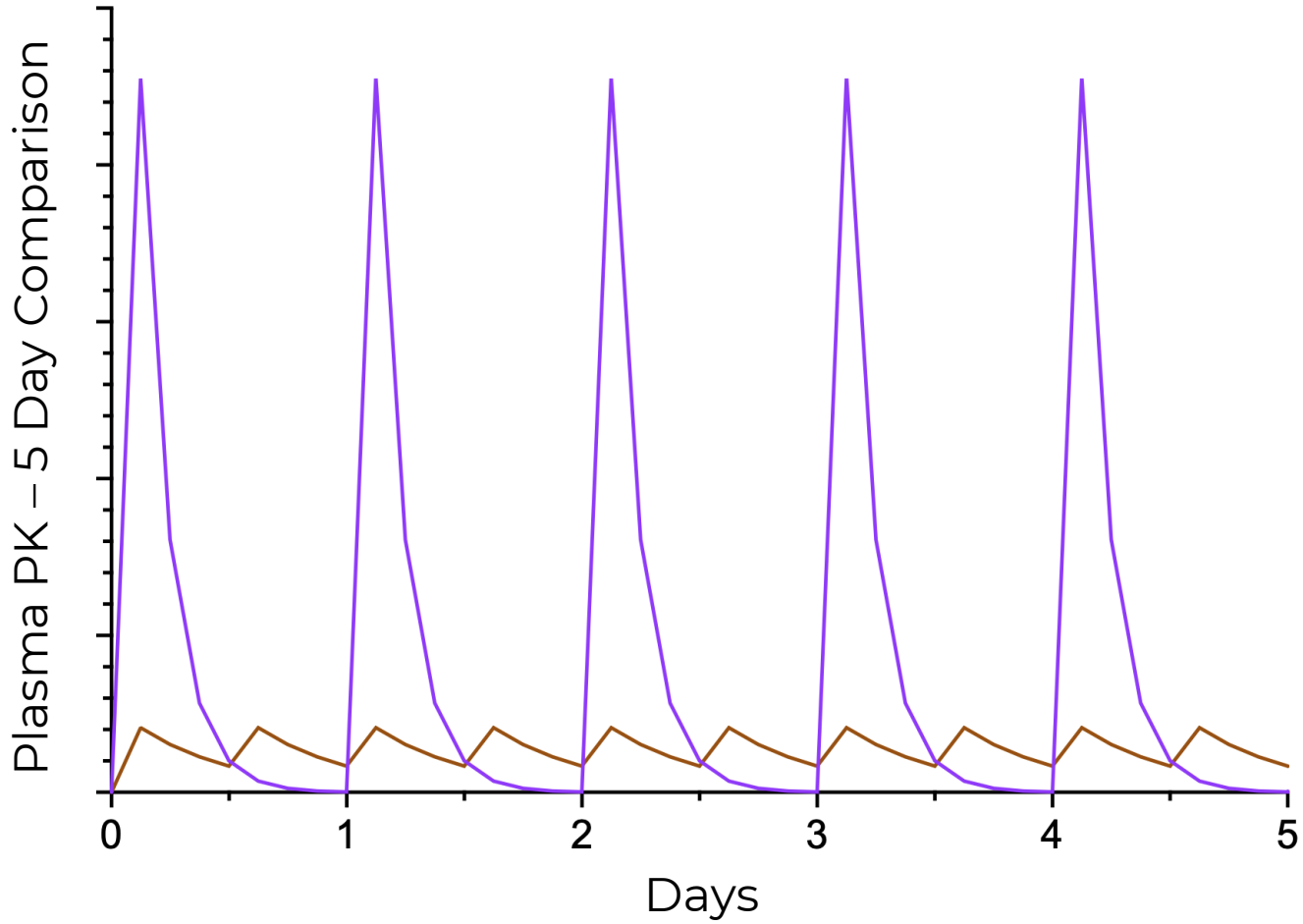
Deep, Cyclic Inhibition



Conceptual illustration of deep cyclic inhibition (purple) vs. chronic pathway ablation (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**

Initial Phase 1 PK, PD and Safety Data for IMM-1-104

First demonstration of novel deep cyclic inhibition mechanism in humans

Deep Cyclic Inhibition (DCI)

