Corporate Presentation

Q2 2024

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 networks

- Multiple ongoing clinical trials with **expected data readouts in the next 12-18 months**
- **Leaders in Hippo pathway** with clinical stage TEAD1 inhibitor **IK-930**
  - Differentiated safety profile emerging from early clinical data & early signs of activity in EHE
  - Focused recruitment in mesothelioma and EHE; **additional clinical data planned for 2H 2024**
  - Broad combination potential including in EGFRm and RASm cancers, starting with osimertinib in NSCLC
- **Novel MEK/RAF molecular glue IK-595** with best in class potential
  - Potential for greater therapeutic index
  - Broad potential across RAF and RAS mutant cancers where prior MEK and RAF inhibitors have not succeeded
  - Cleared safety evaluation of first dosing cohort; dose escalation ongoing
- Closed 2023 with **>$175M in cash; Runway into 2H 2026**

Ikena Wholly-Owned Pipeline and Assets

Development Pipeline Focused on Targeted Oncology

Candidate *Target*	Interventions *Indications*
IK-930 *TEAD*	**Monotherapy** *Hippo-altered cancers including EHE, MPM, other NF2 altered tumors, and additional YAP/TAZ fusion tumors*
	Combination *IK-930+Osimertinib for EGFRm resistant NSCLC* *Additional combos combating therapeutic resistance to other targeted agents*
IK-595 *MEK-RAF*	**Monotherapy** *RAS and RAF altered cancers*
	Combination *Preclinical synergies with multiple agents*

EHE: Epithelioid Hemangioendothelioma | MPM: Malignant Pleural Mesothelioma | NSCLC: Non-Small-Cell Lung Cancer

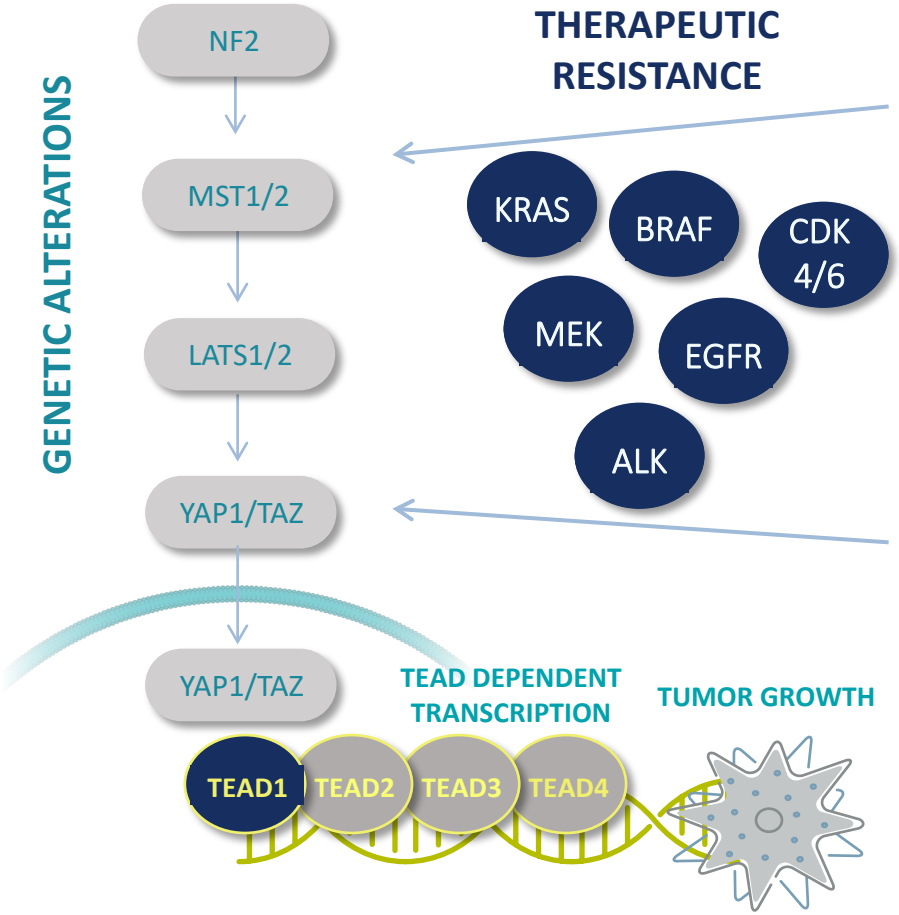
Targeting TEAD & the Hippo Pathway

IK-930

Targeting TEAD Can Address Diverse Patient Populations with High Unmet Need

Two distinct mechanisms: Genetic alterations in Hippo pathway and pathway involvement in therapeutic resistance

Hippo Pathway Activity Triggers TEAD Transcription-Dependent Tumor Growth

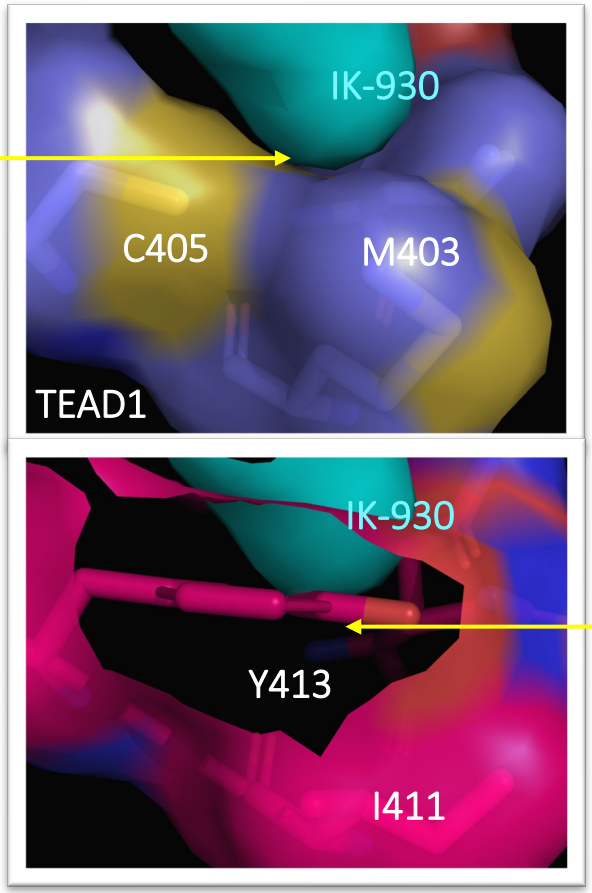


- Multiple genetic alterations lead to pathway activation including NF2 loss of function mutations and YAP/TAZ fusions
- Pathway activated through therapeutic resistance to treatment with other targeted therapies
- Monotherapy **clinically validated** in the field with a panTEAD inhibitor in mesothelioma
- panTEAD inhibition leads to proteinuria which limits continuous target coverage
- IK-930 designed to **optimized therapeutic index** by selectively targeting TEAD1 paralog
- IK-930 demonstrates efficacy equivalent to panTEAD inhibition in mesothelioma models and superior safety in multiple species

EHE: Epithelioid Hemangioendothelioma; MPM: Malignant Pleural Mesothelioma.

