UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 17, 2023

IKENA ONCOLOGY, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-40287**	**81-1697316**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

Ikena Oncology, Inc.
645 Summer Street, Suite 101
Boston, Massachusetts 02210
(Address of principal executive offices, including zip code)

(857) 273-8343
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trade Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	IKNA	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On April 17, 2023, Ikena Oncology, Inc. (the "Company") issued a press release announcing preclinical data in the Company's novel investigational Hippo pathway inhibitor, IK-930. The Company also updated its corporate presentation. A copy of the press release and the Company's updated corporate presentation are attached as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K. The corporate presentation will also be available in the investor relations section of the Company's website at https://www.ikenaoncology.com/.

The information in this Current Report on Form 8-K (including Exhibits 99.1 and 99.2) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Items.

On April 17, 2023, the Company announced preclinical data, summarized below, in the Company's novel investigational Hippo pathway inhibitor, IK-930. IK-930 was designed as a TEAD1-selective inhibitor to avoid on-target renal toxicity expected from panTEAD inhibition. TEAD1 is the most highly expressed TEAD paralog in mesothelioma and epithelioid hemangioendothelioma (EHE). The Company believes the preclinical data support the ongoing IK-930 Phase 1 program in patients with Hippo mutated cancers and the Company's planned expansion into combinations of IK-930 with other targeted therapies in multiple cancer types, including across EGFR and RAS mutated cancers, to potentially delay or even reverse therapeutic resistance. The preclinical data include:

- In nonclinical models and species, IK-930 demonstrated selective inhibition of TEAD1 with equivalent activity to broad TEAD inhibitors and a significantly improved tolerability profile
- IK-930 promotes repressive TEAD1 activity by driving interactions with VGLL4, a signaling partner that reduces expression of pro-growth and anti-apoptotic genes
- Through its binding with TEAD1 and VGLL4, IK-930 potentially blocks chromatin binding of other TEAD paralogs

- In assessing the potential on-target renal toxicity of targeting TEAD, average urinary protein-to-creatinine ratios and histopathology in non-human primates predicted a therapeutic index of less than one for panTEAD inhibitions and a broad therapeutic window for IK-930
- Treatment with IK-930 in combination with multiple targeted agents, such as EGFR, KRAS G12C, and MEK inhibitors, demonstrated a reduction in emergence of drug resistant “persister” cells

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

99.1	Ikena Oncology, Inc. Press Release
99.2	Ikena Oncology, Inc. Corporate Presentation
104	Cover Page Interactive Data File

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Ikena Oncology, Inc.

Date: April 17, 2023

By: /s/ Mark Manfredi
Mark Manfredi, Ph.D.
President and Chief Executive Officer

Ikena Oncology Shares Differentiation Profile of IK-930, a Novel Hippo-Pathway Inhibitor, Including Projected Therapeutic Index Advantages and Breadth of Patient Populations at AACR 2023 Annual Meeting

IK-930 is a potent Hippo-pathway inhibitor that selectively binds TEAD1 and broadly represses oncogenic TEAD signaling

IK-930's differentiated paralog selectivity and robust repressor activity in complex with VGLL4 are key characteristics for potential tumor impact and increased therapeutic index

Non-human primate data demonstrate treatment with IK-930 does not result in any clinical signs of renal toxicity at all doses, in contrast to panTEAD inhibition

Robust preclinical data from IK-930 combinations to combat therapeutic resistance to other targeted therapies suggests broad applicability beyond initial Hippo-altered cancers, including EGFR and RAS mutant cancers

BOSTON, April 17, 2023, – Ikena Oncology, Inc. (Nasdaq: IKNA, "Ikena"), a targeted oncology company forging new territory in patient-directed cancer treatment, today announced that it will present preclinical data in two poster presentations highlighting the Company's novel Hippo pathway inhibitor, IK-930, at the American Association for Cancer Research (AACR) Annual Meeting taking place in Orlando, FL from April 14-19, 2023.

Data being shared today reveals that IK-930 selectively binds and inhibits TEAD1 and further describes the mechanism for its antitumor activity. Key advantages demonstrated in the nonclinical studies include IK-930's superior tolerability and comparable antitumor activity compared to panTEAD inhibition, resulting in a significantly improved projected therapeutic window in cancer patients. IK-930 was designed as a TEAD1-selective inhibitor to avoid on-target renal toxicity expected from panTEAD inhibition. TEAD1 is the most highly expressed TEAD paralog in mesothelioma and epithelioid hemangioendothelioma (EHE). The data being presented support the ongoing IK-930 Phase 1 program in patients with Hippo mutated cancers and the planned expansion into combinations of IK-930 with other targeted therapies in multiple cancer types, including across EGFR and RAS mutated cancers, to potentially delay or even reverse therapeutic resistance.

"IK-930's selectivity profile is the ultimate example of what we are aiming to do at Ikena – creating effective and safe targeted oncology treatments that have the potential to benefit both patients with primary-defined cancers and prevent resistance to other targeted therapies. Targeted oncology came to fruition as a way to develop highly specific therapies that can benefit patients — to spare healthy tissue instead of causing widespread toxicity — it is crucial to take into account a target's function outside of a patient's cancer," said Mark Manfredi, Ph.D., Chief Executive Officer of Ikena Oncology. "Tolerability across multiple nonclinical species, including non-human primates, was central to our design of IK-930 and our enthusiasm about its potential in the clinic."

Highlights from the data in today's poster include:

- In nonclinical models and species, IK-930 demonstrated selective inhibition of TEAD1 with **equivalent activity** to broad TEAD inhibitors and a **significantly improved tolerability profile**

- IK-930 promotes repressive TEAD1 activity by driving interactions with VGLL4, a signaling partner that reduces expression of pro-growth and anti-apoptotic genes
- Through its binding with TEAD1 and VGLL4, IK-930 potentially blocks chromatin binding of other TEAD paralogs
- In assessing the potential on-target renal toxicity of targeting TEAD, average urinary protein-to-creatinine ratios and histopathology in non-human primates predicted a therapeutic index of less than one for panTEAD inhibitions and a broad therapeutic window for IK-930

In addition, tomorrow the Company will present a poster that highlights IK-930's ability to reduce and reverse resistance to other targeted therapies in preclinical models. Highlights include:

- Treatment with IK-930 in combination with multiple targeted agents, such as EGFR, KRAS G12C, and MEK inhibitors, demonstrated a reduction in emergence of drug resistant "persister" cells

"IK-930 was designed by leveraging TEAD biology to rebalance the oncogenic activity of the Hippo pathway, providing a potentially differentiated and tolerable therapeutic option for patients," added Jeff Ecsedy, Ph.D., Ikena Chief Development Officer. "The data presented at AACR today demonstrate the beauty of IK-930's ability to preferentially keep TEAD1 in a transcriptionally repressive state, and to likely block other TEAD paralogs from activating oncogenic transcription. We are thrilled to be able to share this essential differentiation today and look forward to sharing more later this year from our progress with IK-930 in the clinic."

