Kura Oncology Announces Proof of Concept in Angioimmunoblastic T-Cell Lymphoma, Validation of CXCL12 as a Therapeutic Target of Tipifarnib in Peripheral T-Cell Lymphoma

December 2, 2018

– Two CRs, four PRs (46% ORR) observed in advanced AITL patients in Phase 2 trial of tipifarnib in PTCL –

– AITL and other PTCL patients with high CXCL12 expression experienced 50% ORR and 90% clinical benefit with tipifarnib after median of three prior therapies –

– High expression of CXCL12 observed in approximately 40% of PTCL and was associated with poor prognosis for standard-of-care therapy –

– Management to host webcast today at 11:30 p.m. ET / 8:30 p.m. PT –

SAN DIEGO, Dec. 02, 2018 (GLOBE NEWSWIRE) -- Kura Oncology, Inc. (Nasdaq: KURA), a clinical-stage biopharmaceutical company focused on the development of precision medicines for oncology, reported preliminary data in angioimmunoblastic T-cell lymphoma (AITL) and CXCL12+ peripheral T-cell lymphoma (PTCL), the two expansion cohorts in its Phase 2 clinical trial of its lead drug candidate tipifarnib in patients with relapsed or refractory PTCL.

The data, presented today at the American Society of Hematology (ASH) Annual Meeting in San Diego, showed encouraging activity with tipifarnib in late-stage PTCL patients, including a significant association between CXCL12 expression and clinical benefit, and proof of concept in AITL, an aggressive form of T-cell lymphoma often characterized by high levels of CXCL12 expression. A copy of the poster is available on the Company's website at www.kuraoncology.com.

“The mechanism of action of farnesyl transferase inhibitors has remained elusive for several decades,” said Antonio Gualberto, M.D., Ph.D., Head of Development and Chief Medical Officer of Kura Oncology. “Our initial data in HRAS mutant head and neck cancer provided strong evidence of activity in tumors driven by this oncogene. However, many other tumors such as T- and B-cell lymphomas, myeloid leukemias, pancreatic or breast cancers, in which anecdotal evidence of tipifarnib activity has been reported, do not usually carry HRAS mutations. We believe the preliminary results reported at ASH validate our observation that the CXCL12 pathway is a therapeutic target of tipifarnib and provide a potential path to expand the development of tipifarnib well beyond HRAS mutant solid tumors by using CXCL12-related biomarkers to enrich for patients most likely to benefit from treatment. We will continue our efforts to identify these patient subsets and to bring this important drug candidate to patients in need.”

As of November 21, 2018, a total of 39 patients were enrolled in the ongoing Phase 2 trial, including 19 patients with AITL (16 patients in the AITL extension cohort and 3 patients in the previous portion of the study). Six of the 16 AITL patients were not evaluable as of the data cutoff date, including two who were pending initial efficacy assessments. Of the 13 evaluable AITL patients, two achieved a complete response (CR) and four achieved a partial response (PR), for an objective response rate (ORR) of 46% (six of 13). According to the study protocol, the AITL cohort is considered positive when four or more responses are observed.

The study also identified a particularly responsive subset within AITL and non-AITL patients. Specifically, patients with a high ratio of expression of CXCL12 to its receptor CXCR4 experienced a 50% ORR (five of 10) and a 90% clinical benefit rate (nine of 10 with either complete response, partial response or stable disease) with tipifarnib. Patients in this Phase 2 trial had a median of three prior lines of therapy (range 1-7). The high CXCL12/CXCR4 expression ratio had 90% sensitivity and 93% specificity to identify PTCL patients likely to benefit from tipifarnib.

In addition to the Phase 2 clinical data, the results from two ancillary, non-clinical studies were also reported at ASH. In the first, the expression of CXCL12 and CXCR4 was investigated using tumor bank samples of PTCL patients treated with standard-of-care agents. Worse prognosis was observed in PTCL patients with high CXCL12/CXCR4 expression ratio, indicating that CXCL12 is a negative prognostic factor for standard PTCL therapy. In the second study, the effect of the incubation of stroma cells with tipifarnib on CXCL12 secretion was investigated in a mouse model of bone marrow culture. Tipifarnib reduced secretion of the CXCL12 chemokine from the stromal cells, providing a potential mechanism of action for the observed clinical activity.

“To our knowledge, these results position tipifarnib as the first CXCL12 inhibitor with reported proof-of-concept data, marking a significant advancement in our development strategy,” said Troy Wilson, Ph.D., President and CEO of Kura Oncology. “Our data suggest that as many as 40% of PTCL patients express high CXCL12. In addition, the discovery of CXCL12-related biomarkers offers the potential to increase the opportunity for tipifarnib into other hematological and solid tumor indications. We intend to explore those indications while continuing to gather additional data from our ongoing Phase 2 study and expect to provide an update at a medical meeting next year.”