IK-930 Drives TEAD1 Toward a Transcriptional Repressive State

Promotes TEAD1/VGLL4 interaction which broadly blocks oncogenic gene expression

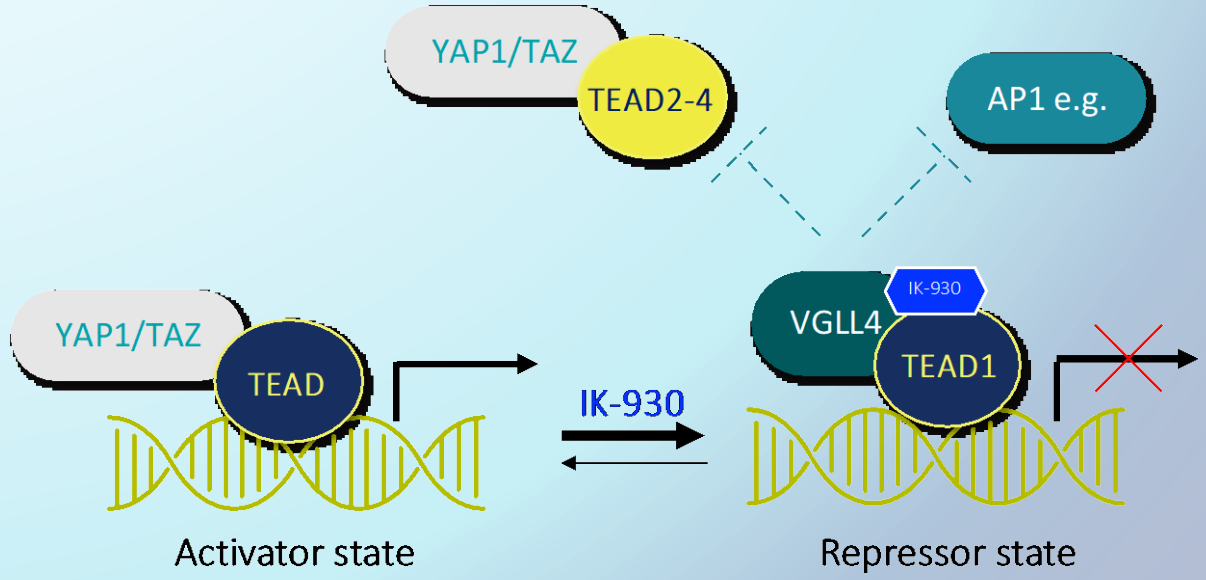


IK-930 is designed to selectively bind TEAD1 while blocking TEAD oncogenic activity across paralogs

Two Opposing States of TEAD

Activator with YAP1 or TAZ (palmitoylation dependent)	Repressor with VGLL4 (palmitoylation independent)

IK-930 Leverages TEAD Biology to Gain Repressive Activity from Both States

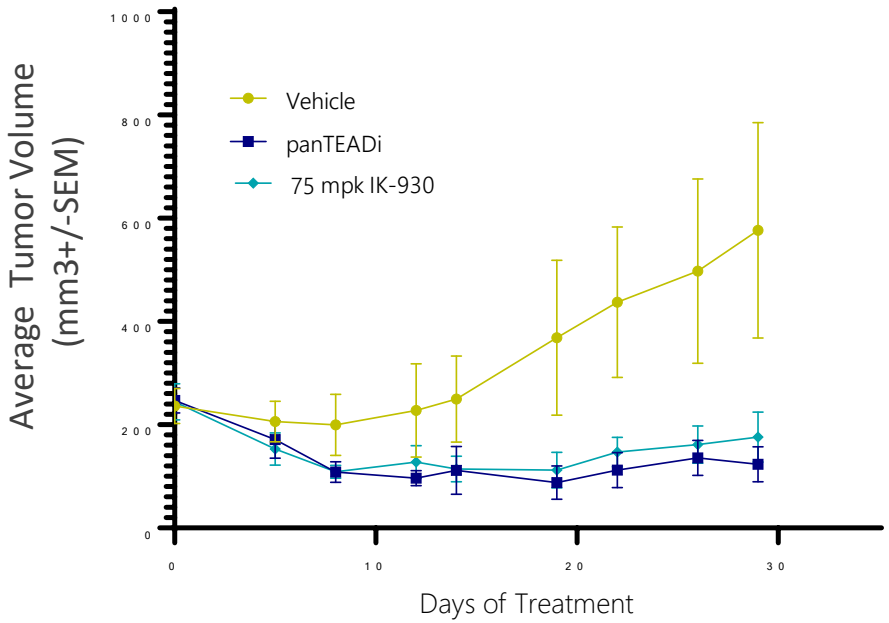


IK-930-TEAD1-VGLL4 complex blocks chromatin access for TEADs and other transcriptional activators

IK-930 Preclinical Data Suggests Similar Efficacy to panTEADi with Differentiated Safety Potential

IK-930 Shows Preclinical Efficacy in Mesothelioma Models Similar to panTEADi

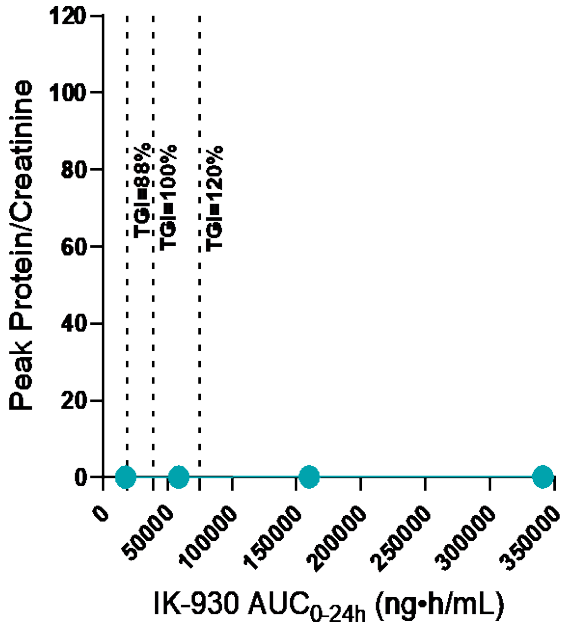
NF2 Deficient Mesothelioma Model



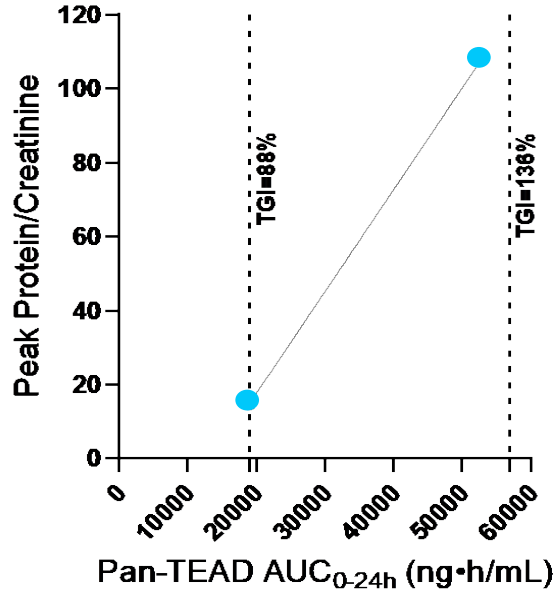
IK-930 showed efficacy across multiple models with different Hippo pathway alterations

IK-930 Does Not Result in Proteinuria at All Tested Doses in Monkeys, in Contrast to panTEADi

IK-930 Monkey 28-day



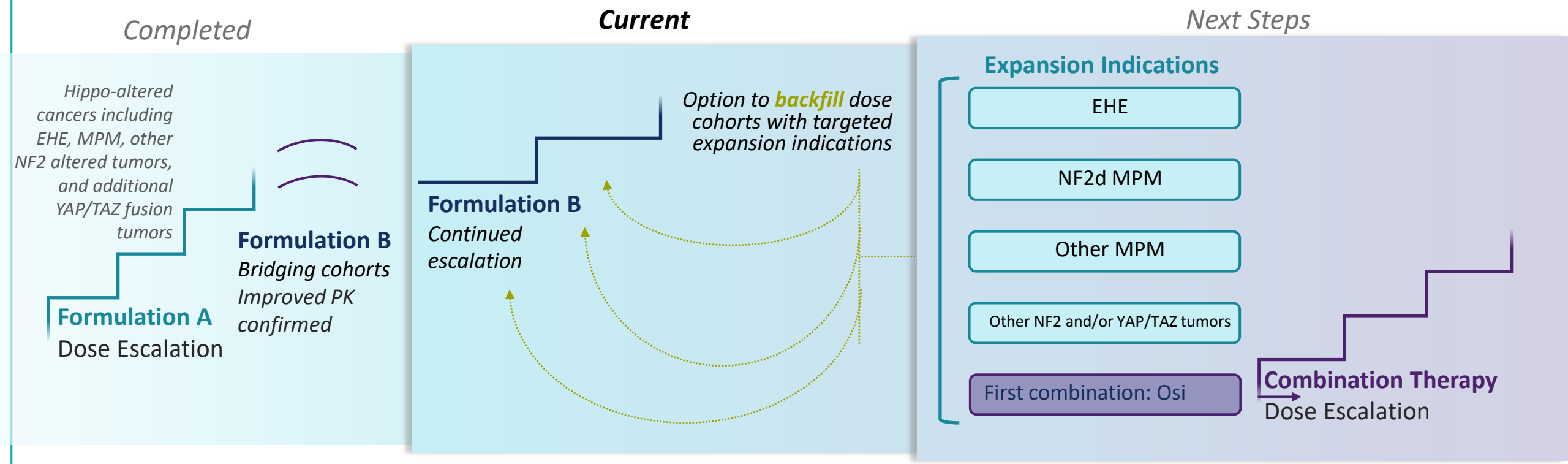
panTEADi Monkey 28-day



Average urinary protein-to-creatinine ratios and histopathology in non-human primates predicted a ***therapeutic index of less than one for panTEAD*** *inhibitors and a* ***broad therapeutic window for IK-930***

