ikena™ ONCOLOGY

Corporate Presentation

First Quarter 2023

Developing Biology-Driven Medicines and Expanding the Impact of Targeted Oncology

We develop differentiated therapies for patients in need that target nodes of cancer growth, spread, and therapeutic resistance in the Hippo and RAS onco-signaling network.

Hippo Pathway

RAS Pathway

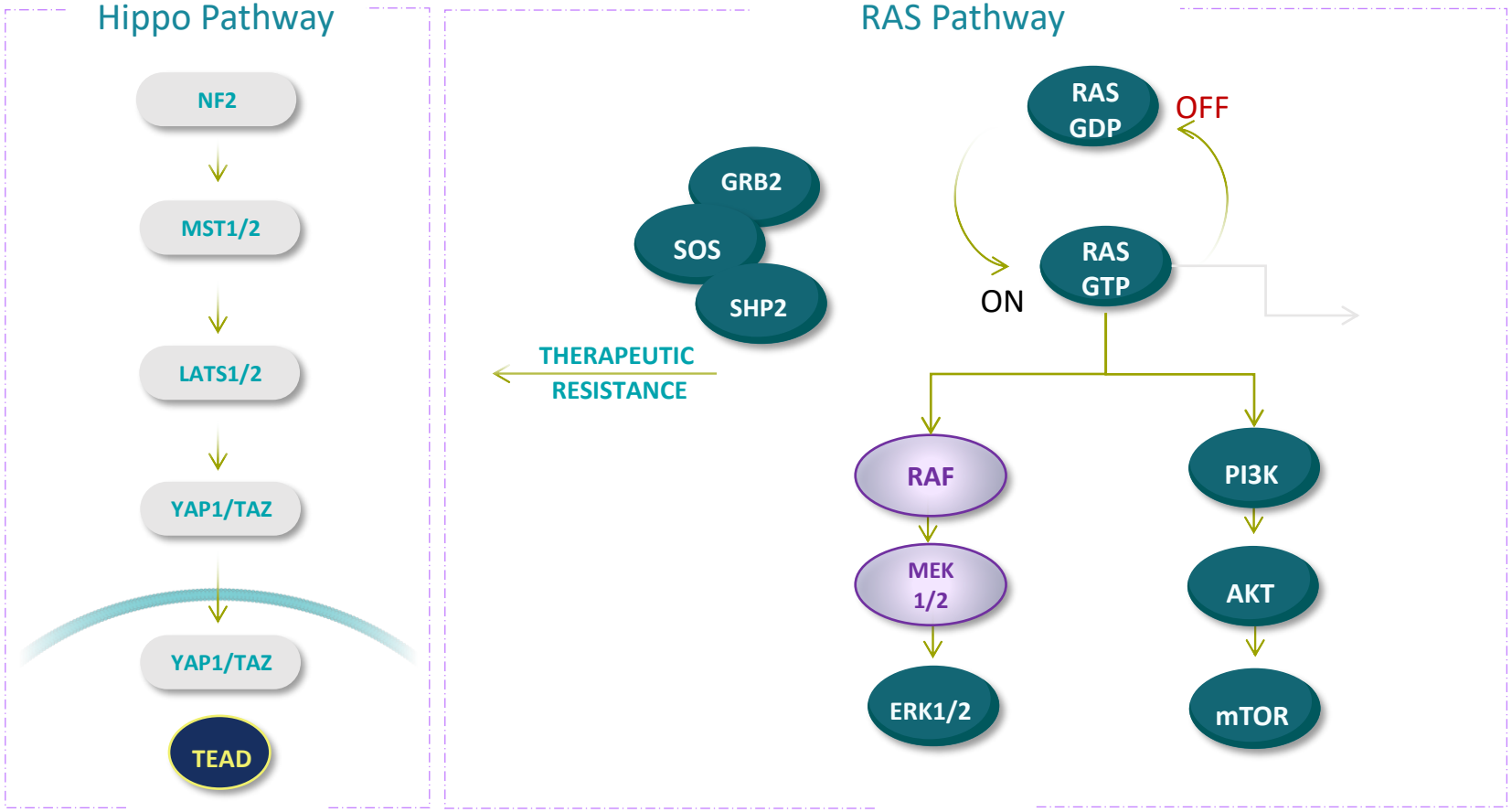
- Multiple ongoing clinical trials with **expected data readouts in the next 12 months**
- **Leaders in Hippo pathway** with clinical stage paralog-selective TEAD inhibitor **IK-930**
  - Initial mono-therapy in mesothelioma and EHE in 2023
  - Combination with osimertinib in NSCLC to start in 2023
  - Next generation Hippo candidate in lead optimization
- **Novel MEK/RAF inhibitor IK-595** in IND-enabling studies
  - IND in 2H 2023 with broad potential across RAF and RAS mutant cancers
- BMS partnered program **IK-175** with **clinical activity in bladder cancer**
  - Potential for **$50M in opt-in fees by early 2024**, $450M in milestones plus global royalties
- **>$170M** in cash; Runway into **2025**

Ikena Wholly Owned Pipeline Focused on Targeted Oncology in Hippo-Ras Oncosignaling Network

		Candidate *Target*	Indications *Interventions*	Partnerships & Rights
Targeted Oncology	*Hippo Pathway*	**IK-930** *TEAD*	Hippo-Altered Cancers *Monotherapy & Multiple Combinations*	ikena ONCOLOGY
		Undisclosed	Hippo-Altered Cancers	ikena ONCOLOGY
	RAS Pathway	**IK-595** *MEK-RAF*	RAS and RAF Altered Cancers; Additional Tumor Types	ikena ONCOLOGY
		Undisclosed	RAS-Mutated Cancers	ikena ONCOLOGY
Immune-Signaling	*AHR Signaling*	**IK-175** *AHR*	Bladder Cancer, AHR Enriched *Monotherapy & Nivolumab Combination*	Bristol Myers Squibb
			Head & Neck Cancer, AHR Enriched *Nivolumab Combination*	Bristol Myers Squibb

Connectivity Across RAS & Hippo Oncosignaling Network

Nodes in the RAS network are intricately connected to each other and other orthogonal pathways, including Hippo



Hippo genetically-altered cancers and Hippo activated resistance

RASm cancers – one of the most common pathway with genetic alteration in cancers – potential benefit from monotherapies and combination therapies

Ikena has deep institutional knowledge and broad capabilities that lay the foundation for discovery programs across the network

Deep knowledge and characterization of the interconnected nature of oncogenic nodes

Proven history of drugging difficult targets

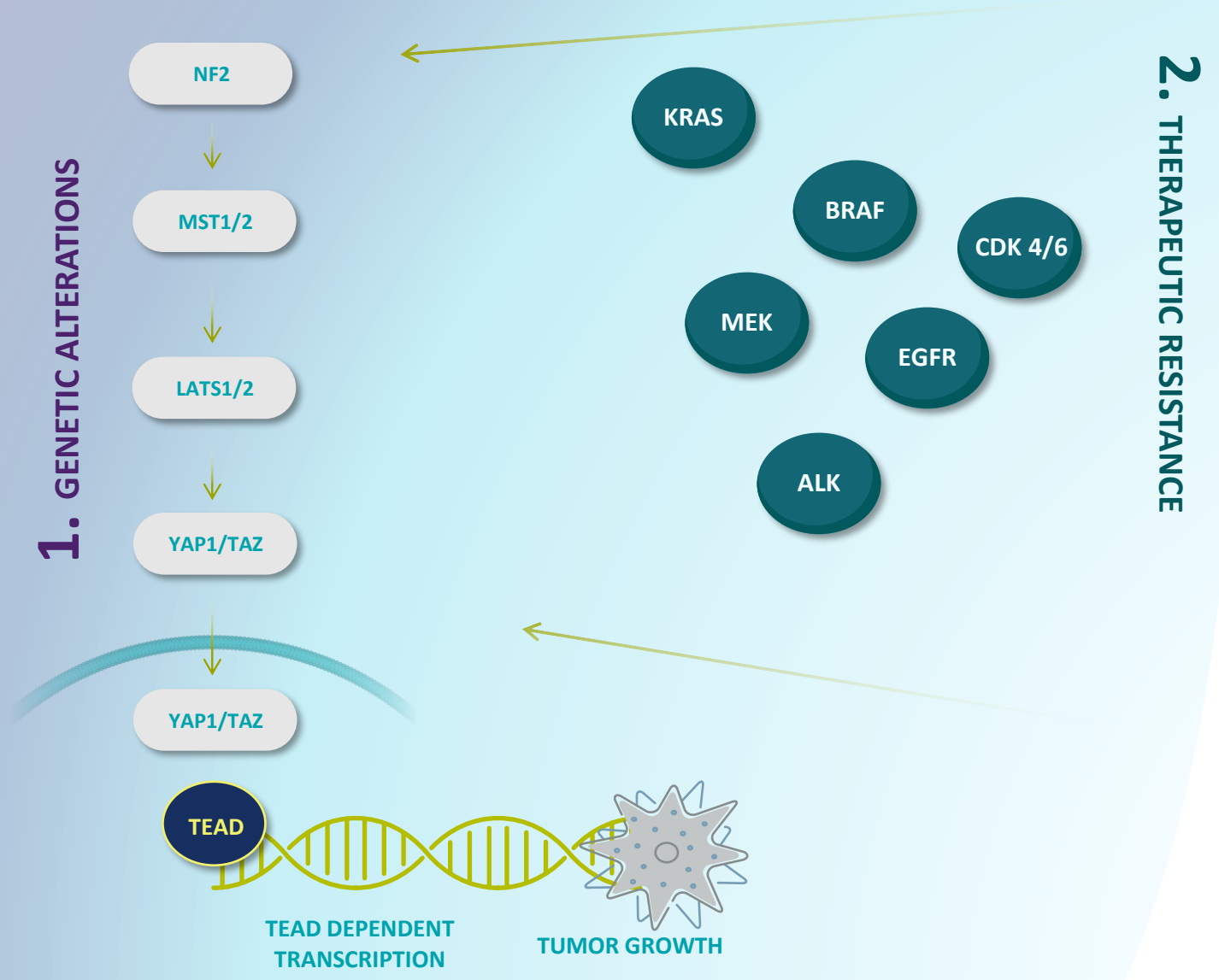
Leaders in drugging the Hippo pathway

Advanced capabilities across biomolecular characterization, structural biology, chemistry, and translational medicine