Presentation Details:

Poster Title: IK-930 A TEAD Paralog Selective Inhibitor for Treating YAP/TAZ-TEAD Dependent Cancers
Session: Novel Antitumor Agents 4
Presenter: Nathan Young, Ph.D., Associate Director of Molecular and Cellular Oncology at Ikena Oncology
Date: Monday, April 17, 2023
Time: 9:00 AM – 12:30 PM ET

Poster Title: IK-930, A Paralog Selective Novel TEAD-Inhibitor, Effectively Attenuates Drug-Tolerant Persister Cell Proliferation
Session: Drug Resistance in Molecular Targeted Therapies 3
Presenter: Daniel Hidalgo, Ph.D., Scientist I, Translational Science at Ikena Oncology
Date: Tuesday, April 18, 2023
Time: 9:00 AM – 12:30 PM ET

Both posters will be available on Ikena's Resources Page on their website following the conference.

About IK-930

IK-930 is an oral, paralog-selective TEAD inhibitor targeting the Hippo signaling pathway. IK-930 selectively binds to TEAD1 and prevents transcription of multiple genes that drive cancer progression. By targeting the Hippo pathway, a key driver of cancer pathogenesis that is genetically altered in approximately 10% of all cancer types, IK-930 could have a differentiating impact across many cancers with high unmet need. Ikena is advancing IK-930 both as a monotherapy in patients with Hippo pathway

mutated cancers and in combination with other approved targeted therapies to combat therapeutic resistance. IK-930 is currently being studied in a Phase 1 clinical trial as a monotherapy in patients with advanced solid tumors with or without gene alterations in the Hippo pathway, including NF2-deficient malignant mesothelioma, Epithelioid Hemangioendothelioma (EHE) with documented TAZ/CAMTA1 fusion genes as well as other solid tumors with either NF2 deficiency or with YAP/TAZ genetic fusions (NCT05228015).

About Ikena Oncology

Ikena Oncology™ is focused on developing differentiated therapies for patients in need that target nodes of cancer growth, spread, and therapeutic resistance in the Hippo and RAS onco-signaling network. The Company's lead targeted oncology program, IK-930, is a paralog-selective TEAD inhibitor addressing the Hippo signaling pathway, a known tumor suppressor pathway that also drives resistance to multiple targeted therapies. The Company's additional research spans other targets in the Hippo pathway as well as the RAS signaling pathway, including developing IK-595, a novel MEK-RAF inhibitor. Additionally, IK-175, an AHR antagonist, is being developed in collaboration with Bristol Myers Squibb. Ikena aims to utilize their depth of institutional knowledge and breadth of tools to efficiently develop the right drug using the right modality for the right patient. To learn more, visit www.ikenaoncology.com or follow us on Twitter and LinkedIn.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding: the timing and advancement of our targeted oncology programs, including the timing of updates; our expectations regarding the therapeutic benefit of our targeted oncology programs; our ability to efficiently discover and develop product candidates; our ability to obtain and maintain regulatory approval of our product candidates; the implementation of our business model, and strategic plans for our business and product candidates. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, those risks and uncertainties related to the timing and advancement of our targeted oncology programs; our expectations regarding the therapeutic benefit of our targeted oncology programs; expectations regarding our new executive officer; our ability to efficiently discover and develop product candidates; the implementation of our business model, and strategic plans for our business and product candidates, and other factors discussed in the "Risk Factors" section of Ikena's Form 10-K for the year ended December 31, 2022, which is on file with the SEC, as updated by any subsequent SEC filings. We caution you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. We disclaim any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent our views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. We explicitly disclaim any obligation to update any forward-looking statements.

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Exhibit 99.2

ikena™ ONCOLOGY

Corporate Presentation

April 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 networks

Hippo Pathway

RAS Pathway

- Multiple ongoing clinical trials with **expected data readouts in the next 12 months**
- **Leaders in Hippo pathway** with clinical stage TEAD1 inhibitor **IK-930**
  - Initial monotherapy dose escalation data in all comers, mesothelioma, and EHE in 2023
  - Broad combination potential including in EGFRm and RASm cancers, starting with osimertinib in NSCLC
- **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
- **>$155M** in cash; Runway into **2025**

Seasoned Executive Team with 50+ INDs and 14 Regulatory Approvals

23
average years of experience

50+
INDs

14
regulatory approvals

Executive Team

Mark Manfredi, Ph.D.
Chief Executive Officer

Sergio Santillana, M.D.
Chief Medical Officer

Jeffrey Ecsedy, Ph.D.
Chief Development Officer

Michelle Zhang, Ph.D.
Chief Scientific Officer

Jotin Marango, M.D., Ph.D.
Chief Financial Officer and Head of Corporate Development

Board of Directors

Owen Hughes
Chair

Iain Dukes, D.Phil.

David Bonita, M.D.

Jean Francois Formela, M.D.

Otello Stampacchia, Ph.D.

Maria Koehler, M.D., Ph.D.

Richard Wooster, Ph.D.

Scientific Advisory Board

George Demetri, M.D.
Professor, Medicine, Harvard Medical School
Director, Center for Sarcoma and Bone Oncology, Dana-Farber Cancer Institute

Kevan Shokat, Ph.D
Professor and Chair, Department of Cellular and Molecular Pharmacology, UCSF
Investigator, Howard Hughes Medical Institute

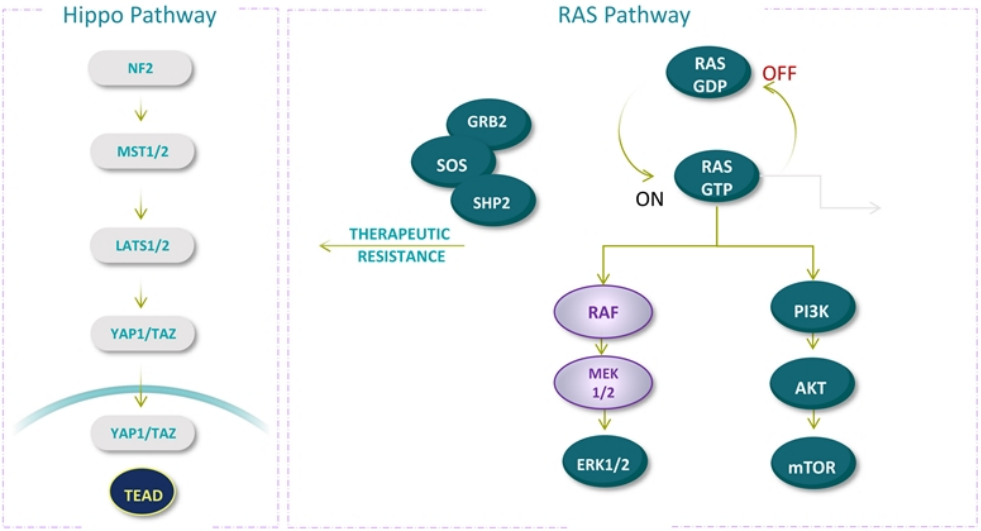
Josep Tabernero, M.D., Ph.D.
Head of Medical Oncology, Vall d'Hebron University Hospital