Initial pharmacokinetic (PK), pharmacodynamic (PD) and safety data support profile for IMM-1-104 believed to be necessary for Deep Cyclic Inhibition (DCI)

Significant PK C_{MAX}

Significant levels of PK C_{MAX} observed (~1uM free fraction C_{MAX} at 160 mg QD p.o. doses)

Short Half-life Observed

Observed IMM-1-104 half-life of approximately 2 hours, as projected in Immuneering's preclinical modeling

Safety Data

IMM-1-104 well tolerated with no dose-limiting toxicities (DLTs) or serious adverse events (SAEs) observed

Trial Timeline Acceleration

Potentially therapeutic doses of IMM-1-104 now likely to be reached earlier than previously planned due to acceleration of trial timeline

RP2D

Recommended Phase 2 Dose (RP2D) now expected in early 2024

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

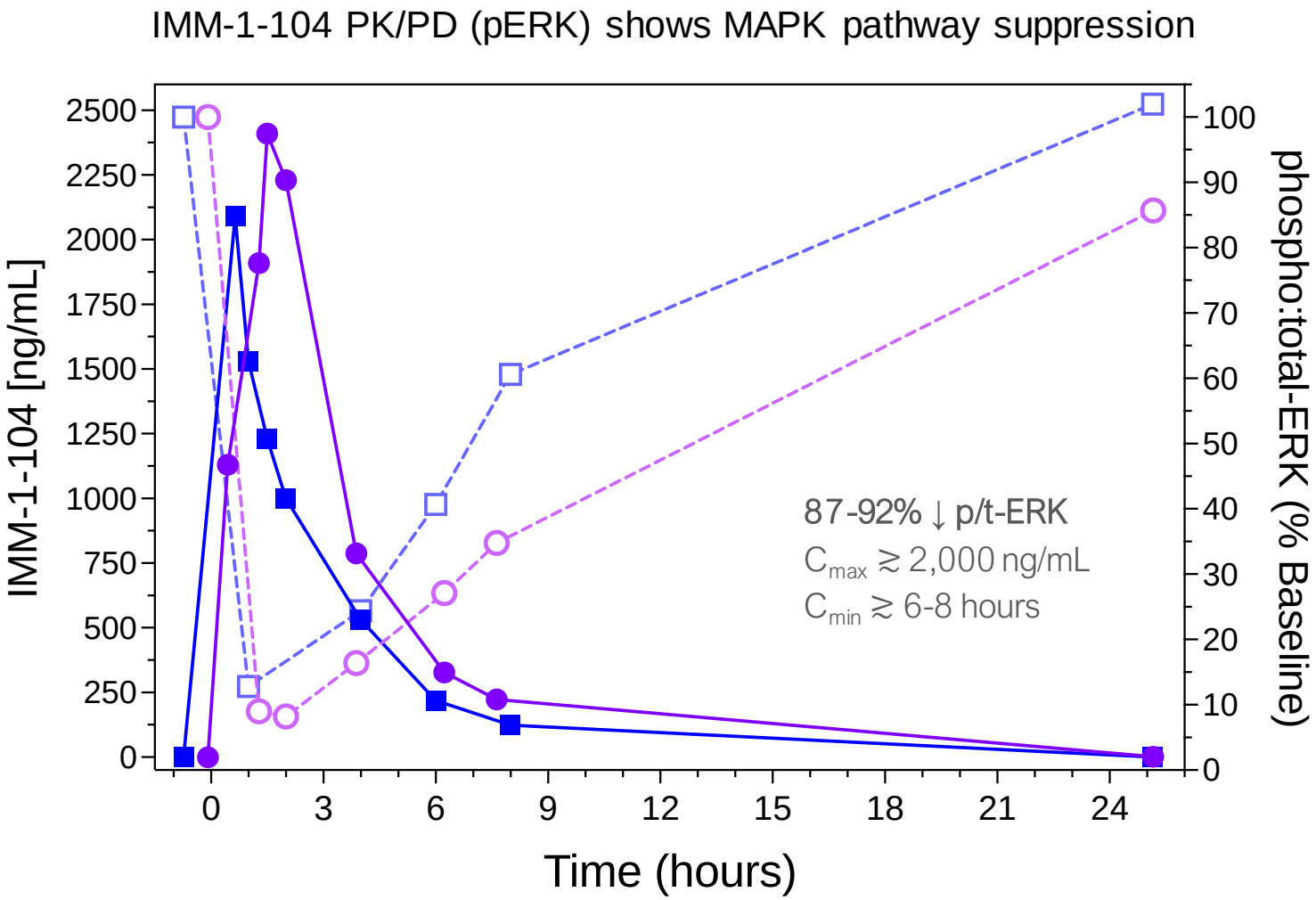
Patient Status Summary for IMM-1-104 Phase 1 Dose Escalation