Targeting TEAD & the Hippo Pathway

IK-930

Hippo Pathway Alterations and Activity Trigger TEAD Transcription-Dependent Tumor Growth



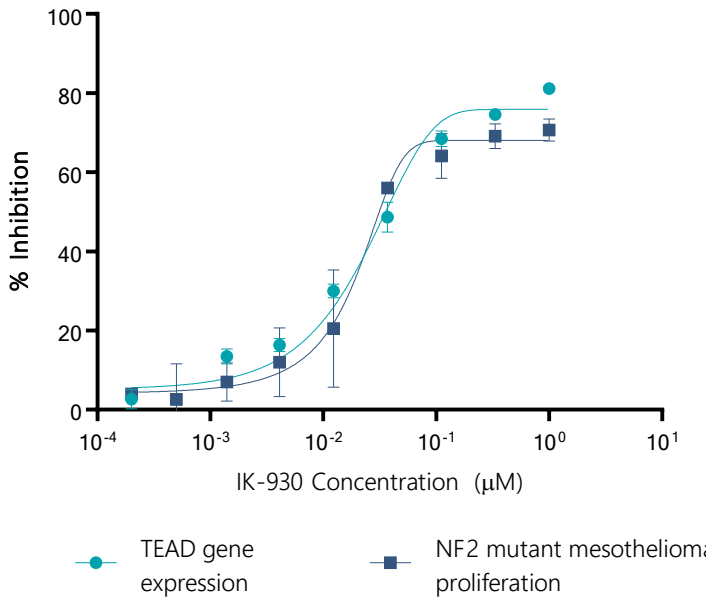
1. **GENETIC ALTERATIONS**: Treat patients with genetic alterations in the Hippo pathway with **IK-930 MONOTHERAPY**. The Hippo pathway is genetically altered in approximately 10% of all human cancers, including 40% of malignant mesothelioma patients and 100% of EHE patients

2. **THERAPEUTIC RESISTANCE**: **COMBINE IK-930** with other targeted therapies. Resistance to multiple targeted therapies and tumor recurrence can be linked to YAP/TEAD activation

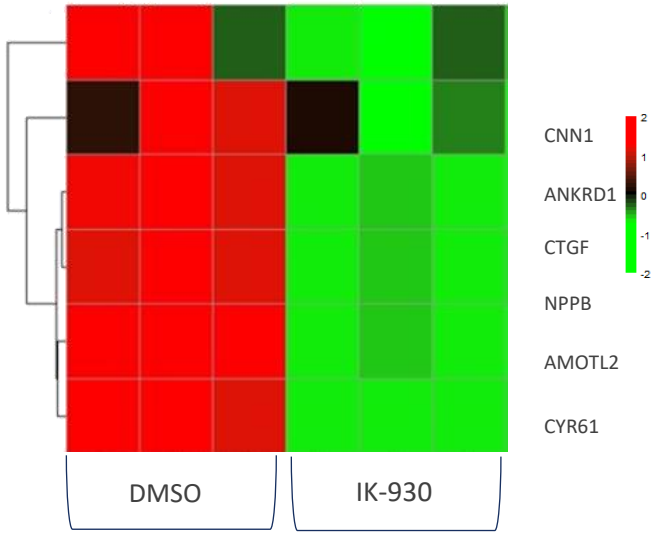
IK-930 is an Oral, Selective, Potent TEAD Inhibitor

IK-930 was well tolerated preclinically while showing significant impact on TEAD dependent gene expression

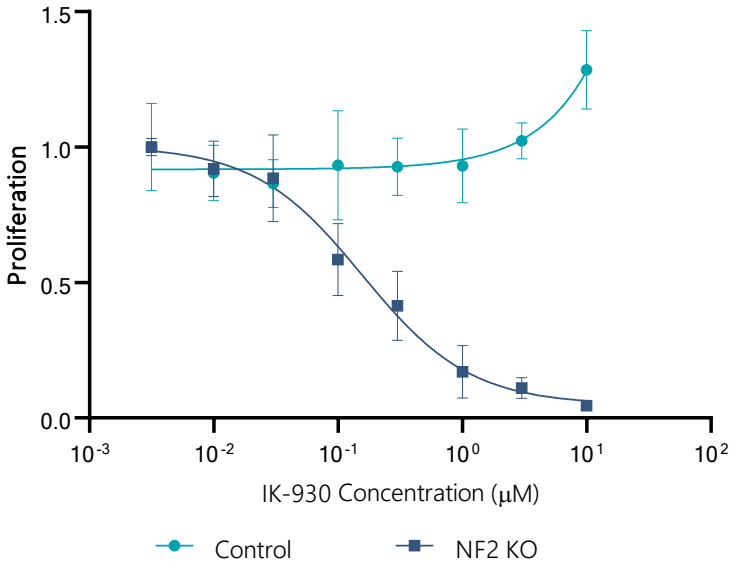
Potent TEAD Inhibition



Robust Inhibition TEAD Target Gene Expression

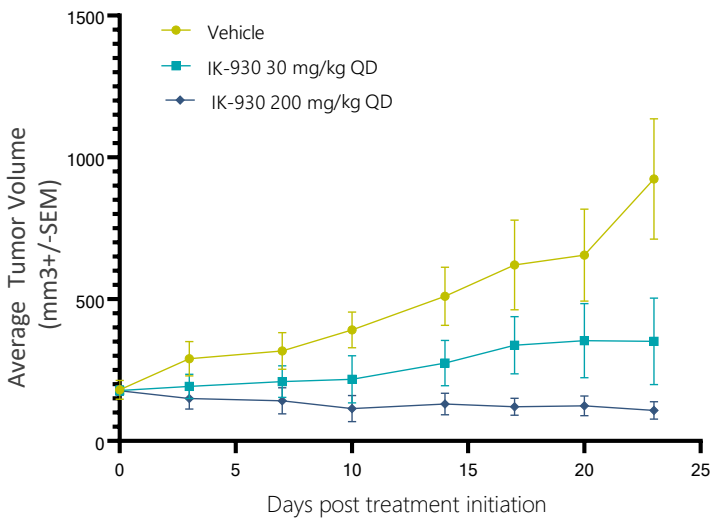


Selective Activity in Hippo-Mutated Cells

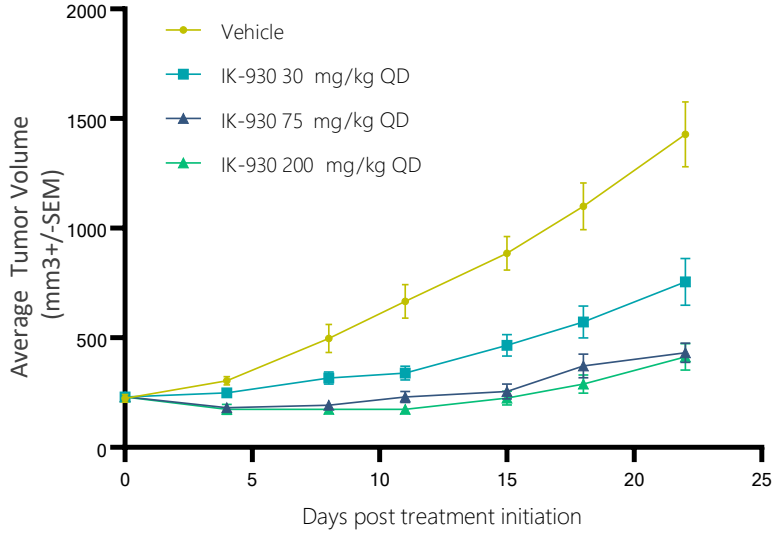


IK-930 Monotherapy Has Potential Across Genetic Mutations in the Hippo Pathway

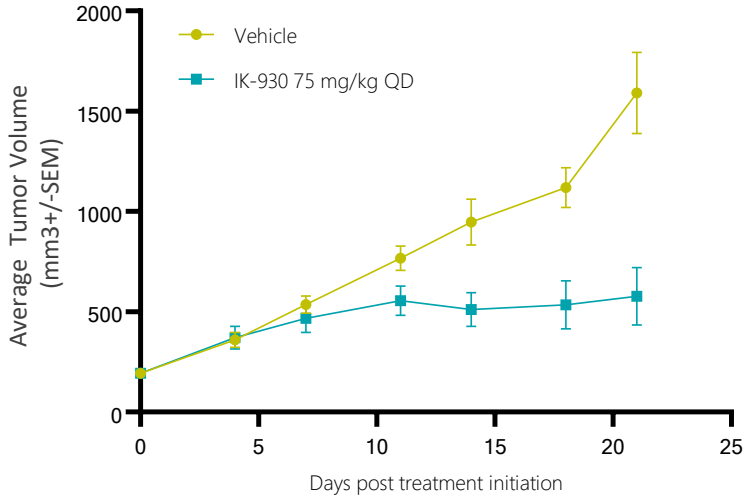
Impact Across Tumor Models for Hippo Pathways Genetic Alterations



NF2 Deficient Mesothelioma Model



LATS1/LATS2 Mutated Mesothelioma Model



YAP1 Amplified HNSCC Model

IK-930 Monotherapy Strategy and Clinical Development Plan; Initial Data Expected in 2H 2023

Growing Monotherapy Opportunity

~125,000 newly diagnosed cancer patients per year in the US with known Hippo pathway mutations and alteration