Current Status of IK-930 Phase 1 Clinical Trial

Dose escalation data from IK-930 phase I trial shows early signs of clinical benefit & safety advantages



IK-930 is designed to **selectively bind TEAD1** while blocking TEAD oncogenic activity across paralogs

Demonstrated **preclinical efficacy equivalent to panTEAD** in mesothelioma models and superior safety in multiple species

IK-930 does not result in proteinuria at all tested doses in monkeys, in contrast to panTEAD inhibition

Favorable clinical safety profile seen in clinical dose escalation

Clinical data update planned for 2H 2024

IK-930 First Signs of Clinical Impact in EHE; Ultra Orphan Indication with No Standard of Care

Epithelioid hemangioendothelioma (EHE)

- 100% defined by Hippo pathway alterations
- 300 patients in the US per year
- **No standard treatment**
  - EHE can range from very indolent to rapidly growing tumors resistant to systemic therapy
  - Aggressive clinical symptoms
  - RECIST has limited value* in capturing changes to disease related symptoms (e.g. pain) and QOL changes

Additional Analysis to Better Qualify QoL Impact in IK-930 Program

- Centrally confirm YAP/TAZ fusions by RNAseq
- Characterize oncogenic mutations by WES
- **Evaluate TEAD dependence and EHE transcriptional signatures by RNAseq**
- Characterize ctDNA molecular response by PCR

All 7 EHE Dose Escalation Patients Demonstrating Initial Clinical Benefit with IK-930 Treatment

7 out of 7 patients reached **stable disease (SD)**

3 out of 7 patients with SD experienced **tumor shrinkage** in multiple target and non-target lesions

3 out of 7 patients continue on treatment with **time on IK-930** ranging from 18 to 26 weeks and ongoing

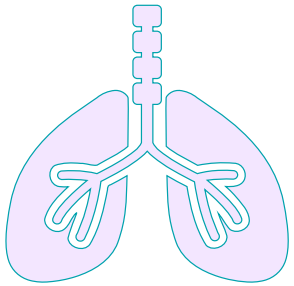
4 out of 7 patients had **improvement of clinical symptoms** and subjective **improvement of QoL**

4*ESMO 2021; Additional Sources: US Incidence MS-2, Pg 28 NCCN 2023; EU Incidence Global Cancer Observatory 2020; NCCN Version 1.2023 Mesothelioma: Pleural; NCCN Patients Guidelines; Image 1_Types; Image 2_Location; Image 3_Asbestos; Brcic et al, 2020

Hippo Pathway is Implicated in Resistance to Multiple Targeted Therapies

IK-930 has the potential to combat resistance and expand the number of patients that could benefit from targeted therapies

Two Clinical Opportunities in EGFR Resistance



First Line Combo with Osi

First line osi combined with IK-930 to potentially prevent the emergence of resistance

Post Resistance Emergence

Treating with IK-930 post the emergence of resistance – negatively selecting for actionable mutations

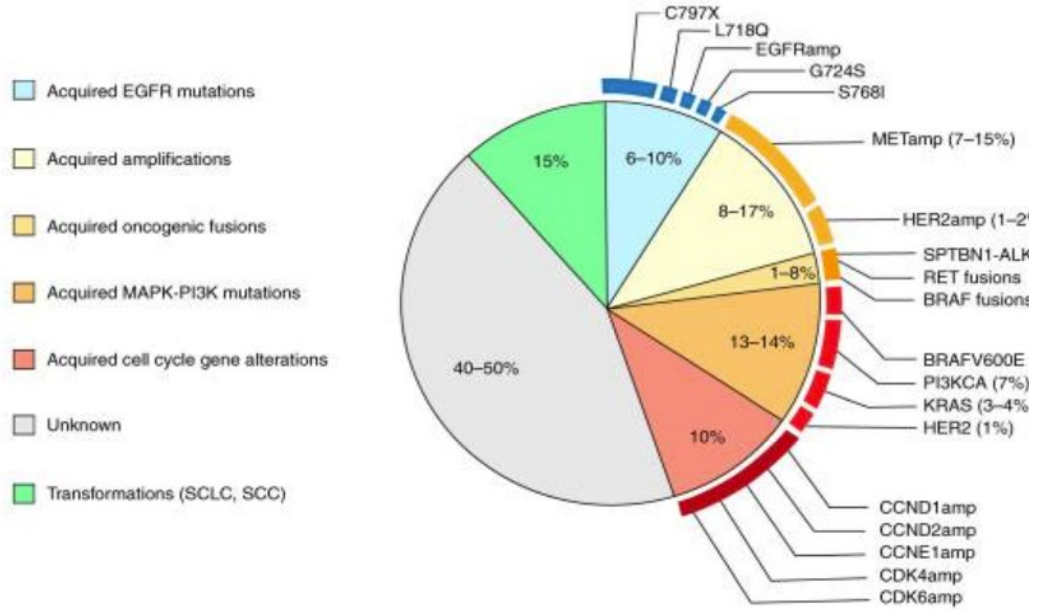
Exploring both as potential paths in clinical program

Clinical supply agreement with AstraZeneca for osimertinib signed in 2022; first combo planned for clinical program

Case Study: Resistance Mechanisms to Osi in EGFRm NSCLC

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

Leonetti, et al., Br J Cancer, 2019



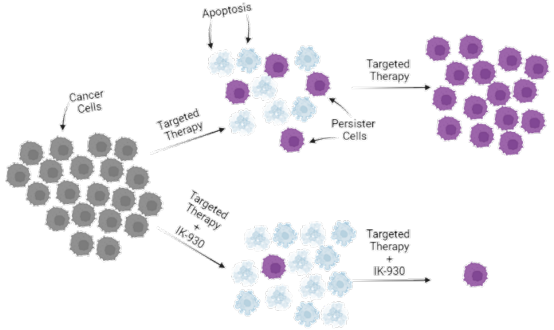
"The biggest hurdle to targeted cancer therapy is the inevitable emergence of drug resistance."

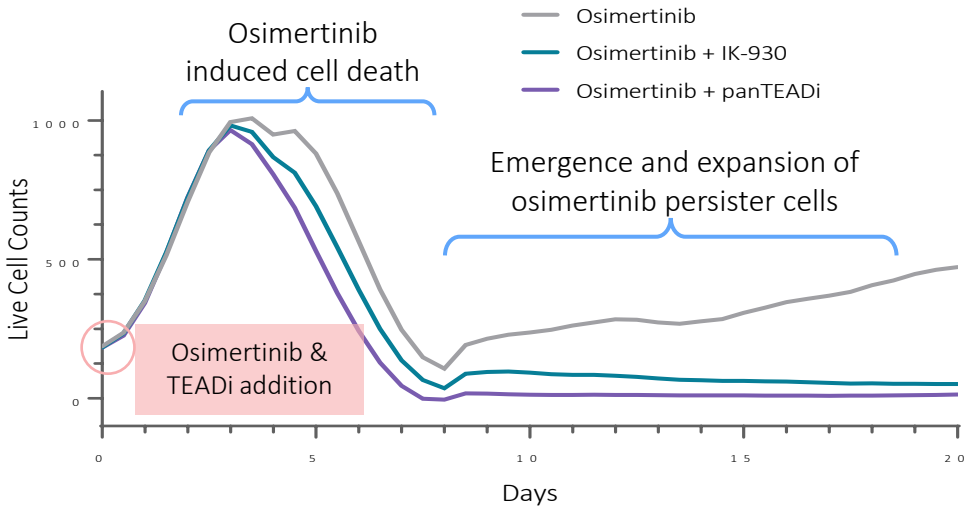
Lim, et al. Journal of Hematology & Oncology 2019