The Phase 2 study was designed to investigate the anti-tumor activity of tipifarnib in patients with relapsed or refractory PTCL. After preliminary data suggested that CXCL12 expression was associated with tipifarnib’s clinical activity, two expansion cohorts were added to enroll patients with tumors expected to overexpress CXCL12: AITL tumors, and those non-AITL tumors that lack a single nucleotide variation in the 3’-untranslated region (3'-UTR) of the CXCL12 gene (CXCL12+ PTCL). CXCL12 is a stroma-derived chemokine that promotes the progression of lymphoma and other hematological and solid tumors carrying the CXCR4 receptor, and our previous results had suggested an association between CXCL12 expression and the most common form of the 3’-UTR CXCL12 variant. In the expansion cohorts, both the presence or absence of this variant and the expression levels of CXCL12 and CXCR4 were assessed.

In the expansion cohorts in the Phase 2 trial tipifarnib was dosed at 300 mg twice daily on days 1-21 of a 28-day cycle. The reported data indicated

that tipifarnib was generally well-tolerated, with adverse events consistent with its known safety profile. The most common treatment-related adverse events (grade ≥ 3) were hematology-related, including neutropenia, thrombocytopenia, leukopenia, febrile neutropenia and anemia.

Last week, the U.S. Patent and Trademark Office (USPTO) issued a new patent for tipifarnib as a method of treating patients with AITL. In May 2018, the USPTO issued a patent for tipifarnib as a method of treating patients with certain CXCL12-expressing cancers, including PTCL. Both patents expand protection for tipifarnib, providing exclusivity in the U.S. to 2037.

Webcast Information

Kura's management will host a webcast at 11:30 p.m. ET / 8:30 p.m. PT today, December 2, 2018, following the conclusion of the poster presentation at the ASH 2018 Annual Meeting. The live audio webcast and slides of the presentation will be available from the Investors and Media section of the company website at www.kuraoncology.com, and will be archived there for 30 days.

About Tipifarnib

Kura Oncology's lead drug candidate, tipifarnib, is a potent and highly selective inhibitor of farnesylation, a key cell signaling process implicated in cancer initiation and development. Tipifarnib was previously studied in more than 5,000 cancer patients and showed compelling and durable anti-cancer activity in certain patient subsets, however no molecular mechanism of action had previously been determined that could explain its activity across a range of diverse clinical indications, including squamous tumors that carry mutant HRAS, as well as in lymphoid, myeloid and solid tumors that do not carry HRAS mutations. Leveraging advances in next-generation sequencing as well as emerging information about cancer genetics and tumor biology, Kura is seeking to identify those patients most likely to benefit from tipifarnib. In November 2018, Kura initiated its first global, registration-directed trial of tipifarnib in patients with recurrent or metastatic HRAS mutant HNSCC.

About Kura Oncology

Kura Oncology is a clinical-stage biopharmaceutical company committed to realizing the promise of precision medicines for the treatment of cancer. The Company's pipeline consists of small molecule drug candidates that target cancer signaling pathways where there is a strong scientific and clinical rationale to improve outcomes by identifying those patients most likely to benefit from treatment. Kura's lead drug candidate is tipifarnib, a farnesyl transferase inhibitor, for which the Company has initiated a registration-directed trial of tipifarnib in recurrent or metastatic patients with HRAS mutant HNSCC. In addition, tipifarnib is being evaluated in multiple other Phase 2 clinical trials in solid tumor and hematologic indications. Kura's pipeline also includes KO-947, an ERK inhibitor, currently in a Phase 1 dose-escalation trial, and KO-539, a menin-MLL inhibitor, currently in IND-enabling studies. For additional information about Kura Oncology, please visit the Company's website at www.kuraoncology.com.

Forward-Looking Statements

This news release contains certain forward-looking statements that involve risks and uncertainties that could cause actual results to be materially different from historical results or from any future results expressed or implied by such forward-looking statements. Such forward-looking statements include statements regarding, among other things, the efficacy, safety and therapeutic potential of tipifarnib and the Company's other product candidates, the conduct, results and timing of Kura Oncology's clinical trials, including the Phase 2 clinical trial of tipifarnib in patients with PTCL, plans regarding future clinical trials and development and commercial activities, the regulatory approval path for tipifarnib and expectations regarding intellectual property and biomarkers related to Kura Oncology's product candidates. Factors that may cause actual results to differ materially include the risk that compounds that appeared promising in early research or clinical trials do not demonstrate safety and/or efficacy in later preclinical studies or clinical trials, the risk that Kura Oncology may not obtain approval to market its product candidates, uncertainties associated with performing clinical trials, regulatory filings and applications, risks associated with reliance on third parties to successfully conduct clinical trials, the risks associated with reliance on outside financing to meet capital requirements, and other risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. You are urged to consider statements that include the words "may," "will," "would," "could," "should," "believes," "estimates," "projects," "promise," "potential," "expects," "plans," "anticipated," "intends," "continues," "designed," "goal," or the negative of those words or other comparable words to be uncertain and forward-looking. For a further list and description of the risks and uncertainties the Company faces, please refer to the Company's periodic and other filings with the Securities and Exchange Commission, which are available at www.sec.gov. Such forward-looking statements are current only as of the date they are made, and Kura Oncology assumes no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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