Ikena Oncology Presents Data at SITC 36th Annual Meeting Describing the Indication Selection Methodology, Translational Data, and Trial in Progress for IK-175

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Data supports and describes the ongoing Phase 1a/b clinical trial of IK-175 as a single agent and in combination with nivolumab in advanced solid tumors

Study evaluates IK-175 in urothelial carcinoma patients including AHR positive enriched subpopulation

BOSTON, Nov. 12, 2021 (GLOBE NEWSWIRE) -- Ikena Oncology, Inc. (Nasdaq: IKNA, "Ikena"), a targeted oncology company navigating new territory in patient-directed cancer treatment, today announced data from multiple presentations at the Society for Immunotherapy of Cancer (SITC) 36th Annual Meeting from their IK-175 AHR antagonist program. The ongoing IK-175 clinical trial is currently recruiting patients in both monotherapy and combination cohorts with nivolumab.

The three poster presentations explore the process of advancing IK-175, an oral selective Aryl Hydrocarbon Receptor (AHR) antagonist, in multiple tumor types, including urothelial carcinoma, a type of bladder cancer with a high prevalence of active AHR signaling. AHR is a transcription factor that facilitates tumor progression by allowing cancer cells to evade the immune system. Cancer cells release multiple different AHR ligands, including kynurenine, activating the pathway and fostering an immunosuppressive effect within the tumor microenvironment. Inhibiting the AHR pathway could promote immune recognition of cancer cells, making it a compelling drug target.

"The data presented at SITC speak to the robust translational approaches we employ across the entirety of our portfolio. Our computational biology methods and diverse patient sample profiling to select potentially AHR-dependent cancer types is a foundation of the IK-175 program plan," said Jeffrey Ecsedy, Ph.D., Chief Scientific Officer at Ikena. "The next layer is the use and development of reliable biomarker assays to prospectively enroll patients with best potential to gain clinical benefit from IK-175. These methods are prime examples of the biomarker-driven patient selection that anchors the Ikena pipeline."

Presentation details:

Poster #: 93
Title: *Computational biology and tissue-based approaches to inform indication selection for a novel AHR inhibitor*
Presenter: Marta Sanchez-Martin, Ph.D., Principal Scientist, Translational Research

- Presentation describes methods used to identify indications dependent on AHR signaling and how patient selection strategies were designed, including:
  - A proprietary RNA-based gene signature of AHR activation, RNA analysis and protein activation
  - Genomic profiling of solid and hematological cancers to identify those harboring AHR gene amplifications
  - Analysis of tissue microarrays of 15 different tumor types to identify those with highest prevalence of nuclear AHR protein expression, reflective of AHR activation
- These analyses revealed that there is a high prevalence of nuclear AHR expression, AHR gene amplification and AHR-target gene expression in urothelial carcinoma, suggesting aberrant AHR activation may play an important role in the progression of this tumor type

Poster #: 58
Title: *Analytical validation of a novel immunohistochemistry assay to determine nuclear AHR expression in human bladder cancer*
Presenter: Lei Wang, Ph.D., Principal Scientist, Translational Research

- Poster reviews the process of developing a novel immunohistochemistry (IHC) assay to measure AHR signaling through nuclear protein expression in tumors
- 199 human bladder cancer formalin-fixed, paraffin embedded (FFPE) samples were used to establish and confirm a cutoff of greater than or equal to 65% cells that are nuclear 2+ and 3+ positive in the tumor region
- The nuclear AHR IHC assay for urothelial carcinoma was developed and analytically validated in a CLIA certified lab and showed greater than or equal to 95% accuracy, specificity, sensitivity, and precision
- The novel assay has been implemented in the ongoing IK-175 Phase 1b clinical study for prospective patient enrichment

Poster #: 550
Title: *TRIAL IN PROGRESS: A Phase 1a/b Study of IK-175, an Oral AHR Inhibitor, Alone and in Combination with Nivolumab in Patients with Locally Advanced or Metastatic Solid Tumors and Urothelial Carcinoma*
Presenter: Jason J. Luke, M.D., FACP, Trial Investigator, UPMC Hillman Cancer Center

- Poster describes the Phase 1 trial of IK-175 (NCT04200963), a first-in-human, open-label, multicenter dose escalation and expansion study to evaluate the safety and tolerability of IK-175 administered as a single agent and in combination with

nivolumab, a PD-1 checkpoint inhibitor in solid tumors and in urothelial carcinoma
    - Primary endpoints include identification of maximum tolerated dose (MTD) and characterizing any dose-limiting toxicities (DLTs)
    - In addition to safety and tolerability of IK-175 as a monotherapy and in combination with nivolumab, the secondary objectives of the study include evaluating disease responses
    - Pharmacokinetics (PK), pharmacodynamics (PD) and preliminary antitumor activity are being evaluated at multiple timepoints within the treatment cycle
- The study is being conducted in adult patients with locally advanced or metastatic solid tumors and urothelial carcinoma, an indication identified to have high frequency of AHR signaling
    - AHR nuclear localization is being measured as a predictive biomarker in patients with urothelial carcinoma
    - Study enriched to include a minimum of 10 patients having a positive AHR nuclear localization test enrolled in the combination arm of the trial
- The trial is currently recruiting for both treatment arms

For more information on the Society for Immunotherapy of Cancer (SITC) 36th Annual Meeting, visit the conference website.

About IK-175
IK-175 is a selective, oral small molecule Aryl Hydrocarbon Receptor (AHR) inhibitor. AHR is activated by multiple ligands, including kynurenine, which drive tumor progression through immunosuppressive effects in the tumor microenvironment. Activated AHR prevents immune recognition of a range of cancers by modulating both innate and adaptive immunity. In *in vitro* human T-cell experiments, IK-175 induces an activated T-cell state, interleukin (IL)-22 gene expression and leads to an increase in pro-inflammatory cytokines, such as IL-2 and IL-9. AHR is a compelling drug target, especially in patients who do not fully benefit from standard of care, including checkpoint inhibitors. Ikena is advancing IK-175 as a single agent and in combination with nivolumab, a PD-1 checkpoint inhibitor, as part of a Phase 1 dose escalation and expansion clinical trial (NCT04200963). Patient populations with urothelial carcinoma are enriched for AHR activation using a novel biomarker. Ikena's IK-175 program is partnered with Bristol Myers Squibb (BMS). BMS has the right to exclusively license the program through the completion of the Phase 1b portion of the clinical trial.

About Ikena Oncology
Ikena Oncology is focused on developing novel therapies targeting key signaling pathways that drive the formation and spread of cancer. Ikena is advancing multiple programs that target tumor markers as well as programs targeting the tumor microenvironment. The Company's lead program, IK-930, is a TEAD inhibitor targeting the Hippo signaling pathway, a pathway that can drive formation and increase survival of tumors and also drives development of resistance to multiple existing therapies. Additional programs include those targeting the RAS signaling pathway and several programs targeting the tumor microenvironment and immune signals, two of which are being developed in collaboration with Bristol Myers Squibb. Ikena's pipeline is built on targeting genetically defined or biomarker-driven cancers and developing therapies that can serve specific patient populations in need of new therapeutic options.
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