IK-930-Osi Combo Delays Tumor Regrowth in vivo and Can Prevent Emergence of Persisters

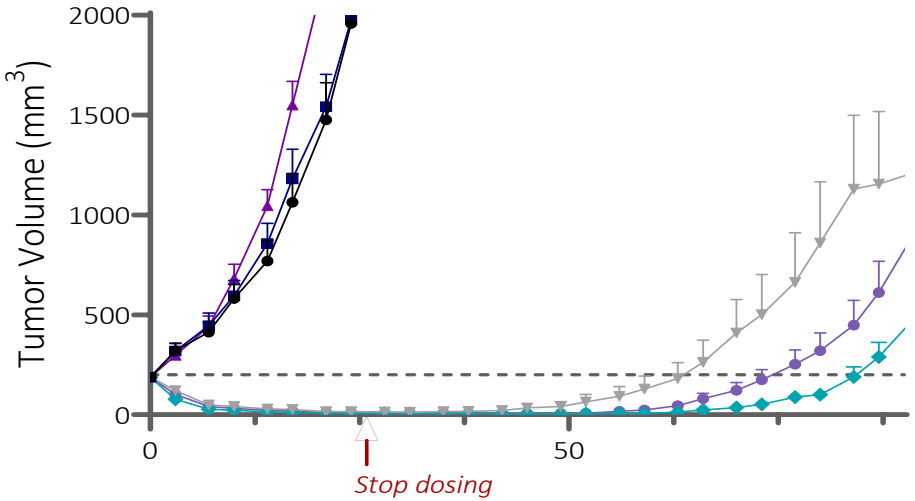
Potential for IK-930 to prevent resistance to EGFR inhibitors and even reverse the effect when given after resistance has already emerged

IK-930 Delays Emergence of Osi-Resistance *Persisters* Comparably to panTEADi





IK-930 + Osi Delays Tumor Regrowth More than panTEADi *in vivo*



Looking Ahead to Robust Monotherapy Data Set in 2H 2024 for First-In-Class Hippo Inhibitor

Continued recruitment in multiple targeted indications including mesothelioma and EHE with valuable partnerships with patient advocacy groups and key investigators

THE EHE FOUNDATION

Mesothelioma Applied® Research Foundation
research - education - support - advocacy

IK-930: First-in-class, paralog-selective TEAD inhibitor

Differentiated safety profile shown in early clinical data

Early signs of activity in EHE

Additional clinical data expected in the second half 2024

MEK-RAF Molecular Glue

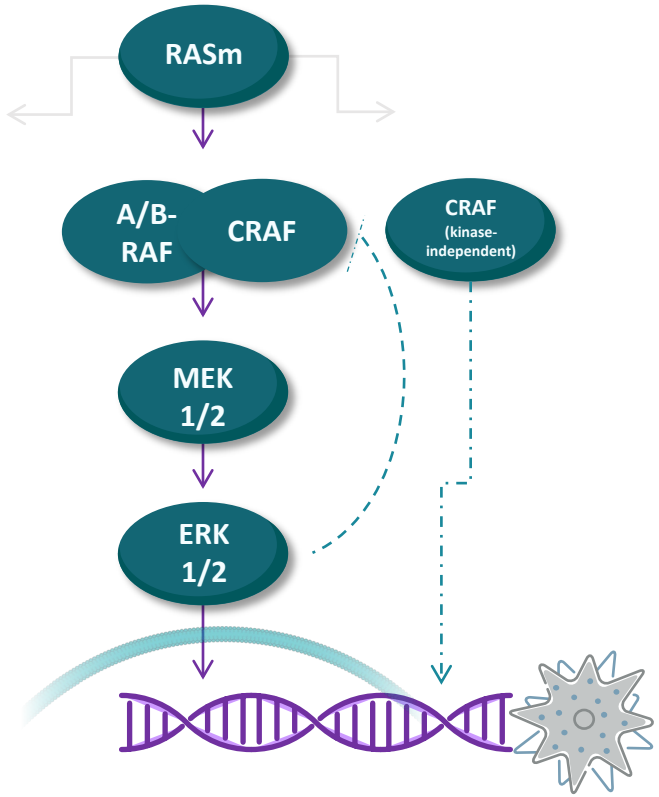
IK-595

ikena ONCOLOGY

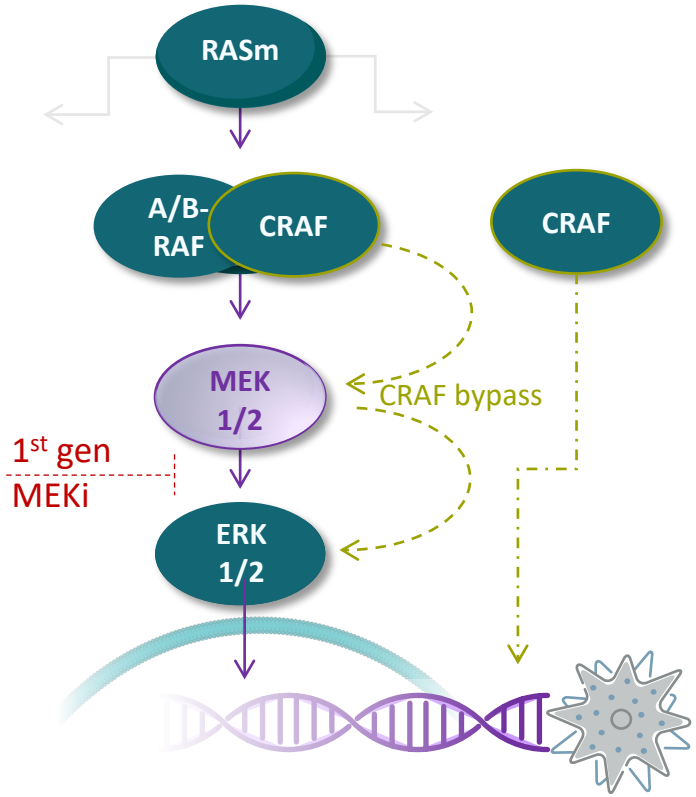
First Generation MEK Inhibitors: Insufficient Targeting Leads to Limited Activity

- 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

MEK's role in driving ERK-mediated tumor growth

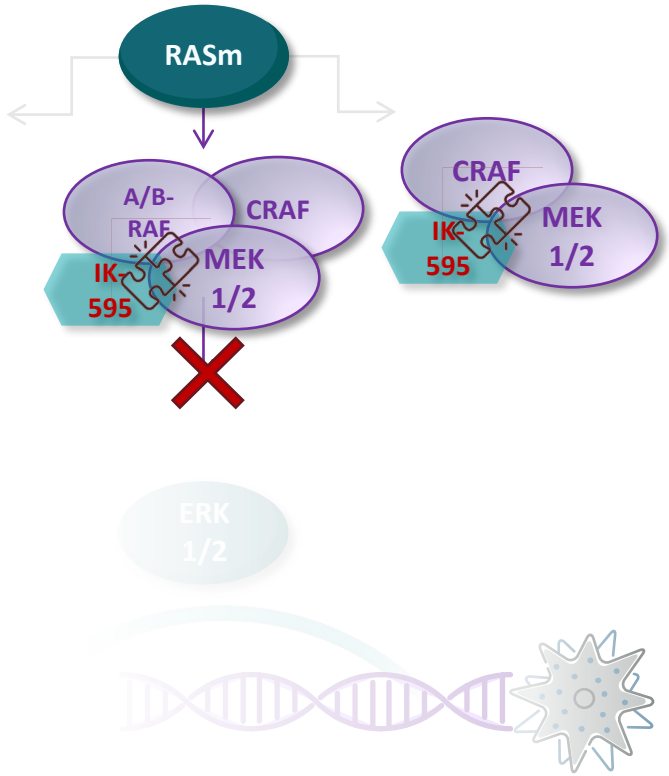


First-gen MEK inhibitors trigger CRAF mediated pathway reactivation



IK-595: A Best-in-Class Dual MEK-RAF Molecular Glue with a Unique MoA and Optimized PK