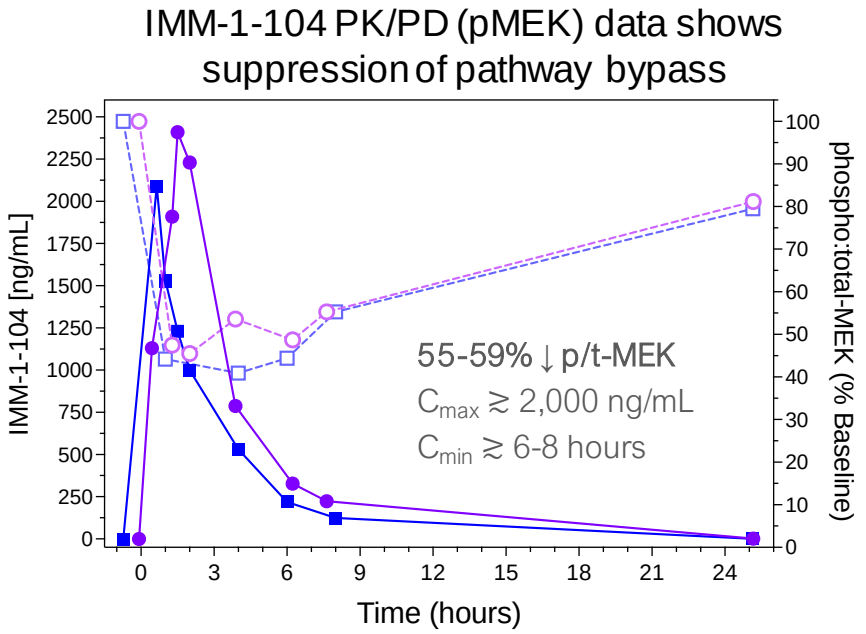
#	Patient	RAS Mutation	Dose Level	Dose	C1D1 ($t_{1/2}$)	C1D15 ($t_{1/2}$)	Mean ($t_{1/2}$)	IMM-1-104 Status
1.	PANCREATIC	KRAS-G12D	**I**	40 mg QD p.o.	1.82 hours	2.10 hours	**1.96 hours**	Off Treatment
2.	COLORECTAL	KRAS-G12V	**II**	80 mg QD p.o.	1.41 hours	1.43 hours	**1.42 hours**	Off Treatment
3.	COLORECTAL	NRAS-Q61L	**III**	160 mg QD p.o.	2.04 hours	1.83 hours	**1.94 hours**	Off Treatment
4.	COLORECTAL	NRAS-Q61K	**III**	160 mg QD p.o.	1.91 hours	1.97 hours	**1.94 hours**	On Treatment
5.	PANCREATIC	KRAS-G12D	**IV**	320 mg QD p.o.	t.b.d.	t.b.d.	t.b.d.	On Treatment

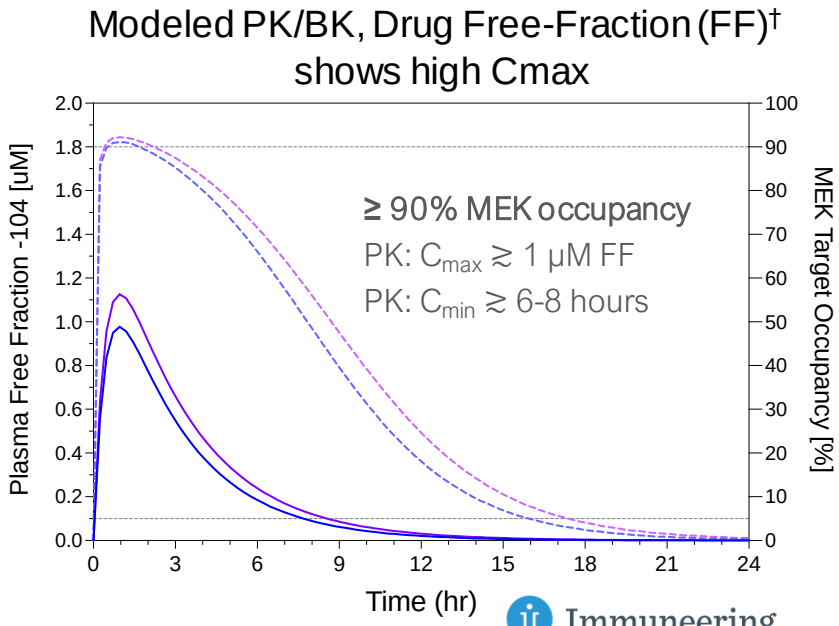
Clinical data timeline reported through April 10th, 2023 (i.e., ~20 weeks since first patient dosed)