Neal Rosen, M.D., Ph.D.
Director, Center for Mechanism-Based Therapeutics and Chair, Medical Oncology, Memorial Sloan-Kettering Cancer Center

Ikena Wholly-Owned Pipeline Focused on Targeted Oncology

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

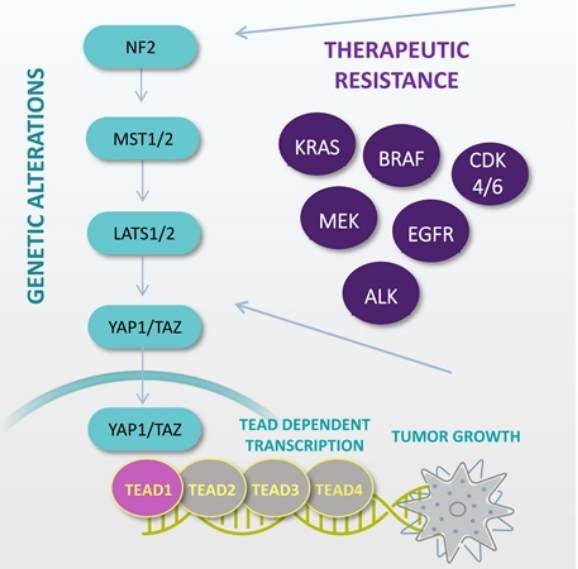
IK-930

ikena ONCOLOGY

IK-930 Well-Positioned to Address Diverse Patient Populations with High Unmet Need

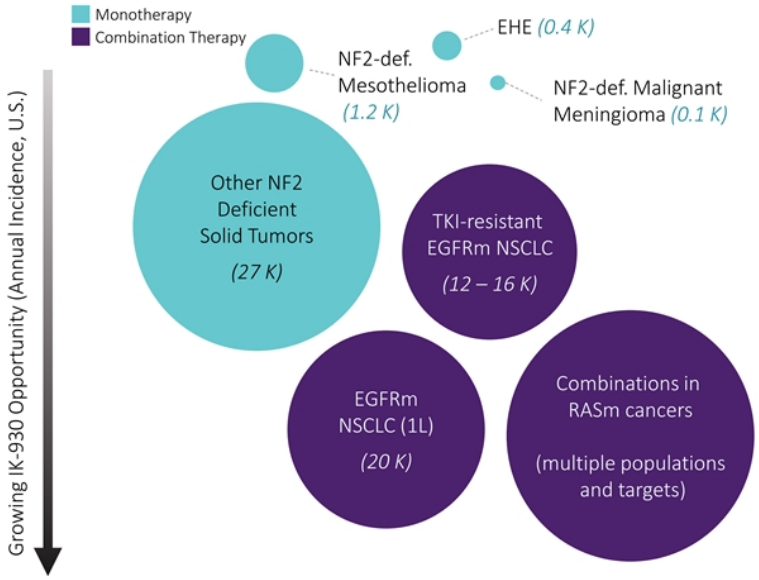
Two distinct mechanisms: Genetic alterations in Hippo pathway and pathway involvement in therapeutic resistance

Hippo Pathway Activity Triggers TEAD Transcription-Dependent Tumor Growth



EHE: Epithelioid Hemangioendothelioma; MPM: Malignant Pleural Mesothelioma.

IK-930 Initial Target Patient Populations



Additional potential opportunities in YAP/TAZ amplified cancers and combinations with RAS pathway agents (MEKi, KRASi)

IK-930 is Potentially both First and Best in Class Targeting Hippo Pathway

IK-930 is a potent Hippo-pathway inhibitor that selectively inhibits TEAD1 and broadly represses oncogenic TEAD activity

IK-930 is a TEAD1 Selective Palmitoylation Inhibitor

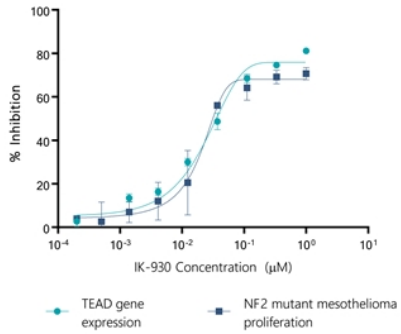
IK-930

	TEAD1	TEAD2	TEAD3	TEAD4
FP (IC_{50} μM)	0.88 ± 0.22	9.23 ± 1.80	> 50	6.58 ± 0.93
Click/Chem(IC_{50} μM)	0.2-0.5	>20	>20	>20
TSA (Kd; μM)	0.32	2.47	/	17.85
Nanobret (IC_{50} μM)	0.091 ± .002	15.53 ± 1.32	> 20	> 20

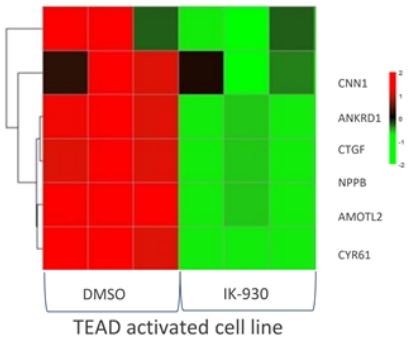
Pan-TEADi

	TEAD1	TEAD2	TEAD3	TEAD4
FP (IC_{50} μM)	0.92 ± 0.25	2.29 ± 0.51	1.18 ± 0.52	1.38 ± 0.58
Click/Chem(IC_{50} μM)	0.2-0.5	2	0.5	2
TSA (Kd; μM)	0.18	1.77	42.82	0.19
Nanobret (IC_{50} μM)	0.030 ± .004	0.51 ± .022	0.041 ± .001	0.32 ± .081

