Kura Oncology Announces Positive Phase 2 Trial of Tipifarnib in Peripheral T-Cell Lymphoma

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– Primary endpoint achieved with 45% and 42% ORR in AITL and CXCL12+ AITL/PTCL-NOS expansion cohorts –

– PTCL patients with tumors characterized by high CXCL12/CXCR4 expression ratio experienced an ORR of 47% and a clinical benefit rate of 82% –

– 50% CR rate and 75% ORR observed in AITL patients with KIR mutations, a CXCL pathway-associated marker –

– Company believes results support multiple registrational opportunities in relapsed/refractory lymphoma and plans to seek regulatory feedback –

– Management to host conference call today at 8:00 a.m. ET –

SAN DIEGO, June 14, 2019 (GLOBE NEWSWIRE) -- Kura Oncology, Inc. (Nasdaq: KURA), a clinical-stage biopharmaceutical company focused on the development of precision medicines for oncology, today announced updated interim data from the ongoing Phase 2 clinical trial of its lead drug candidate, tipifarnib, in patients with relapsed or refractory peripheral T-cell lymphoma (PTCL).

The results, which will be presented during an oral session at 16:45 CET / 10:45 am ET tomorrow at the European Hematology Association (EHA) Annual Congress in Amsterdam, demonstrate ongoing anti-tumor activity and a manageable safety profile in advanced patients with angioimmunoblastic T-cell lymphoma (AITL) as well as non-AITL PTCL. A copy of the presentation is available on the Company's website at www.kuraoncology.com.

"With additional follow up and new patients enrolled in the ongoing Phase 2 study, tipifarnib continues to demonstrate encouraging clinical activity in patients with relapsed or refractory PTCL who have experienced a median of three prior lines of therapy," said Francine Foss, M.D., professor of medicine at the Yale Cancer Center, and a principal investigator in the trial. "Given the grim prognosis for late-stage PTCL patients, these data are exciting because they further validate tipifarnib as a targeted therapy and the potential for CXCL12 pathway biomarkers as effective enrichment strategies in late-stage PTCL patients with few therapeutic options."

The multi-center, single-arm, open-label Phase 2 trial was designed to determine the efficacy, safety and biomarkers of activity of tipifarnib in patients with relapsed or refractory PTCL. Initially, patients were enrolled without selection in the Phase 2 trial. Based upon molecular characterization of the initial patients, the Phase 2 trial was amended to include two expansion cohorts: 1) patients with AITL, an aggressive form of T-cell lymphoma often characterized by high levels of CXCL12 expression (the AITL expansion cohort), and 2) patients with PTCL who lack a single nucleotide variation (rs2839685 A>G) in the 3'-untranslated region of the CXCL12 gene (the CXCL12 SNP+ expansion cohort).

As of the May 24, 2019 data cutoff, a total of 50 relapsed/refractory PTCL patients with a median number of three prior regimens have been enrolled in all stages of the Phase 2 trial. Key preliminary findings include:

- The primary efficacy endpoint was achieved in each of the AITL and CXCL12+ expansion cohorts. Sixteen patients were treated in the AITL cohort and 15 in the CXCL12 SNP+ cohort. Among the 11 evaluable patients in the AITL extension cohort, three achieved a complete response (CR) and two achieved a partial response (PR), for an objective response rate (ORR) of 45% (31% ORR on a modified intent-to-treat basis, mITT). Among the 12 evaluable patients in the CXCL12+ expansion cohort, three achieved a CR and two achieved a PR, for an ORR of 42% (33% ORR by mITT). Two of the five responders in the CXCL12+ expansion cohort were AITL patients.

- When all AITL patients (N=23) and all PTCL not otherwise specified (PTCL-NOS) with available rs2839695 data and absence of this 3'UTR variant (N=17) enrolled in all portions were taken into account, ORR were 53%/39% (PPS/mITT) for AITL and 20%/18% for CXCL12 SNP+ PTCL-NOS.