- **Malignant Mesothelioma:** ~**40%** NF2 loss of function mutations
- **NSCLC: 6%** YAP1 and **29%** TAZ amplification
- **Meningioma:** High frequency of NF2 deficiency; Most common CNS tumor, accounting for **~one-third** of primary CNS tumors
- **Head & Neck Cancers:** Growing body of knowledge on frequent YAP/TAZ amplification and FAT1 (upstream) deficiency
- **Soft Tissue Sarcomas: ~90%** of epithelioid hemangioendothelioma, or **EHE**, have TAZ-CAMTA1 fusions; **10%** of EHE have YAP1-TFE3 fusions

Ongoing Phase 1 Trial
Monotherapy Clinical Development Plan

Dose Escalation → *Currently recruiting; advanced through multiple doses*

All comers

Tumors known to have high incidence of Hippo pathway alterations

Dose Expansion Options →

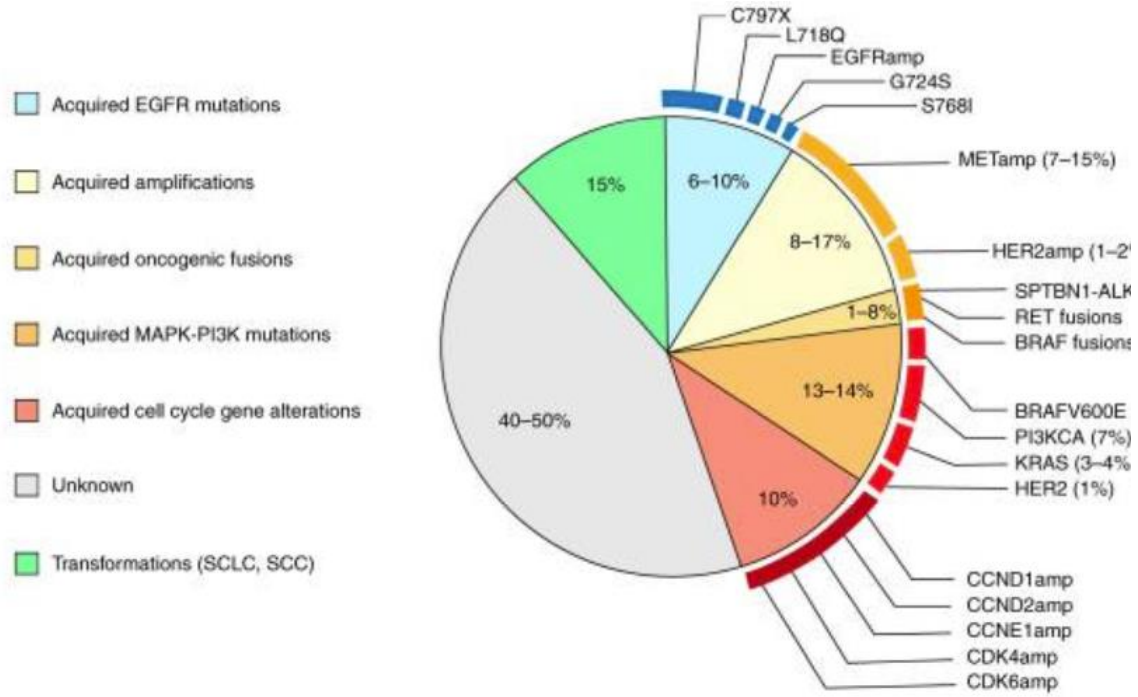
- NF2 deficient mesothelioma
- Epithelioid hemangioendothelioma (EHE)
- NF2 deficient solid tumors; agnostic approach
- YAP/TAZ gene fusion solid tumors; agnostic approach

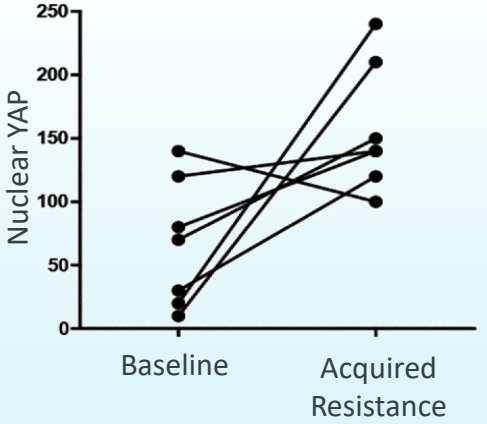
IK-930 Opportunity to Address Emerging Early-Use Osimertinib Resistance

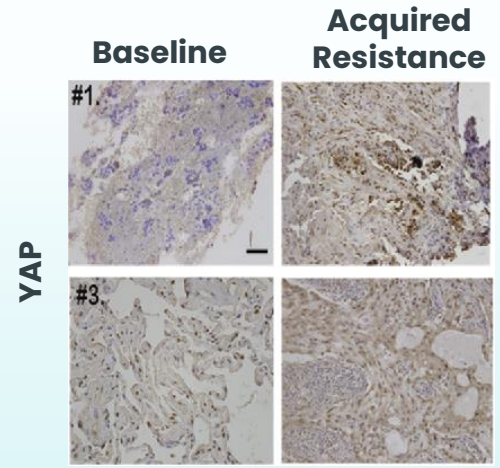
40%+ of patients with Osimertinib resistance have unidentified mechanisms and represent a significant unmet need

Resistance Mechanisms to Osimertinib in EGFRm NSCLC

Leonetti, et al., Br J Cancer, 2019







Lee, et al., BBRC, 2016

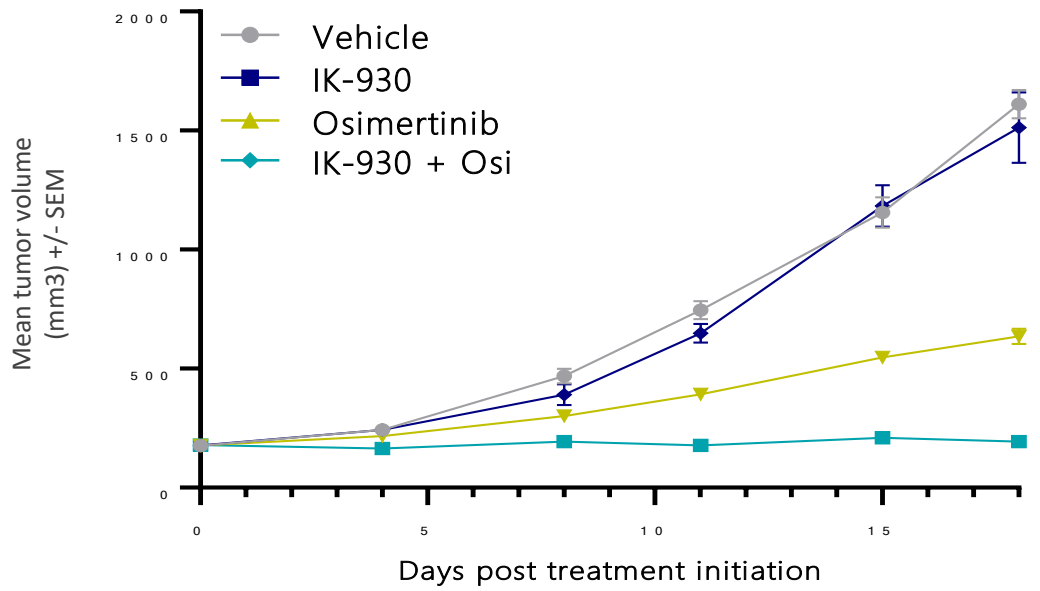
Opportunity for IK-930 combinations to address acquired osimertinib resistance

Opportunity to identify subset of patients in whom addition of IK-930 combo can delay/prevent the emergence of resistance

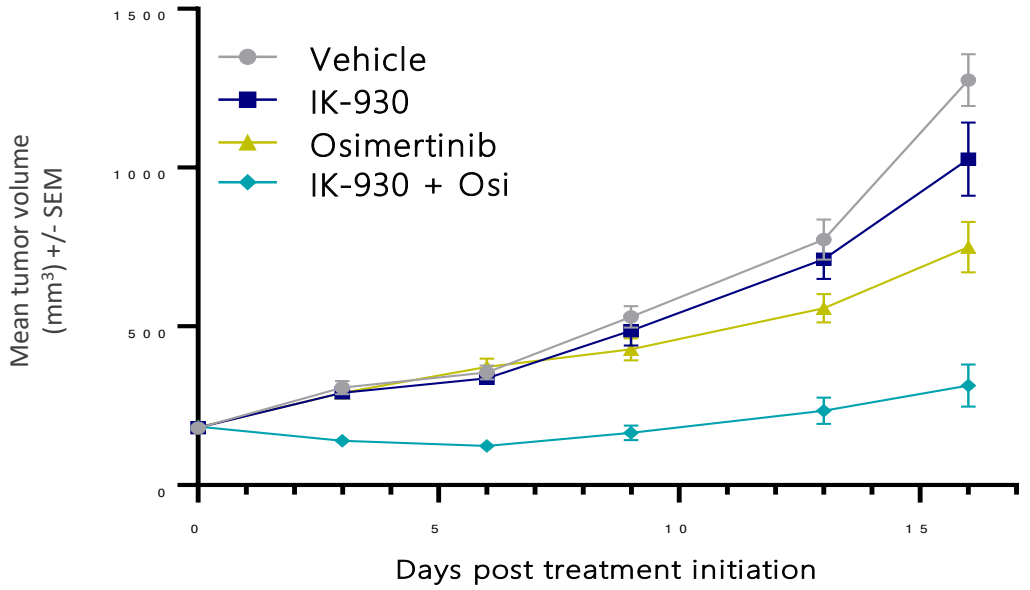
IK-930 Combination with EGFRi shows Improved Anti-tumor Activity