Potent Inhibition of TEAD

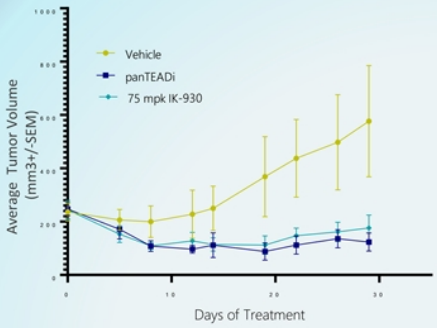


Robust Inhibition TEAD Target Gene Expression

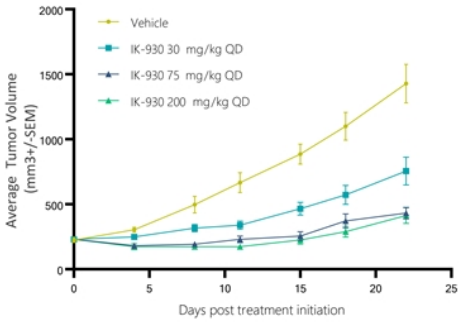


IK-930 Monotherapy Has Potential Across Genetic Mutations in the Hippo Pathway

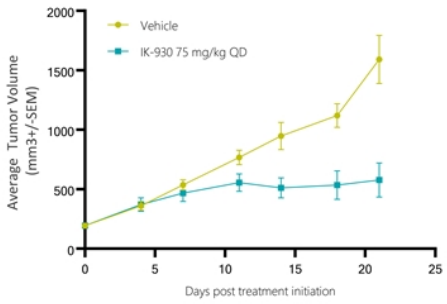
Comparable to panTEADi in NF2 Deficient Mesothelioma with Impact Across Tumor Models for Hippo Pathways Genetic Alterations



NF2 Deficient Mesothelioma Model



LATS1/LATS2 Mutated Mesothelioma Model



YAP1 Amplified HNSCC Model

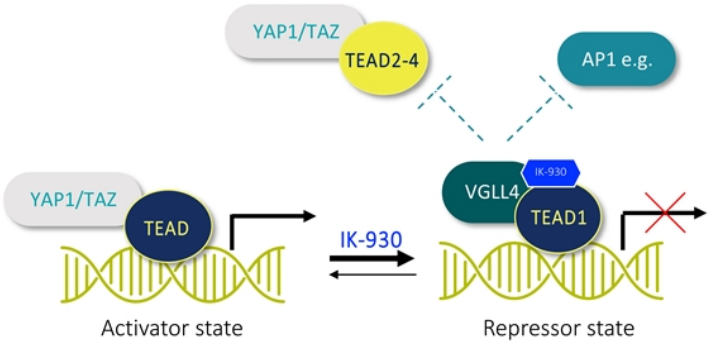
IK-930 Mechanism Drives TEAD1 into Tumor-Repressive Activity

Leveraging the two opposing states of TEAD through binding TEAD1 to inhibit palmytoilation and promoting VGLL4 interactions

Two Opposing States of TEAD

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

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



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

IK-930 Is Designed to Balance Efficacy and On-Target TEAD Renal Tox

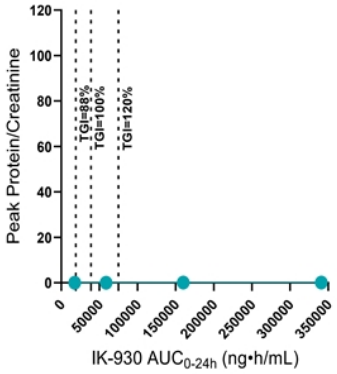
Prior attempts to target the Hippo pathway have not been able to balance anti-tumor activity and kidney toxicity

Designing a Targeted Treatment to Maximize Antitumor Activity and Minimize On-Target Tox

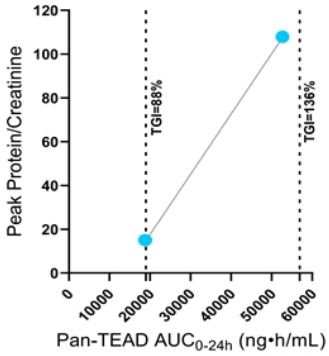
- panTEAD inhibition has been seen to drive proteinuria and frank kidney toxicity (Kaneda et al, AACR 2019)
- In preclinical models it has been seen that YAP1 is required for podocyte (highly specialized kidney cell) viability (Schwartzman et al., 2016)
- IK-930's selectivity provide a far wider potential therapeutic window while demonstrating equivalent activity in multiple in vivo models
- 28-Day Monkey Study
  - IK-930: No clinical signs or renal changes observed; all doses
    - No toxicity to other systems
  - panTEADi
    - Decreased activity, ataxia observed in both dose groups
    - High dose halted on day 18 due to mortality and morbidity