IK-595 glues 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

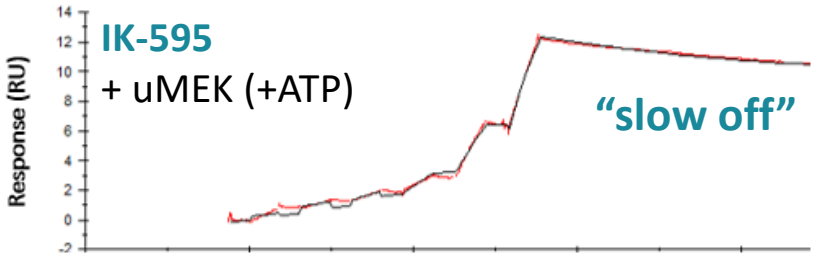
- ✓ Inhibit MEK mediated ERK1/2 phosphorylation
- ✓ Prevent MEK phosphorylation by RAF
- ✓ Alleviate therapeutic resistance through CRAF mediated bypass and pathway reactivation
- ✓ Block CRAF kinase independent activities
- ✓ Optimized PK profile to target IC90 plasma concentrations widening the therapeutic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

IK-595 could address cancers traditional MEK inhibitors have been unable to treat

- KRAS, NRAS (and other such as non-V600E BRAF) tumors signal through B, C, and A RAF as dimers and first generation MEK inhibitors are not effective (due to feedback activation and kinase independent functions)
- IK-595 could be active in KRAS and NRAS tumors by preventing both feedback activation and by inhibiting the kinase independent function of CRAF

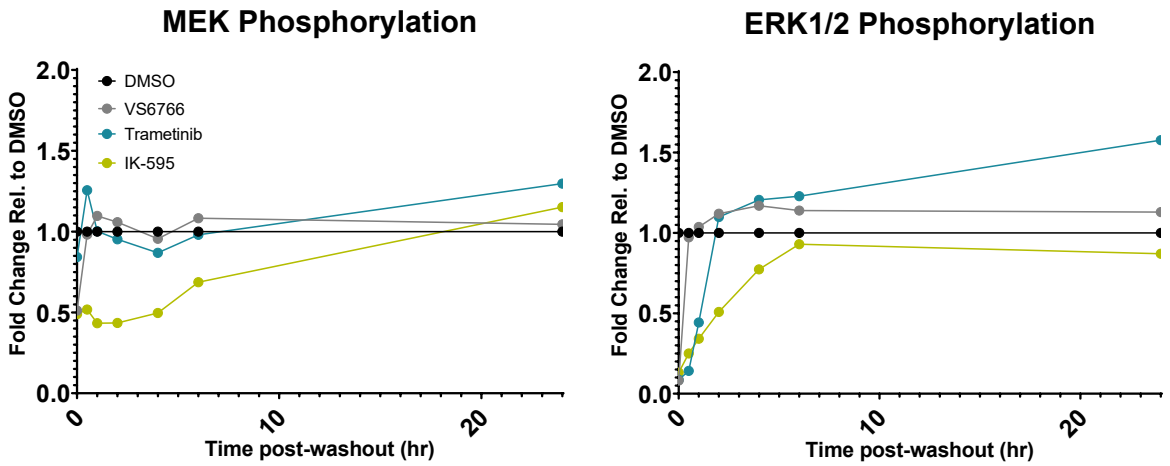
IK-595 Tight Binding and Slow Off Right Prolongs Inhibition; Strong Stabilization of MEK-CRAF, MEK-BRAF, MEK-ARAF

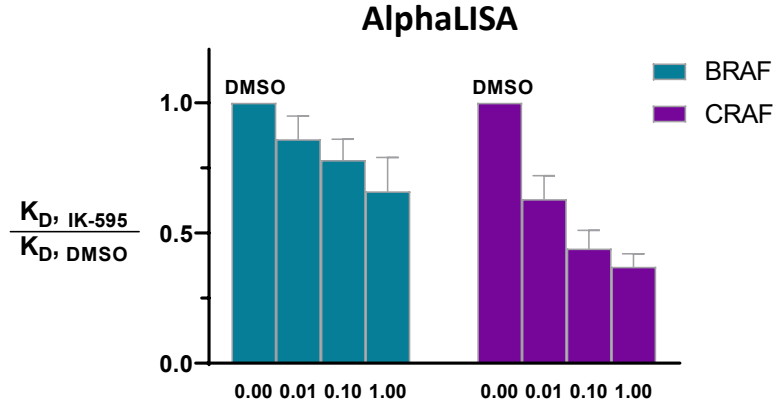
IK-595 binds to MEK with much slower off-rate kinetics compared to other assets



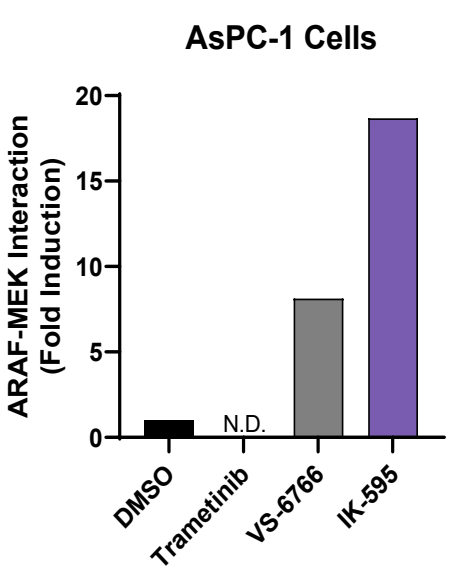
MEK	On Rate ($M^{-1}s^{-1}$)	Off Rate (s^{-1})	Affinity (nM)
IK-595 (to MEK)	8.24 E+04	**6.09 E-04**	7.39

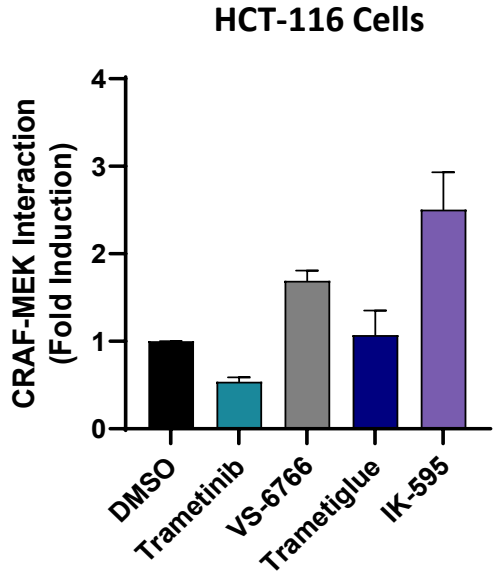
Slow off rate allows for intermittent dosing schedules





MEK-BRAF: $K_{D,\ DMSO}$ = 16.3 nM
MEK-CRAF: $K_{D,\ DMSO}$ = 5.9 nM

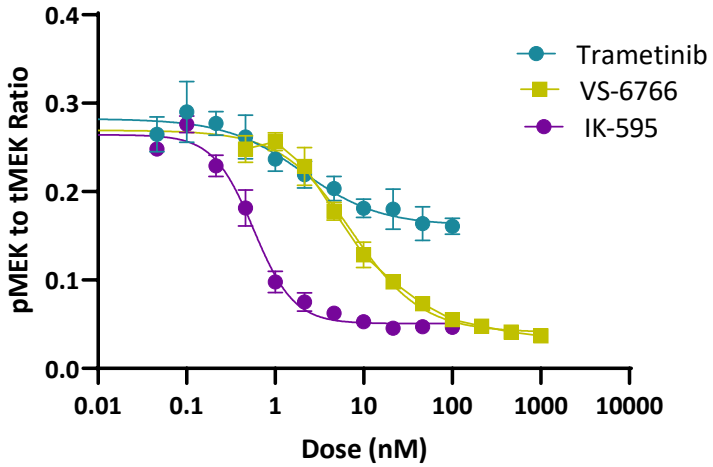




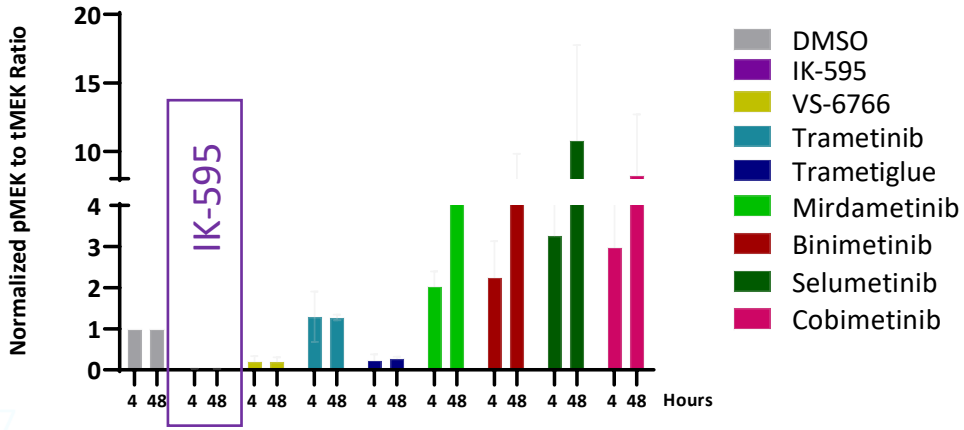
IK-595 Leads to More Durable Pathway Suppression than Other MEK Inhibitors