Multiple EGFRm Lung Cancer Models Show Benefit of IK-930-Osi Combination

H1975 Tumor Model

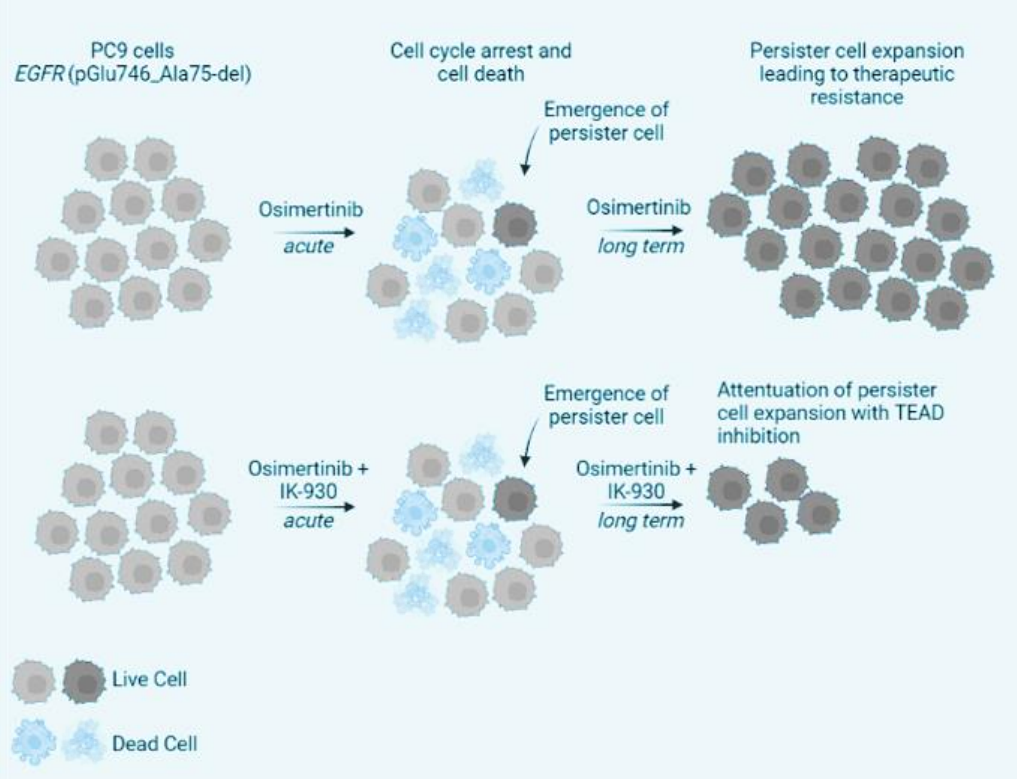


PC9 Tumor Model

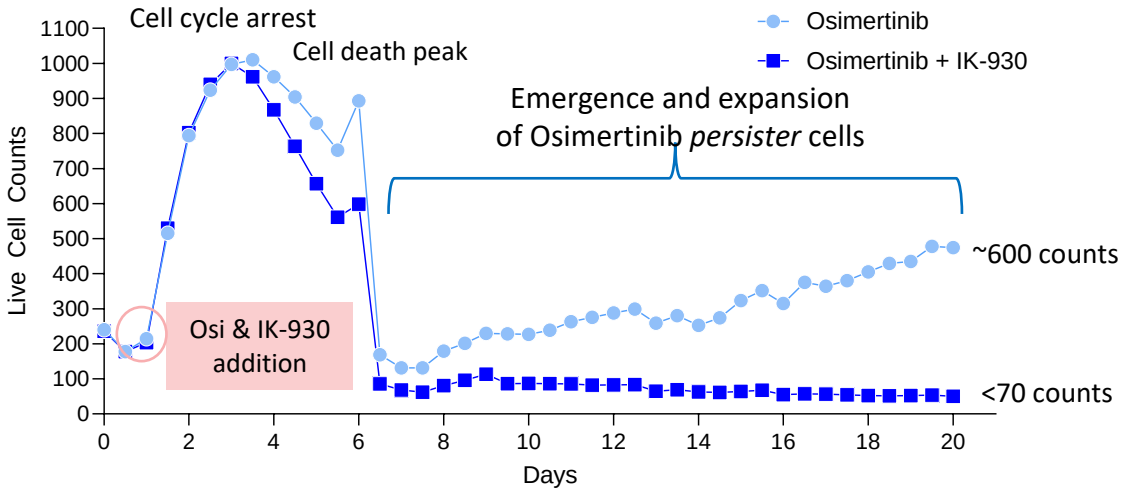


IK-930 Has Pre-Clinical Impact on Refractory *Persister* Cells

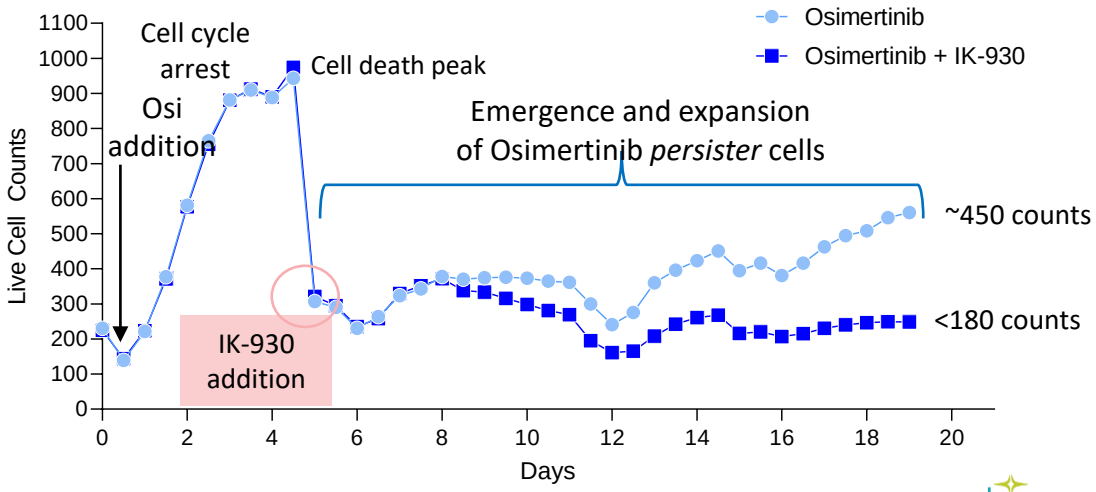
*Potential for IK-930 to **prevent** resistance to EGFR inhibitors and even **reverse** the effect when given after resistance has already emerged*



IK-930 + Osi Combined Prevents Emergence of *Persisters*



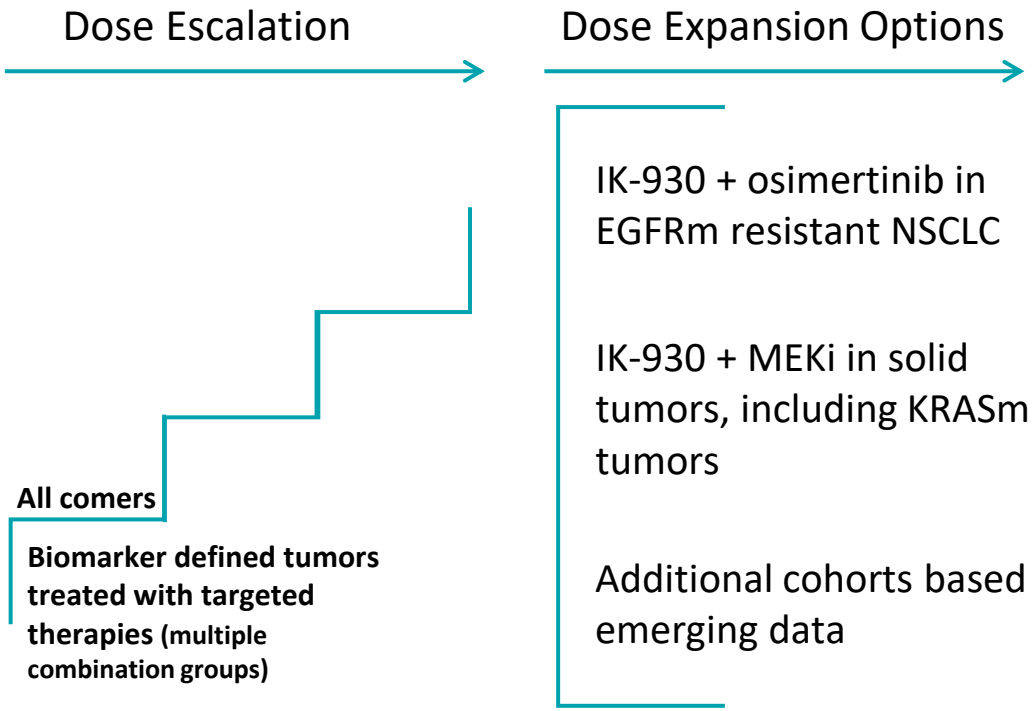
IK-930 Addition after *Persister* Emergence Attenuates Expansion



IK-930's Potential to Combat Therapeutic Resistance to Other Targeted Therapies

Combination strategy represents an independent mechanism and potential opportunity for IK-930

Combination Clinical Development Plan
First Cohort to Initiate in 2023



Addressing a Leading Limitation of Targeted Therapy - Primary and Secondary Therapeutic Resistance

Resistance to multiple targeted therapies and tumor recurrence can be linked to **YAP/TEAD activation**

Overcoming resistance mechanisms and escape could **deepen and prolong responses and address *de novo* resistance**, allowing more patients to respond to target therapies overall

"…underlying mechanisms through which malignant tumor cells acquire or develop resistance to anti-cancer treatment. The Hippo signaling pathway appears to play an important role in this process."
Zeng et al. Cancers 2021

"The biggest hurdle to targeted cancer therapy is the inevitable emergence of drug resistance."
Lim, et al. Journal of Hematology & Oncology 2019

"Despite [targeted oncology's] immense progress, advanced cancer is ultimately lethal for most patients due to treatment resistance."
Aldea, et al. Cancer Discovery 2021