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

IK-930 Monkey 28-day

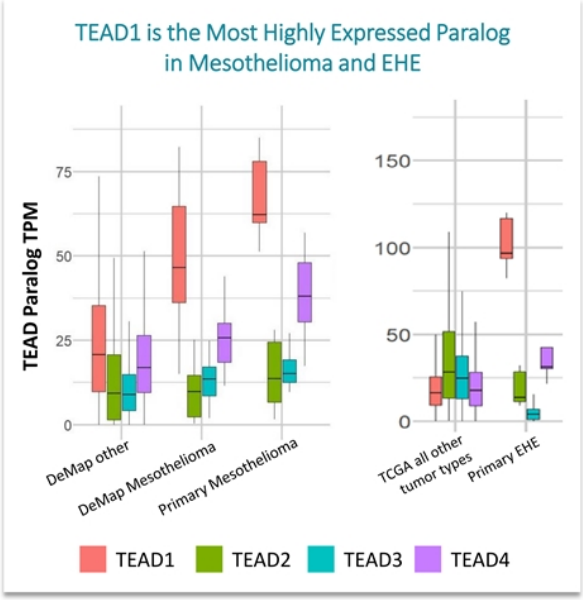


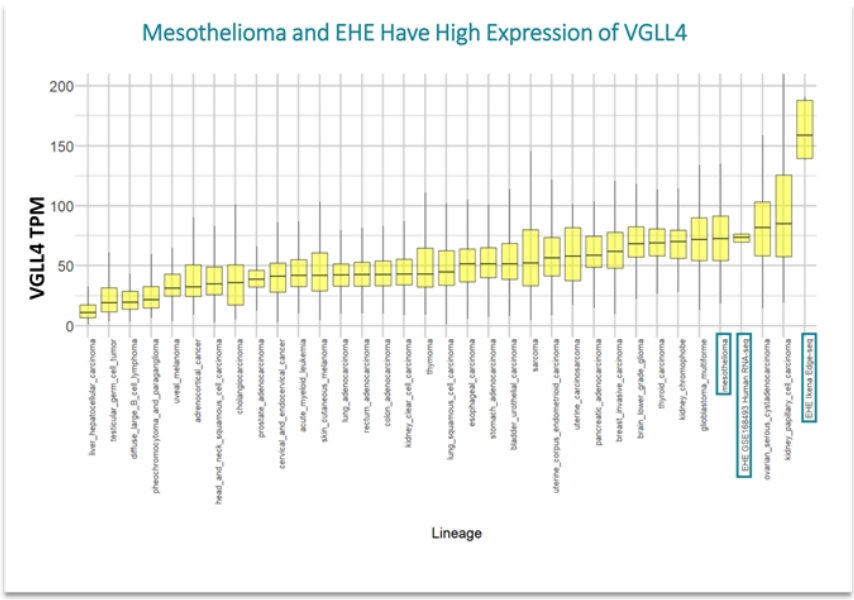
panTEADi Monkey 28-day



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*

TEAD1 and VGLL4 are Highly Expressed in IK-930's Initial Target Indications





IK-930 Monotherapy Clinical Strategy; 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 → **Dose Expansion Options**

Currently recruiting; advanced through multiple doses

All comers

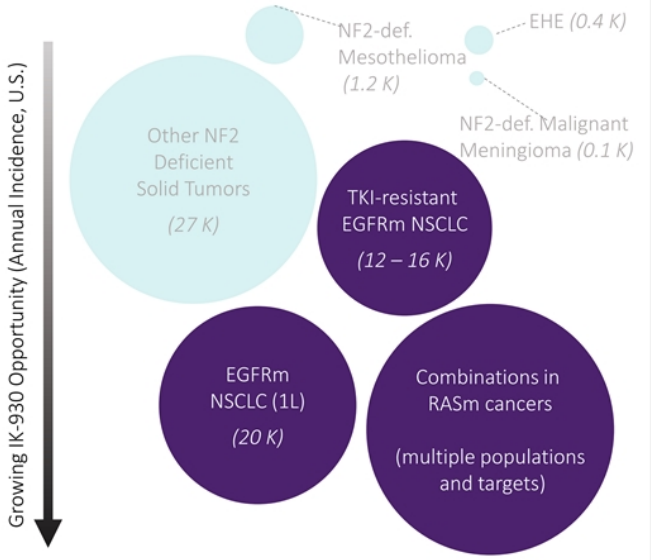
Tumors known to have high incidence of Hippo pathway alterations

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

The Hippo Pathways 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

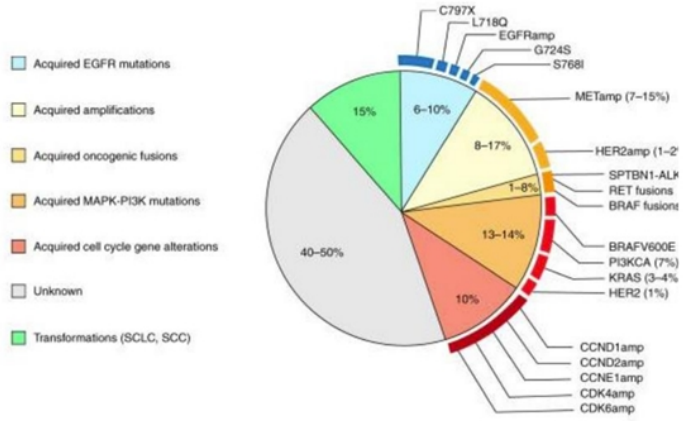
Combating Therapeutic Resistance is a Major Need



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

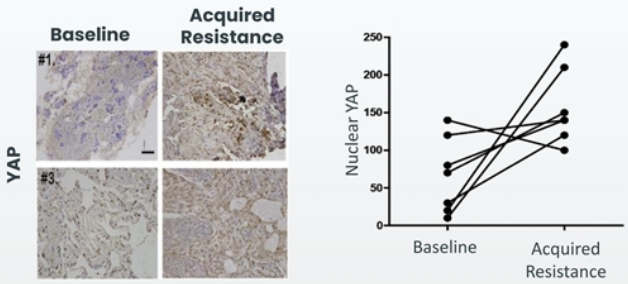


"The biggest hurdle to targeted cancer therapy is the inevitable emergence of drug resistance."

Lim, et al. Journal of Hematology & Oncology 2019

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

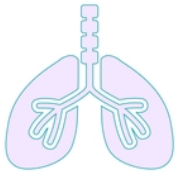
YAP Nuclear Localization Post Osi Treatment Linked to Acquired Resistance



Lee, et al., BBRC, 2016

There is a growing body of data linking the Hippo pathway to resistance to multiple targeted therapies, including osimertinib

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

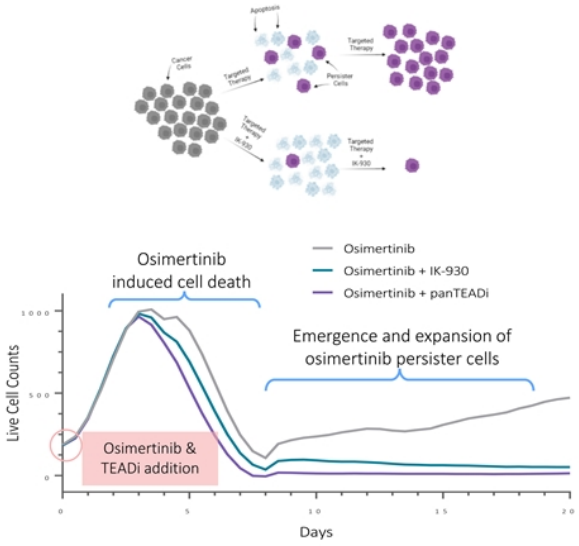
Exploring both as potential paths in clinical program

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

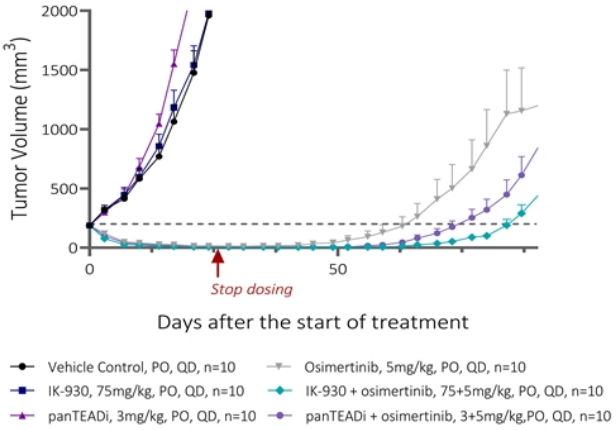
IK-930-Osi Combo Delays Tumor Regrowth *in vivo* and Can Prevent Emergence of *Persisters*