IK-595 Potently Inhibits MEK Phosphorylation In Vitro

***In vitro* MEK Phosphorylation (AsPC-1 cells)**

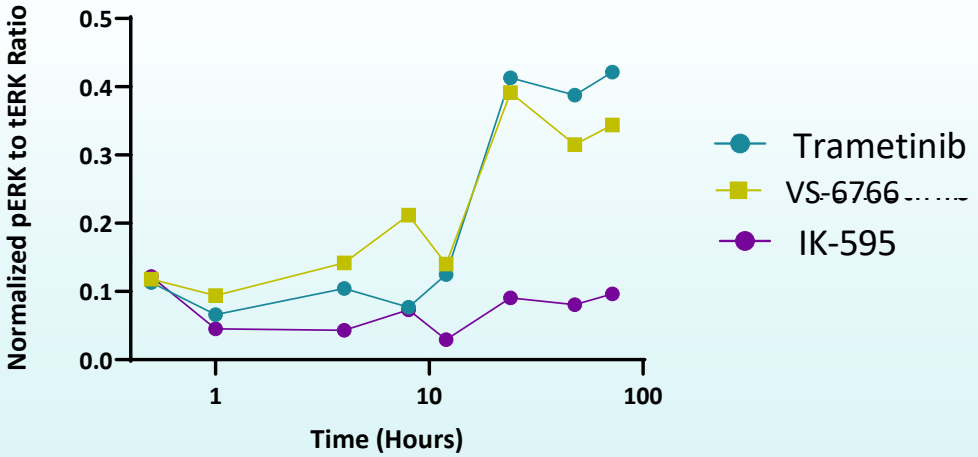


***In vitro* MEK Phosphorylation (HCT116 cells)**

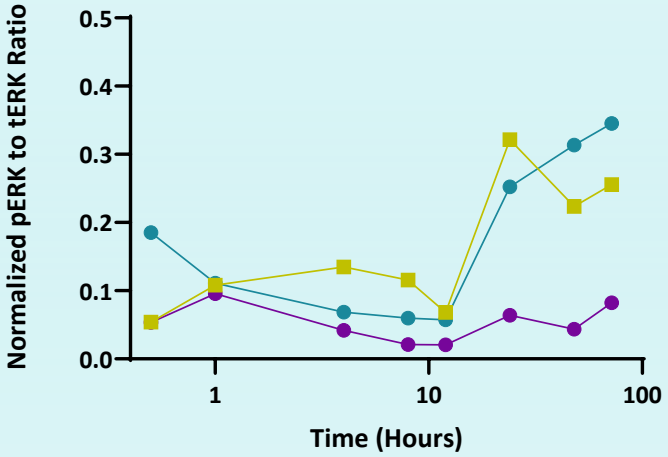


IK-595 Demonstrates Robust and Prolonged pERK Inhibition in Multiple Cell Lines

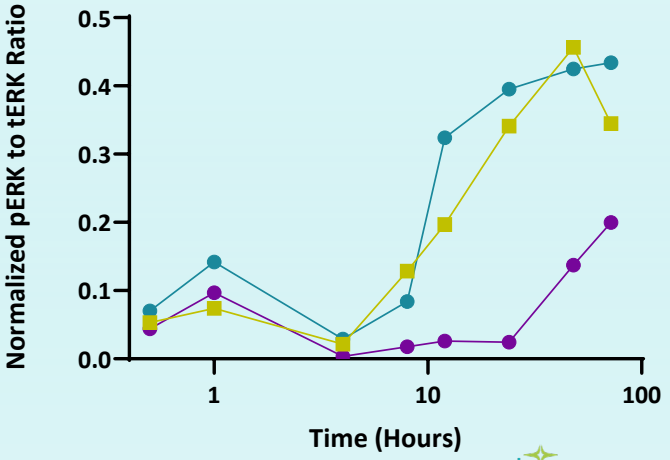
AsPC1 (KRASmut Pancreatic)



NCI-H2122 (KRASmut Lung)



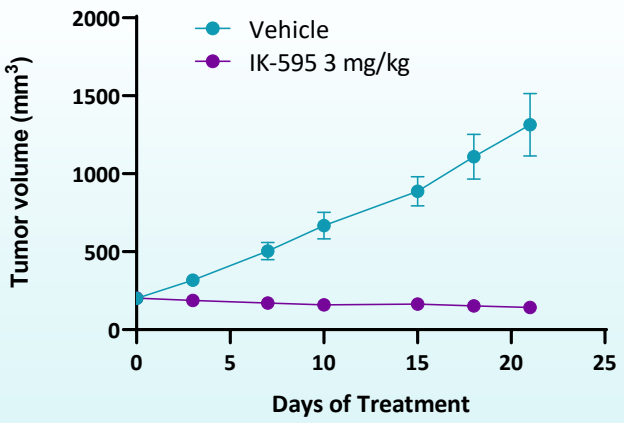
5637 (CRAF Amplified Bladder)



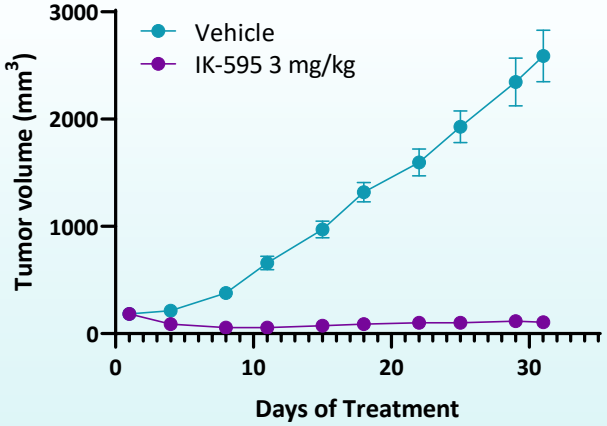
Robust Efficacy in RAS & RAF Models; High Sensitivity in CRAF Dependent Models