Ikena Leads the Field in Targeting the Hippo Pathway

- **IK-930**: First-in-class, paralog-selective TEAD inhibitor
  - Ongoing phase 1 clinical trial currently in dose escalation
    - Monotherapy cohorts in NF2 mutant mesothelioma and EHE (100% YAP/TAZ)
    - Multiple planned combination cohorts combating therapeutic resistance
      - Data shows potential to prevent and reverse resistance to EGFR inhibitors
  - **Additional data on advantages of paralog-selectivity and combination approach in 1H 2023**
  - **Initial clinical data expected in 2H 2023**
- **Next-gen Hippo program** in lead optimization

MEK-RAF Complex Inhibitor

IK-595

ikena ONCOLOGY

The RAS Pathway is Highly Implicated in Cancer

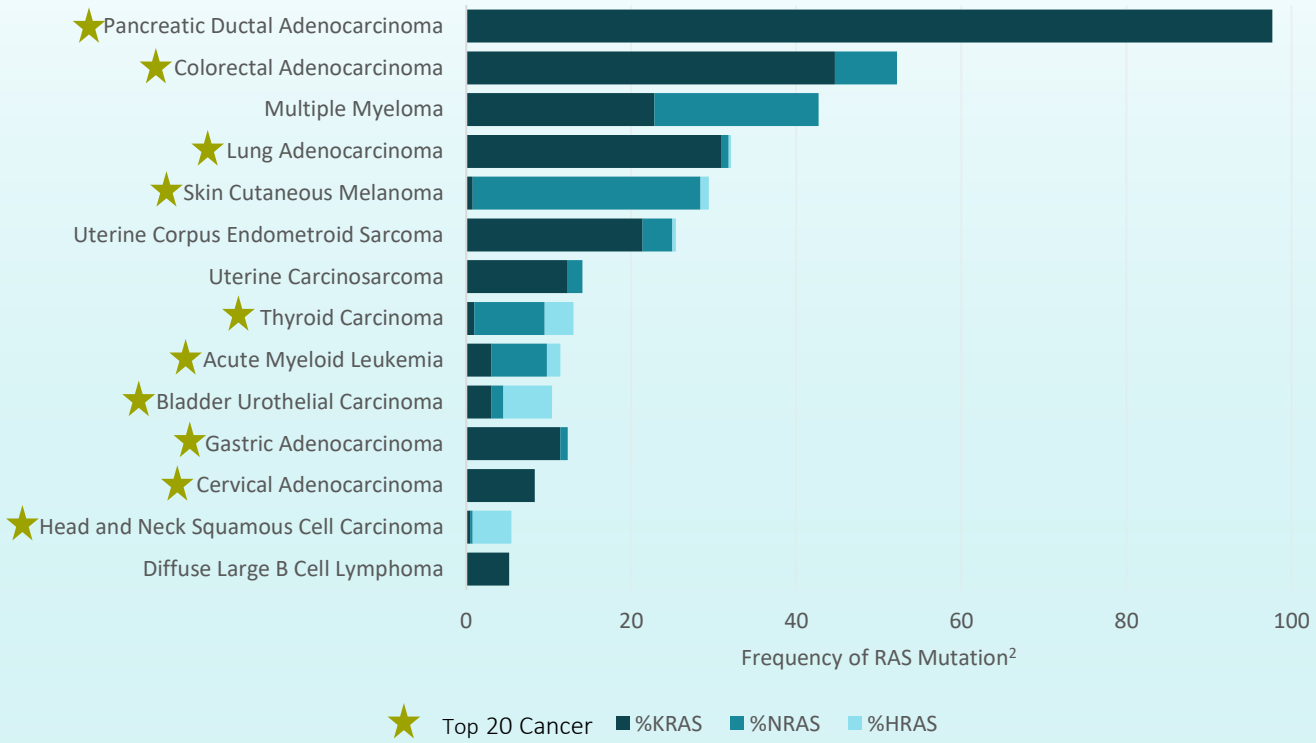
Targeting within the pathway could be impactful for a massive and diverse population

The **RAS pathway** is potentially implicated in **over half a million new cancer diagnoses each year** in the US alone[1]

New approaches in targeting the pathway need to consider key learnings

- Approved inhibitors can paradoxically activate MEK/ERK signaling
- CRAF is implicated as a key signaling bypass mechanism for targeted therapies, and has kinase independent activity that drives RAS mutant cancers

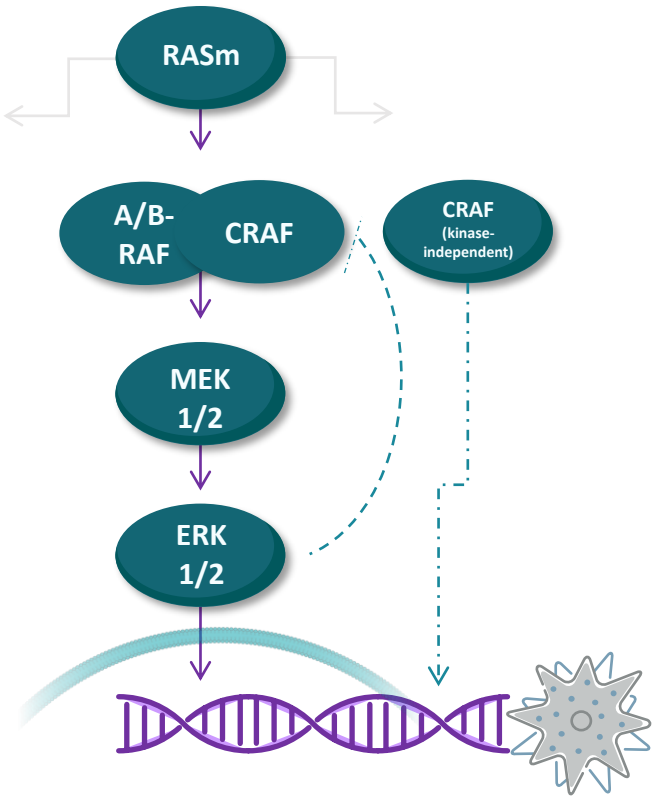
10 of the 20 most common cancers worldwide are associated with RAS pathway mutations



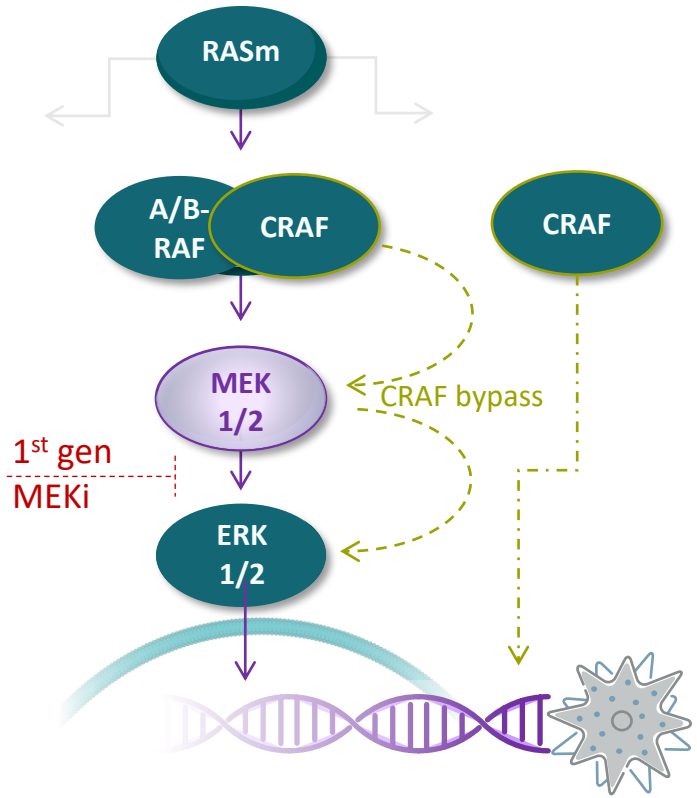
[1]ACS and https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3457779/
[2]Cox. Nature Reviews Drug Discovery (2014); World Cancer Research Fund International

First Generation MEK Inhibitors: Insufficient Targeting Leads to Limited Activity

MEK's role in driving ERK-mediated tumor growth



First gen MEK inhibitors trigger CRAF mediated pathway reactivation



Approved MEK inhibitors like trametinib and binimetinib block MEK kinase activity

Feedback in the pathway however triggers CRAF activation

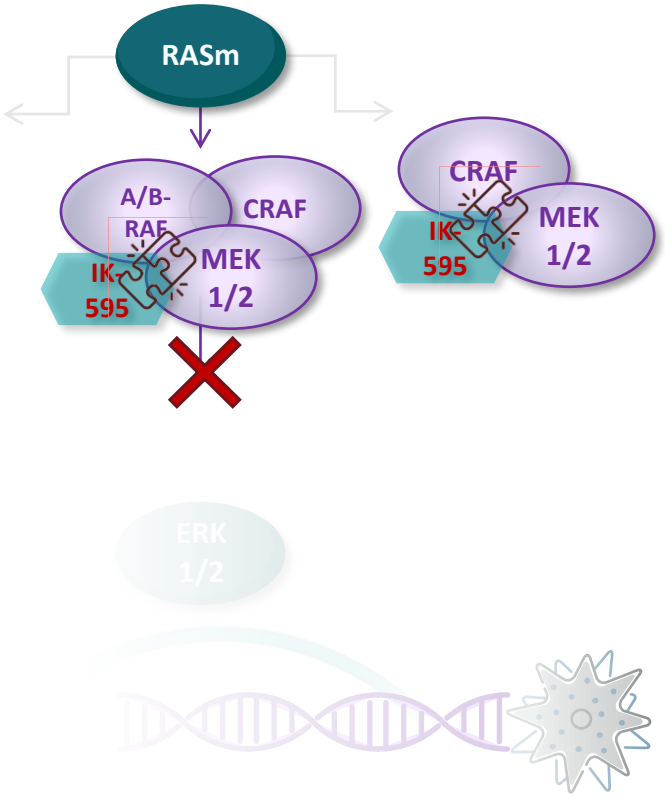
Cancer's survival mechanism utilizes CRAF to reactivate the pathway and bypass inhibition