*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

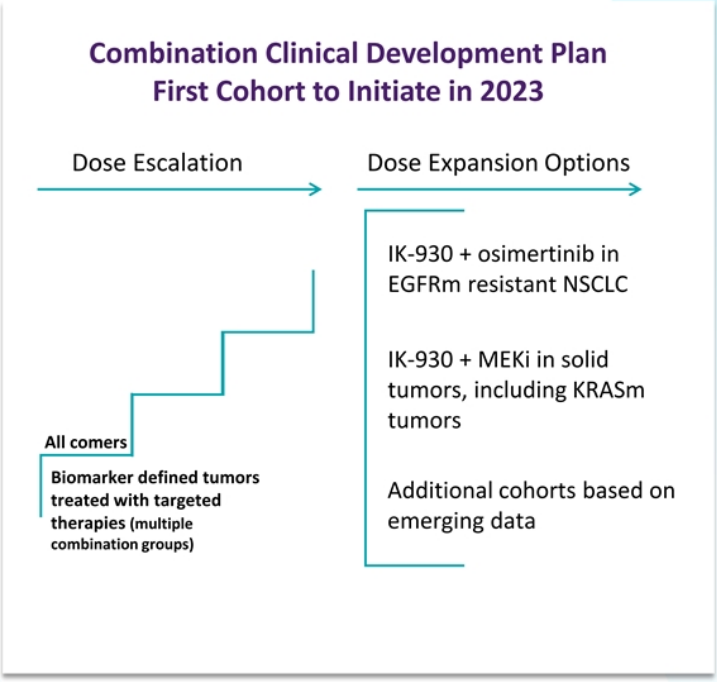


IK-930 + Osi Delays Tumor Regrowth More than panTEADi *in vivo*



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

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



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

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 presented at AACR 2023**
  - **Initial clinical data expected in 2H 2023**
- **Additional research in Hippo pathway leading next-gen efforts**

MEK-RAF Complex Inhibitor

IK-595

The RAS Pathway is Highly Implicated in Cancer

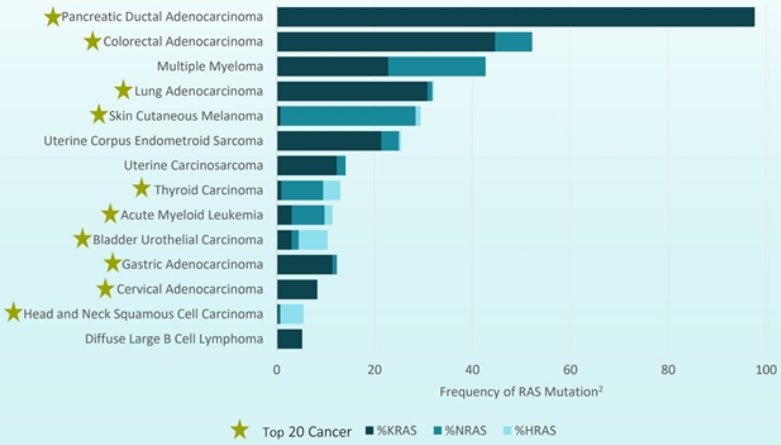
Targeting within the pathway could be impactful for a massive and diverse population

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

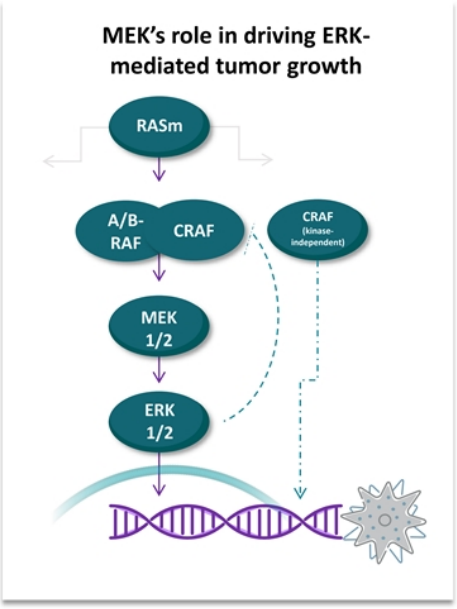
- Approved inhibitors can paradoxically activate MEK/ERK signaling
- CRAF is implicated as a key signaling bypass mechanism for targeted therapies, and has kinase independent activity that drives RAS mutant cancers

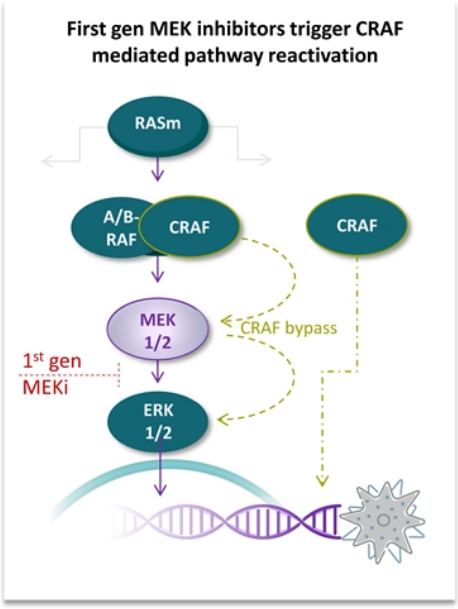
10 of the 20 most common cancers worldwide are associated with RAS pathway mutations



[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





Approved MEK inhibitors like trametinib and binimetinib block MEK kinase activity

Feedback in the pathway however triggers CRAF activation

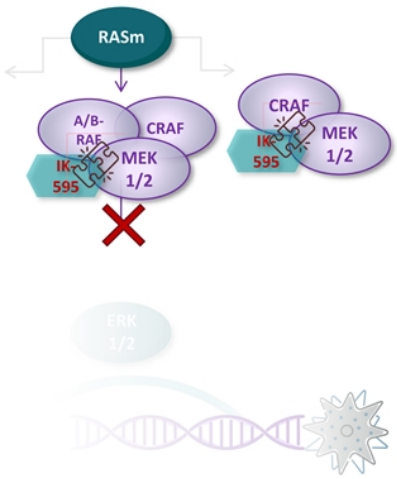
Cancer's survival mechanism utilizes CRAF to reactivate the pathway and bypass inhibition

