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

April 17, 2023

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 (GLOBE NEWSWIRE) -- 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 1 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's 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 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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