Additionally, approved inhibitors miss blocking kinase-independent CRAF function that can trigger tumor growth

Leads to incomplete pathway inhibition

IK-595: A Best-in-Class Dual MEK-RAF Complex Inhibitor

IK-595 traps MEK & RAF in an inactive complex to prevent CRAF bypass and kinase-independent CRAF function



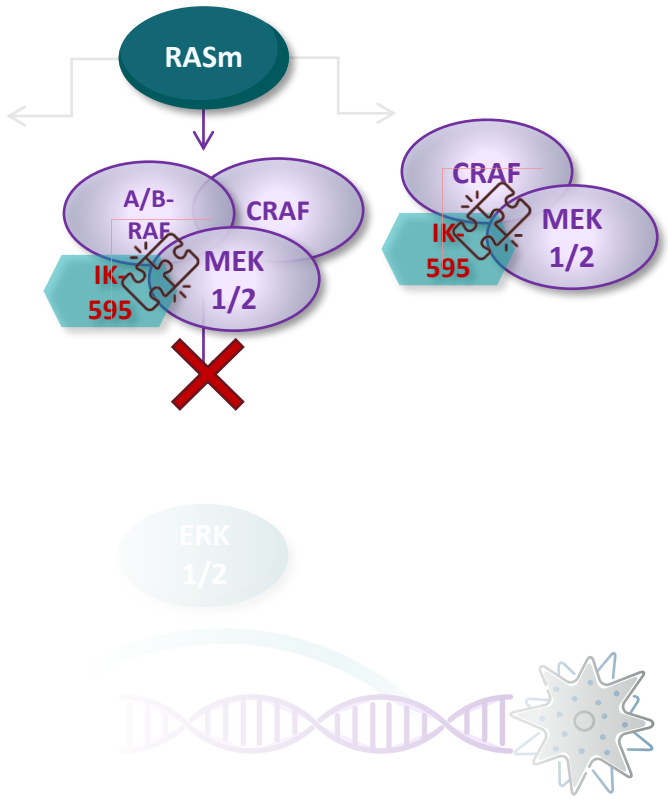
Key IK-595 Advantages

IK-595 is designed to and has shown preclinical evidence of superior profile than first generation and in-development MEK inhibitors

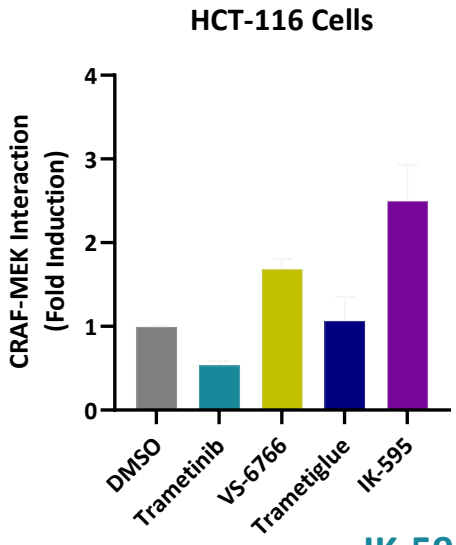
- ✓ Inhibit MEK mediated ERK1/2 phosphorylation
- ✓ Prevent MEK phosphorylation by RAF
- ✓ Alleviate therapeutic resistance through CRAF mediated bypass and pathway reactivation
- ✓ Block CRAF kinase independent activities
- ✓ Optimized PK profile to target IC90 plasma concentrations widening the therapeutic window

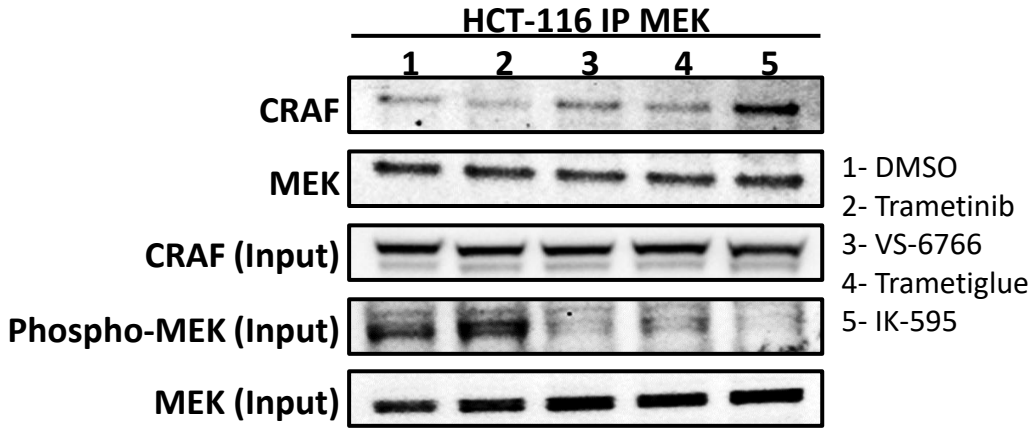
Key Advantages of IK-595 Including Robust Stabilization of MEK-CRAF Complex

IK-595 traps RAF and MEK in a stable, inactive complex providing advantages in blocking both bypass in the pathway and kinase-independent CRAF function



IK-595 Stabilizes CRAF-MEK Complex



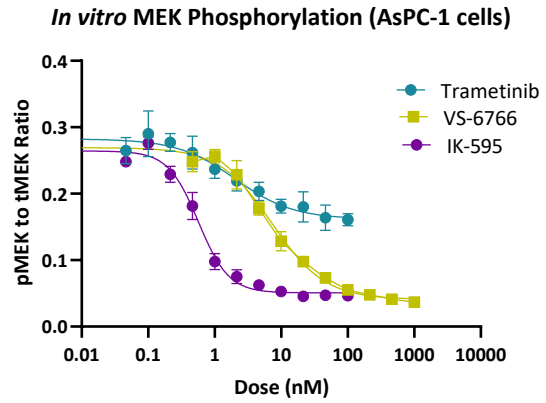


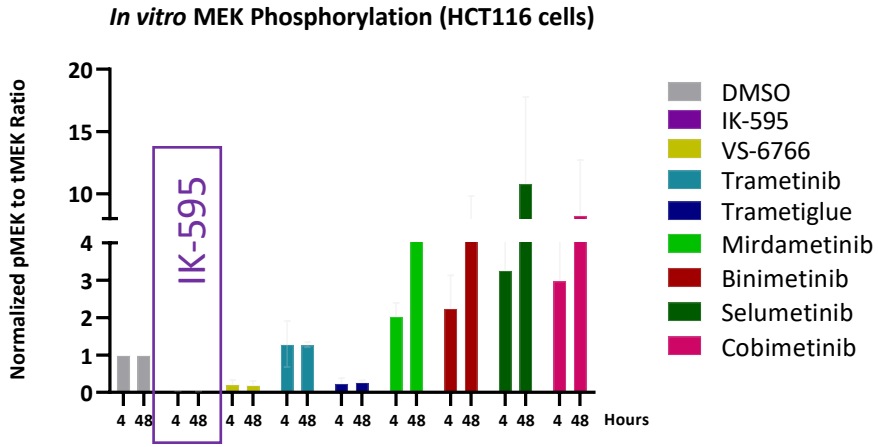
IK-595 Potency Adds to Best-in-Class Potential

Assay	Cellular pERK IC_{50}	Biochem uMEK IC_{50}	Cellular pMEK 4h / 48h IC_{50}	Proliferation AsPC-1 CTG IC_{50}
IK-595	0.1 nM	3 nM	0.6/1 nM	1.3 nM

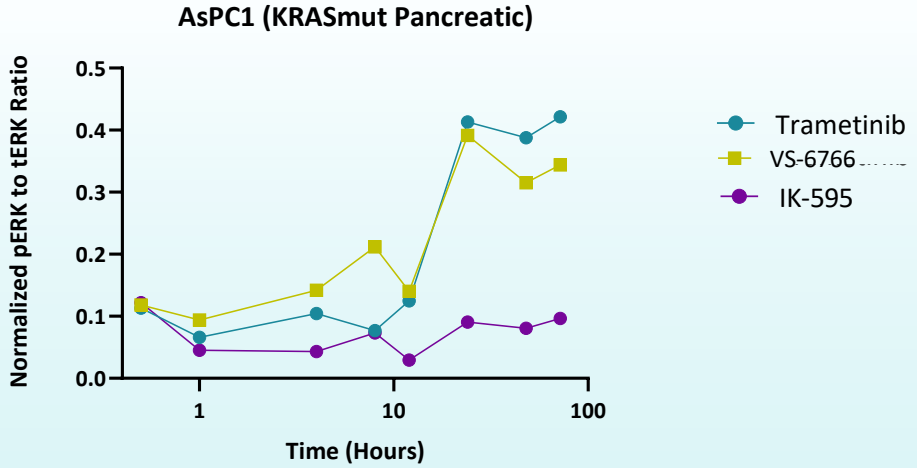
IK-595 Leads to Significantly More Durable Pathway Suppression than Other MEK Inhibitors

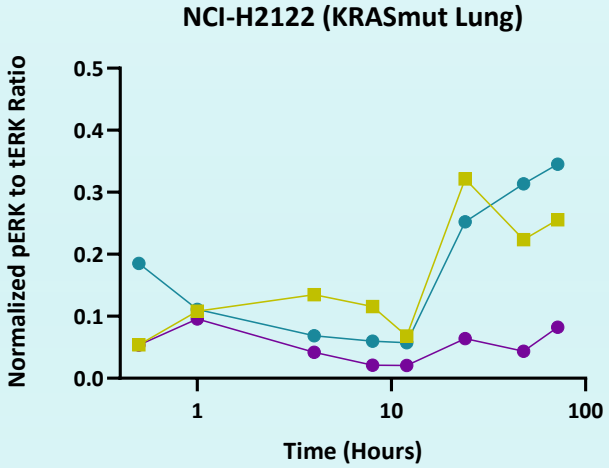
IK-595 Potently Inhibits MEK Phosphorylation In Vitro