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



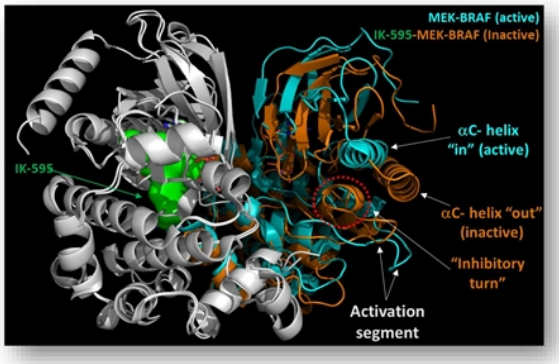
Key IK-595 Advantages

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

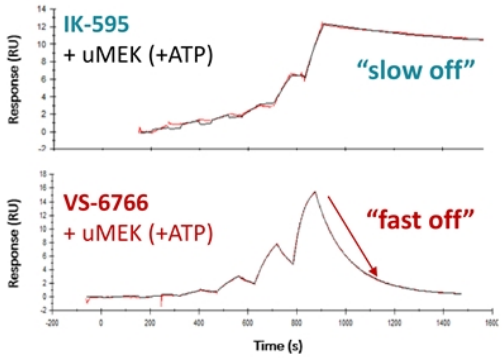
- ✓ Inhibit MEK mediated ERK1/2 phosphorylation
- ✓ Prevent MEK phosphorylation by RAF
- ✓ Alleviate therapeutic resistance through CRAF mediated bypass and pathway reactivation
- ✓ Block CRAF kinase independent activities
- ✓ Optimized PK profile to target IC90 plasma concentrations widening the therapeutic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

Key Advantages of IK-595 Including Robust Stabilization of MEK-RAF 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



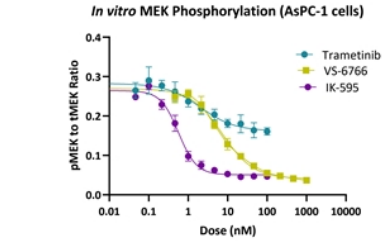
IK-595 binds to MEK with much slower off-rate kinetics compared to other assets with similar MoA

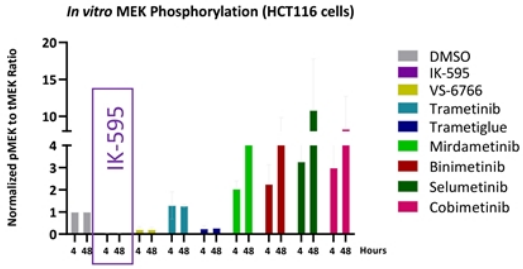


MEK	On Rate ($M^{-1}s^{-1}$)	Off Rate (s^{-1})	Affinity (nM)
IK-595 (to MEK)	8.24 E+04	**6.09 E-04**	7.39
VS-6766 (to MEK)	1.69 E+05	**7.08 E-03**	41.83

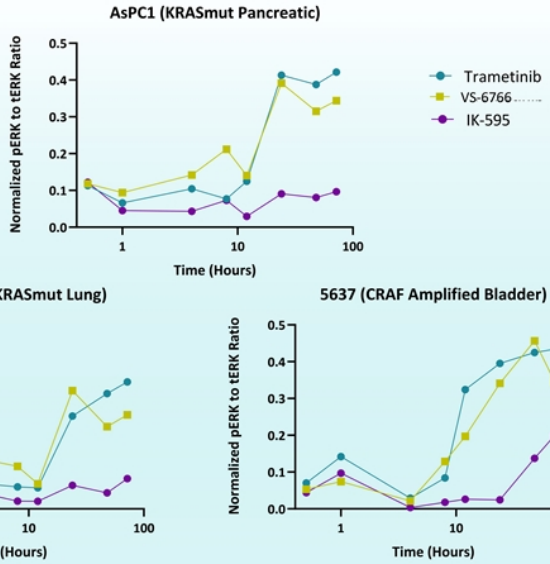
IK-595 Leads to More Durable Pathway Suppression than Other MEK Inhibitors

IK-595 Potently Inhibits MEK Phosphorylation In Vitro





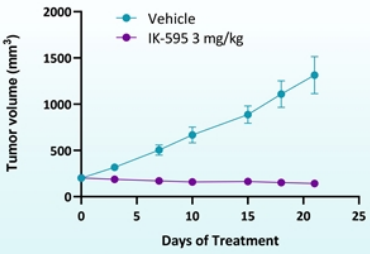
IK-595 Demonstrates Robust and Prolonged pERK Inhibition in Multiple Cell Lines



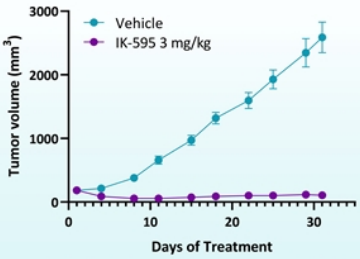
Robust Efficacy in RAS & RAF Models; High Sensitivity in CRAF Dependent Models