Antitumor Activity Across Models at Tolerated IK-595 Doses

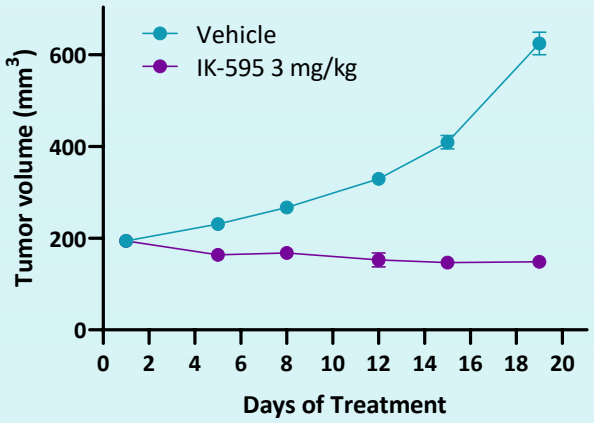
AsPC-1: KRAS G12D Pancreatic Model



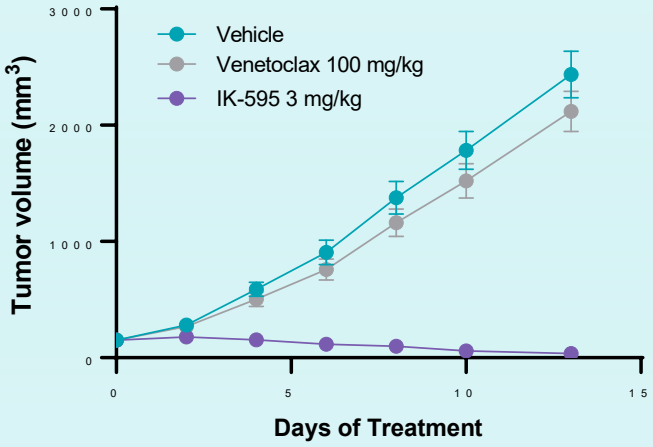
NCI-H2122: KRAS G12C Lung Tumor Model



5637: CRAF Amplified Bladder Tumor Model

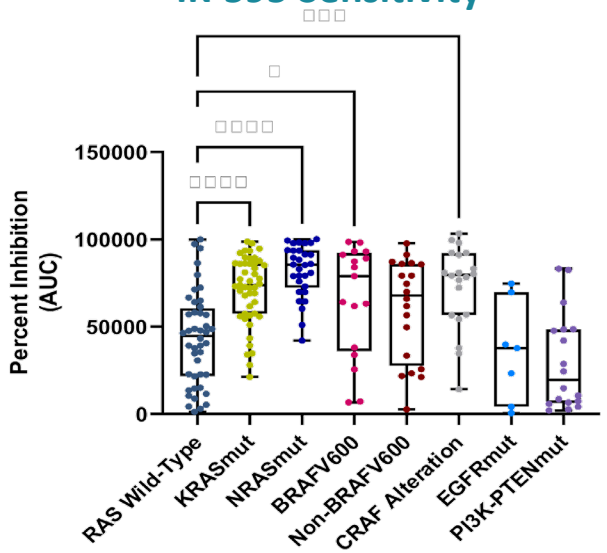


OCI-AML-3: NRAS Q61L Acute Myeloid Leukemia



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

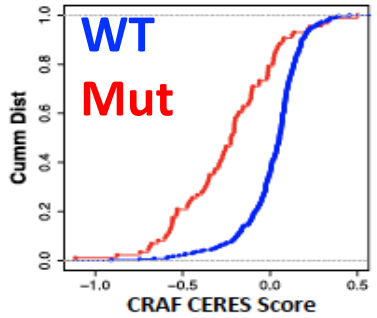
IK-595 Sensitivity



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

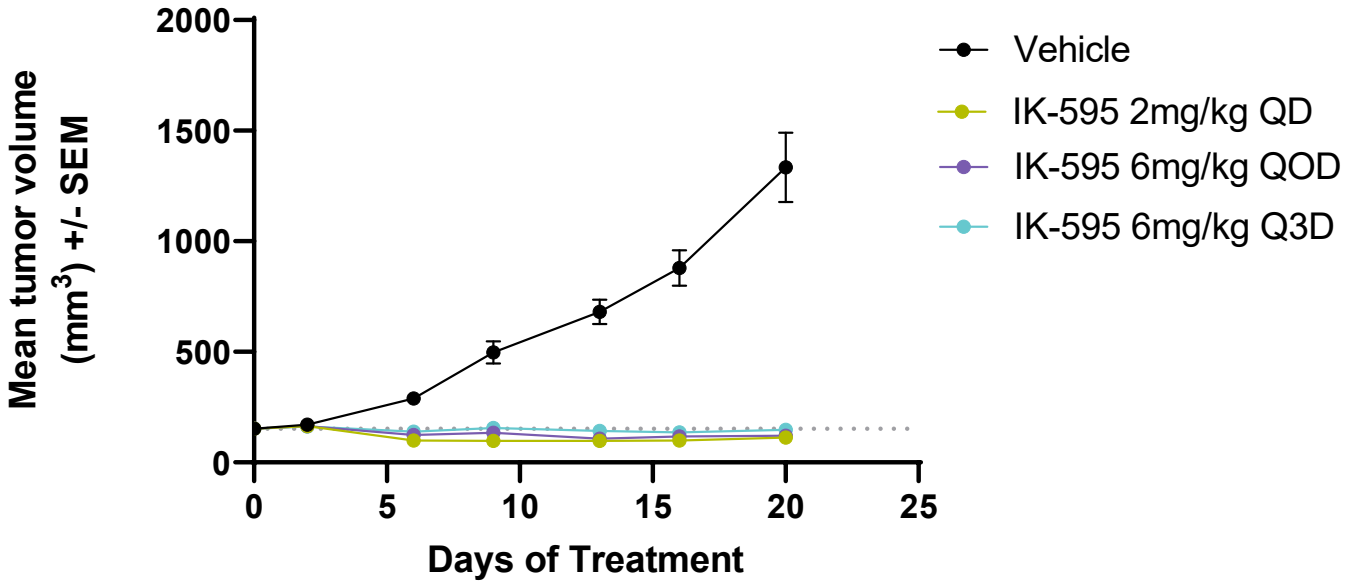
NRAS and KRAS – CRAF CERES Score

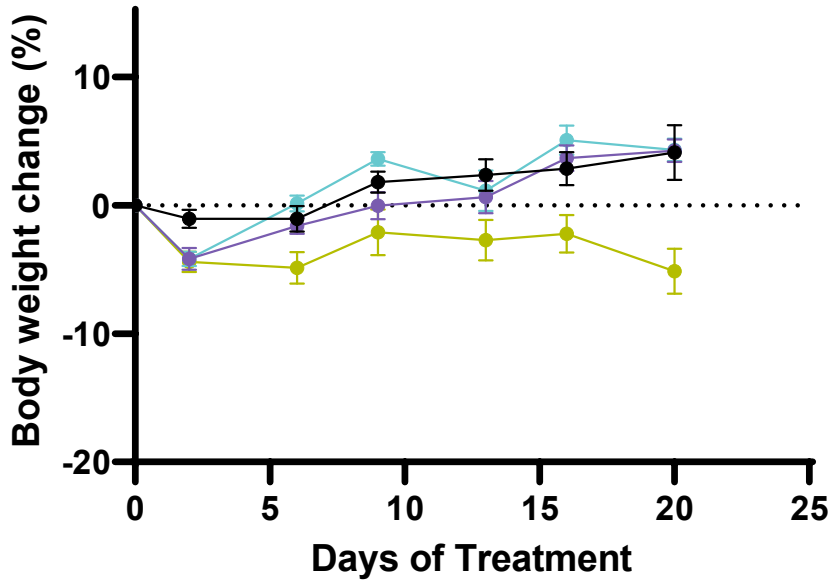
Jones, 4th RAS-Targeted Drug Development Summit 2022