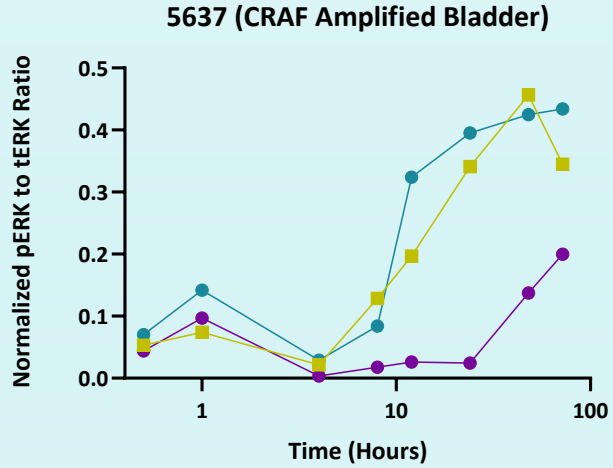




IK-595 Demonstrates Robust and Prolonged pERK Inhibition in Multiple Cell Lines



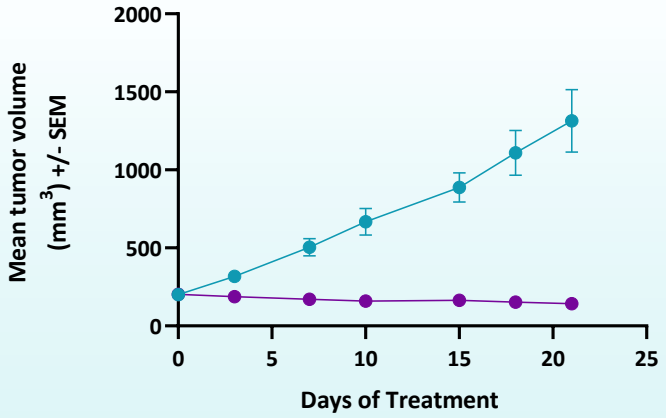




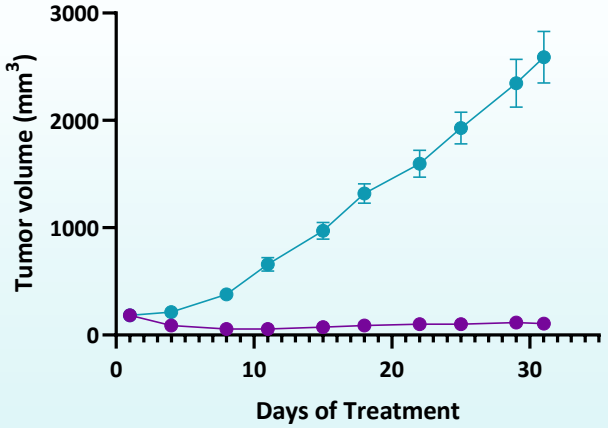
Robust Preclinical Efficacy in RAS and RAF Cancers with Great Sensitivity in CRAF Dependent Models

Antitumor Activity Across Models at Tolerated IK-595 Doses

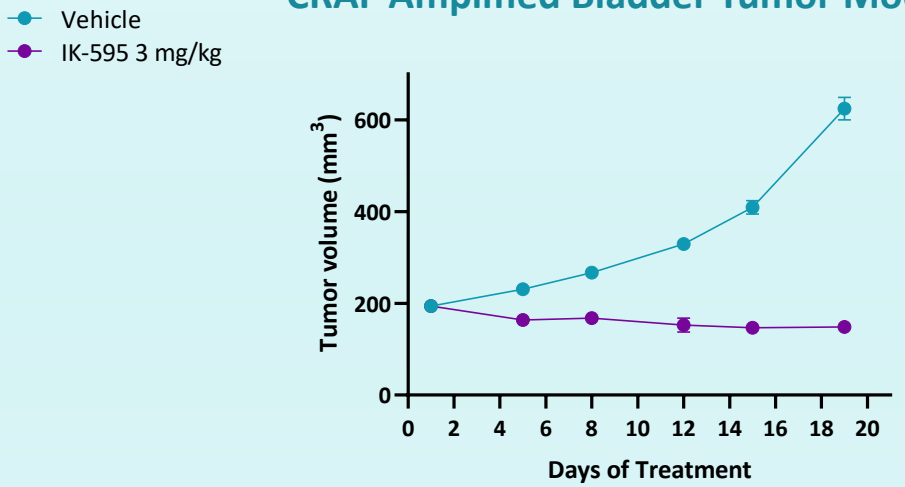
KRAS G12D Pancreatic Model



KRAS G12C Lung Tumor Model

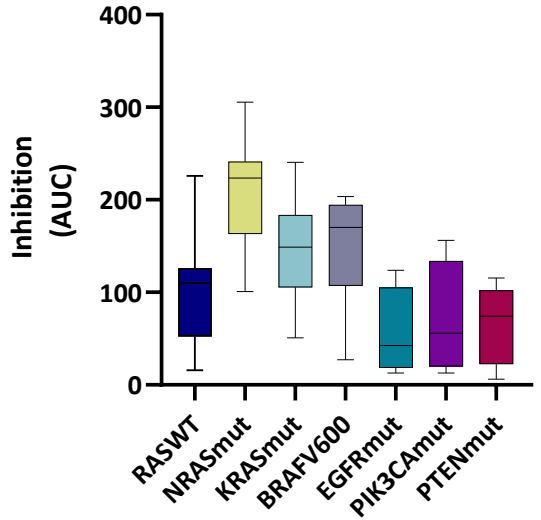


CRAF Amplified Bladder Tumor Model



Efficacy achieved with both continuous and intermittent dosing of IK-595

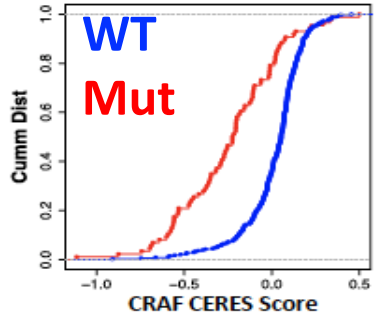
IK-595 Sensitivity



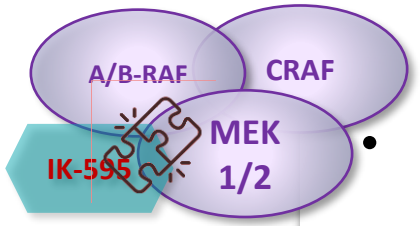
IK-595 has greatest sensitivity in NRAS and KRAS mutant cell lines which are dependent on CRAF

NRAS and KRAS – CRAF CERES Score

Jones, 4th RAS-Targeted Drug Development Summit 2022



IK-595: Best-in-Class Next Generation MEK-RAF Complex Inhibitor



- Novel, best-in-class inhibitor that traps MEK and RAF in an inactive complex for more complete inhibition of the pathway
- Durable, potent inhibition of the pathway demonstrated through multiple data sets
- Mechanisms prevents CRAF bypass and kinase-independent CRAF function
- Preclinical efficacy in multiple disease models
- Difficult to treat CRAF-dependent tumors show high sensitivity to IK-595 in cell lines
- **IND planned for 2H 2023**

Targeting AHR to Counter Immunosuppressive TME

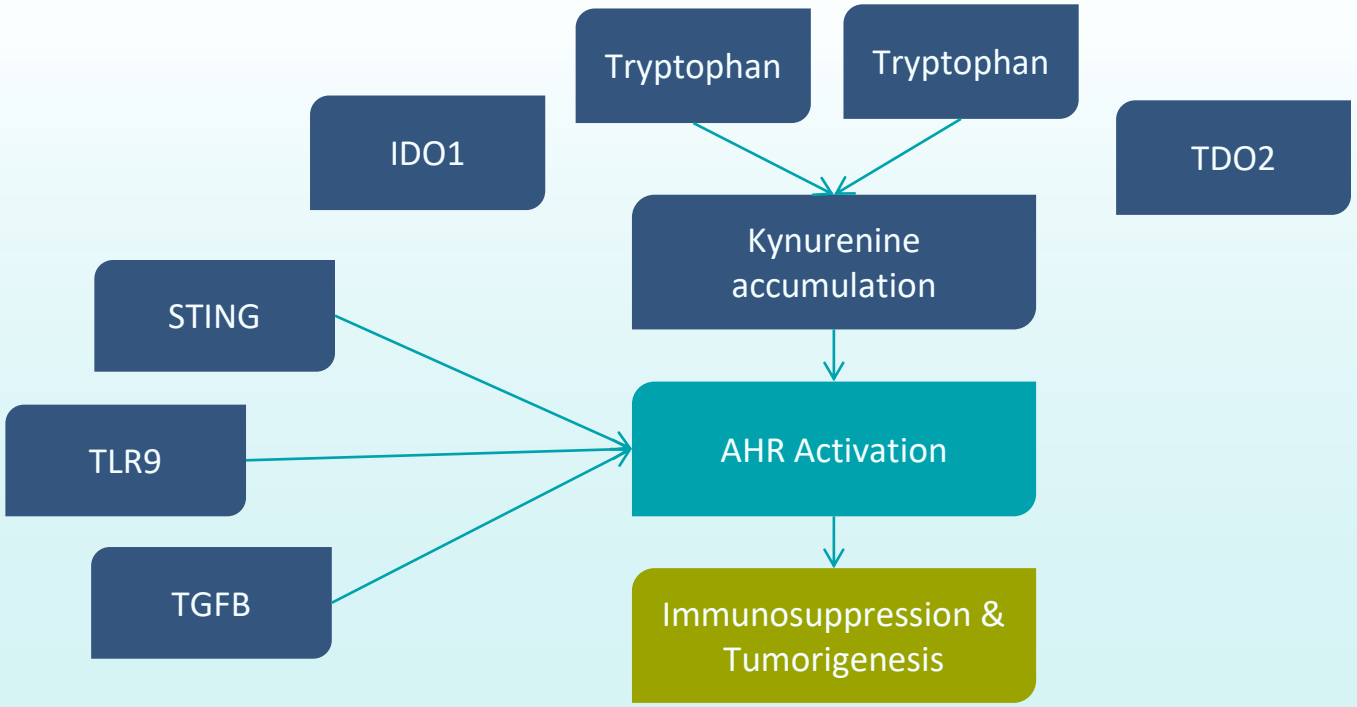
IK-175

Bristol Myers Squibb™

ikena ONCOLOGY

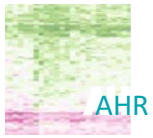
AHR's Role in Immune Signaling & Identifying Bladder Cancer as Key Population