- **No DLTs or SAEs observed;** No drug-related AEs beyond grade 1 have been reported in dose levels III or IV
- Early PK data were approximately dose linear with no drug accumulation
- **Actively enrolling patients at 320 mg QD p.o. with 2 additional patients already consented** (KRAS-G12V Pancreatic and KRAS-G12S Colorectal)

~ 90% Pharmacodynamic Inhibition of pERK







- Dose Level III: Cycle 1 Day 1 (C1D1) PK (solid), BK (dotted), and PD (dotted) for patient 3 (purple) and 4 (blue), both at 160 mg QD p.o.
- PK plasma: pre-dose (0), 0.5, 1, 1.5, 2*, 4, 6, 8, 24 hours; PD plasma: PK-matched without 0.5 or 1.5 hours (*poor sample quality for Pt.4 at 2 hour)
- PD method: A549 ($KRAS^{G12S}$) cells were exposed to patient plasma for 2-hours before quantifying phosphorylated and total ERK and MEK

† Hoare, Sam RJ. "Analyzing kinetic binding data." Assay Guidance Manual [Internet] (2021)

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

First Time in Humans

IMM-1-104
(Dual MEK inhibitor)

IND cleared; First patient dosed on Nov 21, 2022

Dose Escalation Phase 1a*

Bayesian Design (mTPI-2) escalation in select solid tumor types*

≤12 patients expected

Dose Evaluation Phase 1b*

Dose Evaluation and RP2D

~12-20 patients expected; "bake off" between dose levels per Project Optimus

Dose Expansion - Phase 2a**

Expansion 1:

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

Expansion 2:

- **RAS Mutated Melanoma** (~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

- **RP2D = Recommended Phase 2 Dose**
- **PGx = Pharmacogenomics**

Phase 1 Sites

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	

- Investigator enthusiasm remains high
- Broad RAS inclusion criteria (Solid Tumors, All Histologies)

Milestones

Program	Milestone	Expected Timing
IMM-1-104	Initial Phase 1 pharmacokinetic (PK) and safety data	**COMPLETE**
IMM-1-104	Initial Phase 1 pharmacodynamic (PD) modeling data and additional PK and safety data	**COMPLETE**
IMM-1-104	Additional trial updates	On a periodic basis
IMM-1-104	RP2D and Additional Safety data	**Early 2024**
IMM-6-415	IND filing	Q4 2023

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Differentiated Approach

- Targeting **Universal-RAS** patient population versus limited single mutation targeted approaches
- **Once-Daily Oral Dosing**
- **Deep cyclic inhibition** targeted, based on:
  - **Manyfold higher C_{MAX}**
  - and **short half-life**
- Approach designed to **spare healthy cells** and potential to **limit adaptive resistance**
- **Monotherapy-Focused** initially, with combination potential

IMM-1-104 Demonstrated 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** that identified counterintuitive and novel deep cyclic inhibition approach
- **Validated using** proprietary **bioinformatics & 3D tumor growth assays**

Key Inflection Points Expected in Near Term

- **Initial Phase 1 PK, PD, safety data support profile for** IMM-1-104 believed to be necessary for **Deep Cyclic Inhibition**
- **Investigator enthusiasm high**; broad inclusion criteria
- **Additional trial updates expected on a periodic basis; RP2D** expected in early 2024
- **IMM-6-415** IND expected in Q4 2023
- **Cash runway projected into Q4 2024**

Thank you

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