In Vivo Efficacy Demonstrated Following Intermittent Dosing of IK-595

KRAS G12V Lung Cancer Model with Multiple IK-595 Dosing Schedules



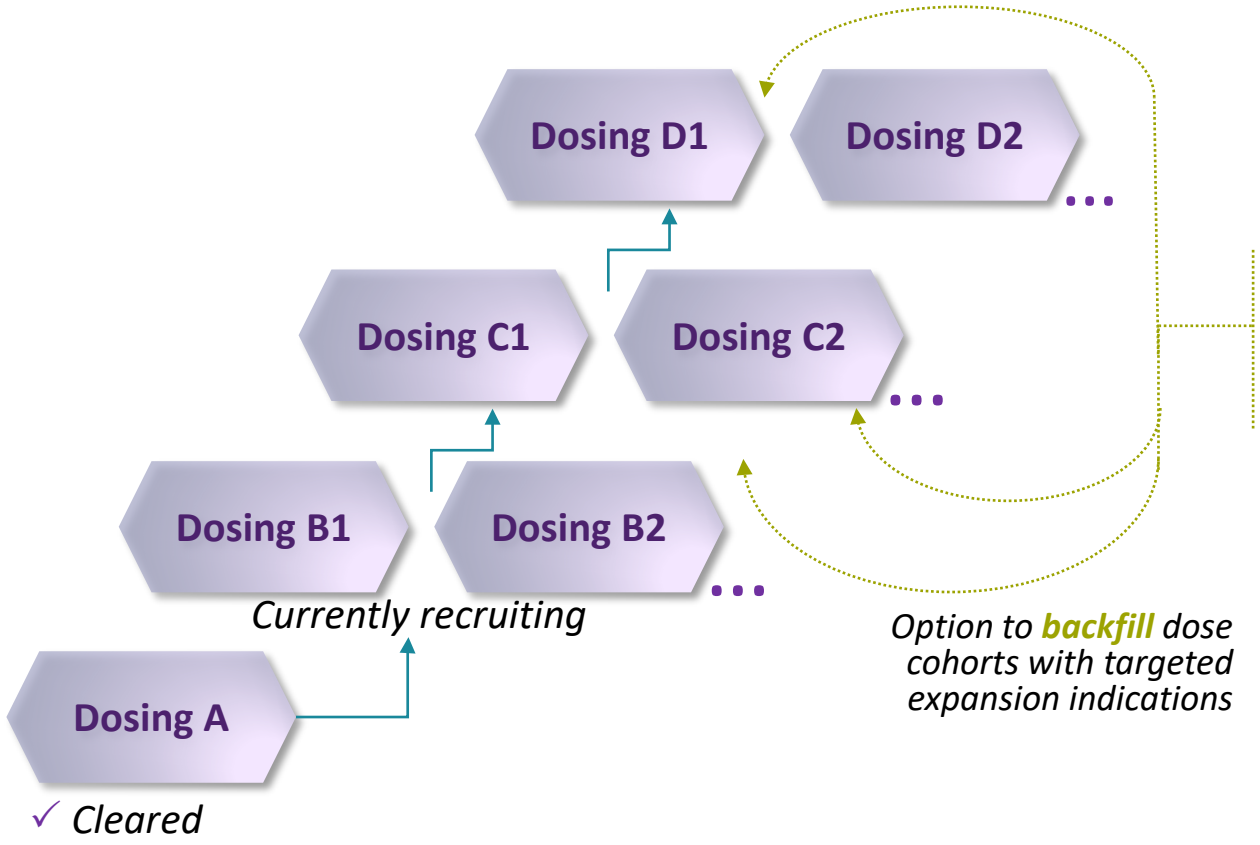


QD, QOD, and Q3D dosing show equivalent efficacy in multiple CDX models with better tolerability for intermittent schedules

IK-595 Clinical Program Explores Multiple Dosing Schedules and Targeted Indications

Dose Escalation & Dose Schedule Exploration

Recruiting only targeted patients into dose escalation including any with RAS or RAF mutations



Dose Expansion and Combinations Following Dose Schedule Selection

Potential indications where IK-595 could be differentiated from other MEK inhibitors

Monotherapy expansions and potential backfill populations

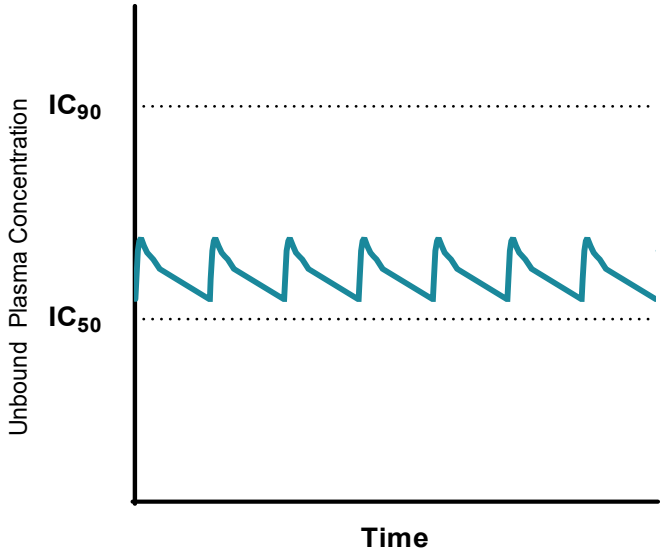
- NRASm CRC and/or melanoma
- KRASm solid tumors including pancreatic, CRC, NSCLC
- BRAFm type II/III
- CRAFm tumors
- Combinations including potentially w/ other targeted therapies in RAS/RAF pathway, mAbs, chemo

IK-595 Designed for Therapeutic Index Optimization

$T_{1/2}$ optimized to enable dosing schedules to hit above IC_{90} and achieve impact while allowing for holiday

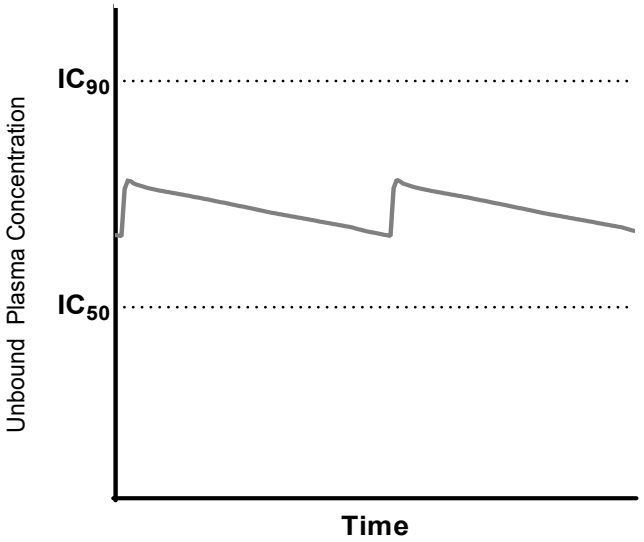
Trametinib

Clinical PK
2 mg QD



VS-6766

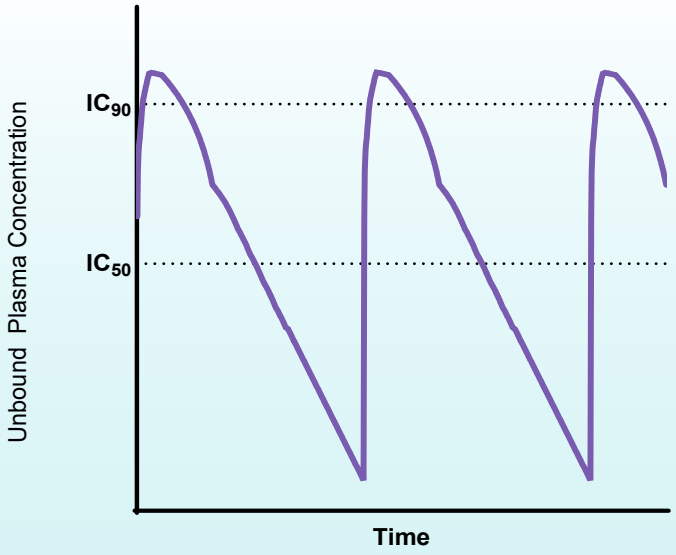
Clinical PK
3.2 mg twice/week



Clinical doses of trametinib and VS-6766 do not reach plasma concentrations above pERK IC_{90} due to the very long human $T_{1/2}$ of trametinib (72-120 hrs) and VS-6766 (60-100 hrs)

IK-595

Human Predicted PK



Shorter human $T_{1/2}$ of IK-595 allows flexibility in dosing schedules

Enables transient plasma concentrations above IC_{90} & recovery before next dose

Ikena Wholly Owned Pipeline

Pipeline Focused on Targeted Oncology

Candidate *Target*	Interventions *Indications*	IND Enabling	Phase 1	Upcoming Milestones
IK-930 *TEAD*	**Monotherapy** *Hippo-altered cancers including EHE, MPM, other NF2 altered tumors, and additional YAP/TAZ fusion tumors*			Next data 2H 2024 including MPM and new formulation PK/PD
	Combination *IK-930+Osimertinib for EGFRm resistant NSCLC* *Additional combos combating therapeutic resistance to other targeted agents*			Initiation of Osimertinib post monotherapy dose finding in 2H 2024
IK-595 *MEK-RAF*	**Monotherapy** *RAS and RAF altered cancers*			Clinical execution in 2024
	Combination *Preclinical synergies with multiple agents*			Initiation post monotherapy dose finding

EHE: Epithelioid Hemangioendothelioma | MPM: Malignant Pleural Mesothelioma | NSCLC: Non-Small-Cell Lung Cancer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