Antitumor Activity Across Models at Tolerated IK-595 Doses

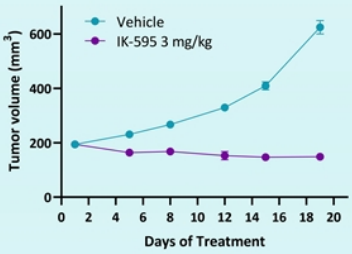
AsPC-1: KRAS G12D Pancreatic Model



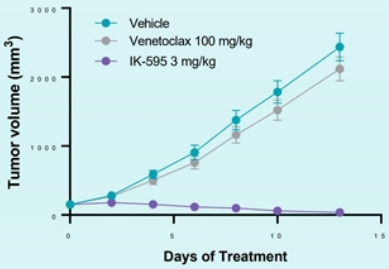
NCI-H2122: KRAS G12C Lung Tumor Model



5637: CRAF Amplified Bladder Tumor Model

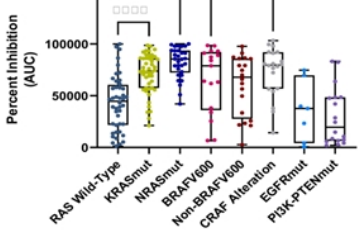


OCI-AML-3: NRAS Q61L Acute Myeloid Leukemia



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

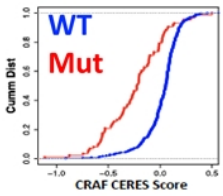
IK-595 Sensitivity



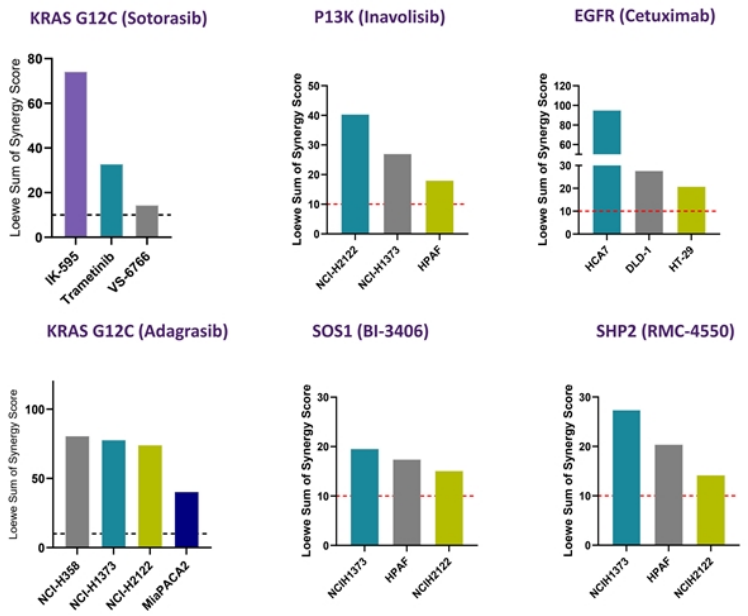
IK-595 has greatest sensitivity in NRAS and KRAS mutant cell lines which are dependent on CRAF

NRAS and KRAS – CRAF CERES Score

Jones, 4th RAS-Targeted Drug Development Summit 2022



IK-595 shows Significant Synergy Levels with Multiple Combination Agents



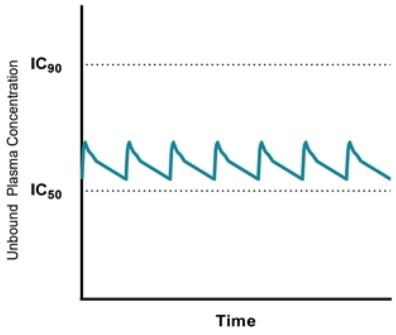
- High synergy scores show the potential for future potential combinations for IK-595
- Demonstrated the potential for expansion to larger patient populations within the RAS pathway
- Also shows potential to address needs in cancer populations where primary mutations fall outside the pathway but engage RAS biology

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

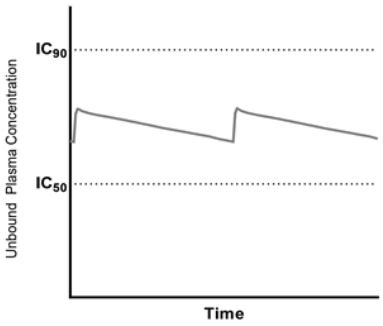
Trametinib

Clinical PK
2 mg QD



VS-6766

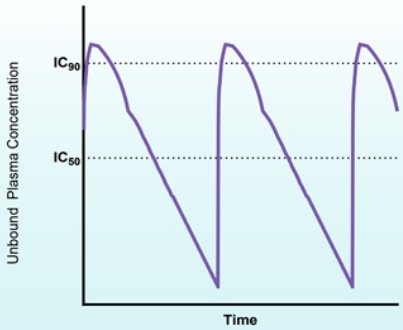
Clinical PK
3.2 mg twice/week



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

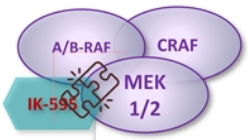
Human Predicted PK



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

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

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
- Designed with half life for optimization of therapeutic index and flexible dosing schedules
- **IND planned for 2H 2023**

Targeting AHR to Counter Immunosuppressive TME

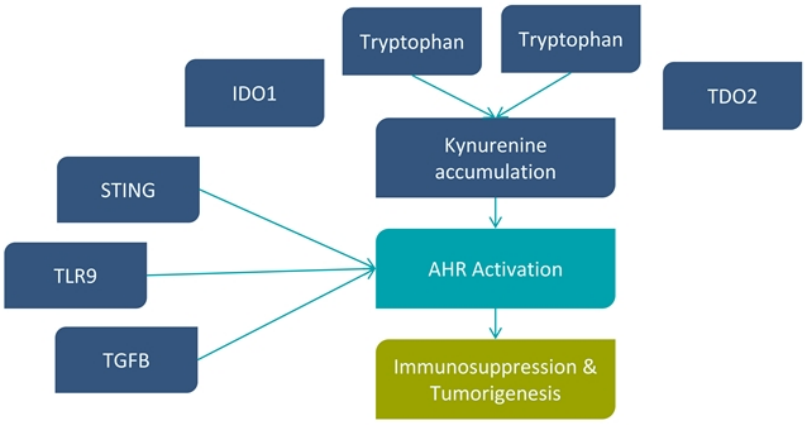
IK-175

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

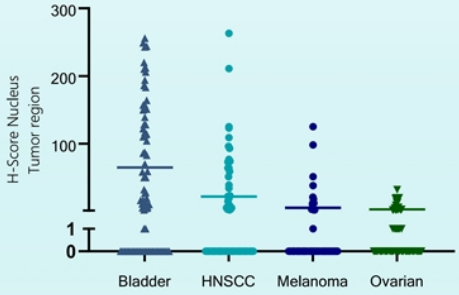
Novel Assays to Optimize Indication Selection

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)

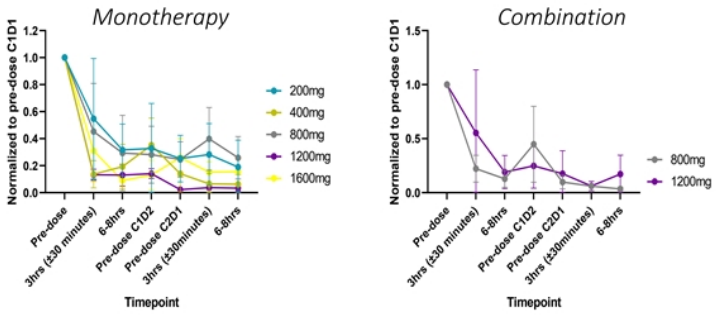
Pharmacodynamics seen at all doses

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

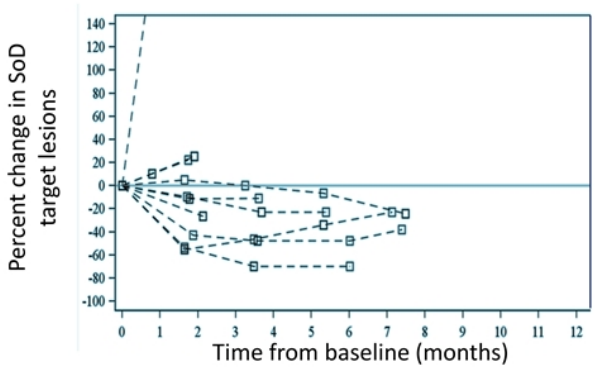
Initial Clinical Urothelial Carcinoma Data Demonstrated Encouraging Anti-Tumor Activity

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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