Activated AHR can prevent immune recognition of cancer through both the innate and adaptive immune systems



AHR modulates activity in both the innate and adaptive immune systems

Novel Assays to Optimize Indication Selection

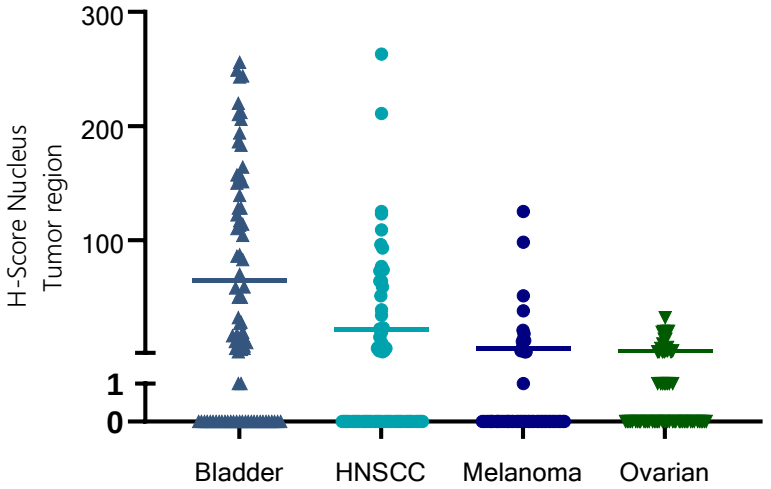


Proprietary transcriptional signature

Gene amplification

Proprietary IHC

Tumor Microarray Result



IK-175 Ph1 Study Ongoing in Urothelial Carcinoma Patients

Patients have exhausted SOC and progressed on CPIs

Clinical data presented at SITC 2022 including dose escalation (all-comers), and both mono and combo stage 1 expansion cohorts in urothelial carcinoma

- 43 total patients; 40 evaluable for anti-tumor activity
- 20 dose escalation
- 20 dose expansion (10 mono, 10 combo)

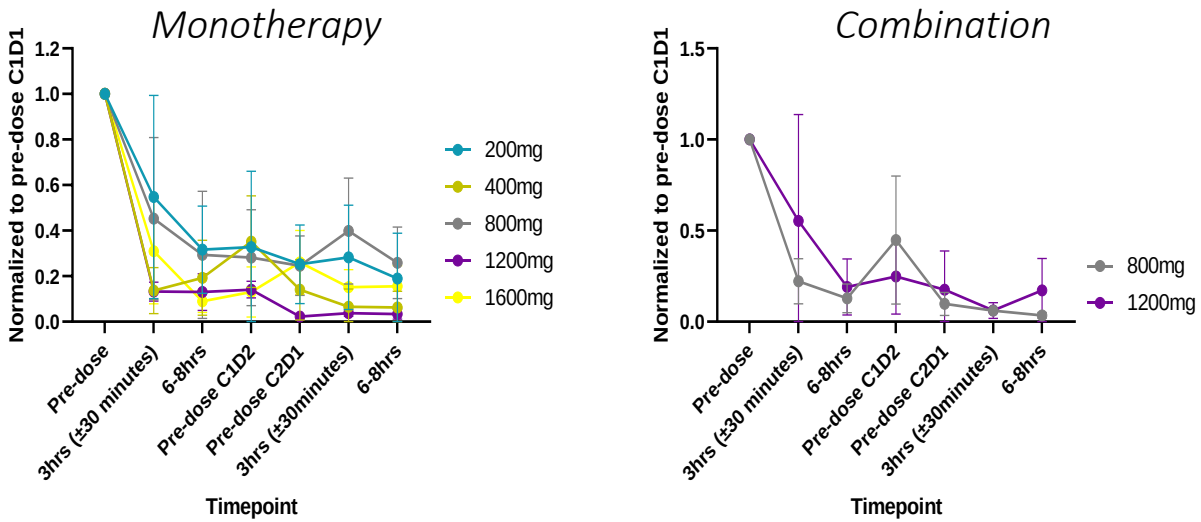
Pharmacodynamics seen at all doses

No DLTs observed

IK-175 was well tolerated with a predictable and manageable safety profile

Encouraging anti-tumor activity and duration of response seen in IK-175 nivolumab combination expansion cohort

Pharmacodynamics at All Doses



Last-line, Heavily Pre-treated Patients

Demographics of Evaluable Urothelial Carcinoma Patients in Initial Clinical Analysis

	Monotherapy (n=10)	Combination (n=10)
Prior lines of anti-cancer therapy		
1-3	2	4
4-10	8	6
ADC experienced	9	6

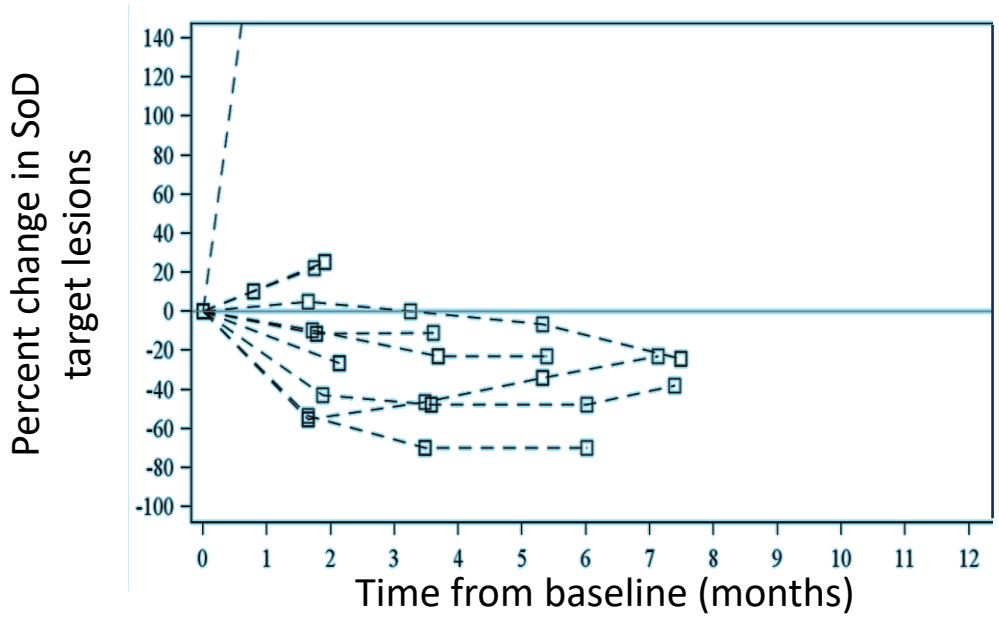
Initial Clinical Data in Urothelial Carcinoma Demonstrated Encouraging Anti-Tumor Activity

Clear evidence of monotherapy activity contributing to combination responses
Heavily pretreated patients exhausted all options -- failed checkpoints and have had up to 10 prior lines of therapy
Mono partial response ongoing over 15 months; Combo partial responses ongoing over 5 months

Initial Clinical Data from Stage 1 of Expansion Cohorts

	Monotherapy (n=10)	Combination (n=10)
Best overall response		
Confirmed partial response	1 (10%)	2 (20%)
Stable Disease	1 (10%)	2 (20%)
Progressive disease	6 (60%)	6 (60%)
ORR, n(%)	1 (10%)	2 (20%)
DCR, n(%)	2 (20%)	4 (40%)

Stage 1 of Combination Cohort in Urothelial Carcinoma Showed 40% DCR with Encouraging Anti-Tumor Activity



Combo result represent meaningful potential for patient population with significant and ongoing DoR

Stage 2 of expansion cohorts ongoing

Ikena Wholly Owned Pipeline Focused on Targeted Oncology in Hippo-Ras Oncosignaling Network

		Candidate *Target*	Indications *Interventions*	Partnerships & Rights	Discovery / IND Enabling / Phase 1	Upcoming Milestone
Targeted Oncology	*Hippo Pathway*	**IK-930** *TEAD*	Hippo-Altered Cancers *Monotherapy & Multiple Combinations*	ikena ONCOLOGY		Initial data expected 2H 2023
		Undisclosed	Hippo-Altered Cancers	ikena ONCOLOGY		Progressing research toward add 'l candidate
	RAS Pathway	**IK-595** *MEK-RAF*	RAS and RAF Altered Cancers; Additional Tumor Types	ikena ONCOLOGY		IND in 2H 2023
		Undisclosed	RAS-Mutated Cancers	ikena ONCOLOGY		Progressing research toward add 'l candidate
Immune-Signaling	*AHR Signaling*	**IK-175** *AHR*	Bladder Cancer, AHR Enriched *Monotherapy & Nivolumab Combination*	Bristol Myers Squibb		Presented initial data at SITC'22; continued trial progress
			Head & Neck Cancer, AHR Enriched *Nivolumab Combination*	Bristol Myers Squibb		Phase 1 ready


ikena™
ONCOLOGY