- Thirty-four patients had available gene expression data. Patients with a high ratio of CXCL12 expression to its receptor CXCR4 (N=17) experienced an ORR of 47% and a clinical benefit rate of 82% (CR+PR+SD) with tipifarnib.

- Next-generation sequencing of 16 AITL patients revealed a high rate of mutation/variation (50%) of the killer cell immunoglobulin-like receptors, including KIR3DL2. KIR3DL2 mutation at C336R was concurrent with Q386E and was associated with outcome from tipifarnib therapy. Four of the eight KIR3DL2 C336R/Q386E patients achieved a CR, two achieved a PR and two achieved stable disease (SD) for a CR rate of 50%, an ORR of 75% and a clinical benefit rate of 100%. Furthermore, high KIR3DL2 mutant variant allele frequency KIR3DL2 was predictive of complete response to tipifarnib in AITL. Tumors with KIR3DL2 mutations expressed low levels of CXCL5 and its receptor CXCR1 and CXCR2, a potential mechanism of resistance to tipifarnib.

- Tipifarnib was generally well-tolerated in this Phase 2 trial, with adverse events consistent with its known safety profile. The most frequently observed treatment-related adverse events (grade ≥ 3) were hematology-related, including thrombocytopenia, neutropenia, leukopenia, anemia, febrile neutropenia and lymphopenia.

“We believe that these data validate our prior observations of tipifarnib as a CXCL12 pathway inhibitor and constitute the first clinical proof-of-concept of farnesyl transferase inhibitors in CXCL12-driven tumors. AITL and related lymphomas encompass approximately one-third of PTCL cases and represent a significant unmet medical need,” said Antonio Gualberto, M.D., Ph.D., Head of Development and Chief Medical Officer of Kura Oncology. “We are also very encouraged by the discovery of KIR3DL2 mutations, the characterization of mechanisms of sensitivity and resistance to tipifarnib in lymphoma, and the development of robust molecular tools for the selection and/or stratification of PTCL patients. These findings are a testimony of the potential for success of our precision medicine approaches.”

Poster Presentation Explores CXCL12 Overexpression in Tipifarnib Responders

Separately, Kura has been evaluating the potential to use CXCL12 pathway biomarkers to enrich for clinical activity in other hematologic malignancies. In addition to AITL, high CXCL12 expression was observed in tumors from other lymphoma patients, including patients with PTCL-NOS, diffuse large B-cell lymphoma (DLBCL) and mycosis fungoides, the most common form of cutaneous T-cell lymphoma (CTCL). Lymphoma patients with CXCL12 reference sequences also appeared to have a higher chance of clinical benefit from tipifarnib treatment. The identification of these CXCL12 reference sequences in responders to tipifarnib across multiple hematologic malignancies will be presented in a poster presentation at 17:30 CET / 11:30 am ET tomorrow at the EHA Annual Congress in Amsterdam. A copy of the poster is also available on the Company’s website at www.kuraoncology.com.

“These data represent the first prospective validation of CXCL12 pathway biomarkers to enrich for clinical activity of tipifarnib in PTCL. We believe these data support the potential to register tipifarnib in both the AITL and PTCL-NOS patient populations, and we look forward to seeking regulatory feedback on next steps for this program,” said Troy Wilson, Ph.D., President and CEO of Kura Oncology. “In addition, based on our growing body of clinical and preclinical data, we believe CXCL12 pathway biomarkers may have the potential to unlock the therapeutic value of farnesyl transferase inhibition across multiple hematologic and solid tumor indications, including DLBCL, acute myeloid leukemia (AML), CTCL and pancreatic cancer.”

Conference Call and Webcast

Kura’s management will host a webcast and conference call at 8:00 a.m. ET today, June 14, 2019 to discuss the results from the Company’s Phase 2 trial of tipifarnib in PTCL. The live call may be accessed by dialing (877) 516-3514 for domestic callers or +1 (281) 973-6129 for international callers and using conference ID #1273055. A live webcast of the call will be available from the Investors and Media section of the Company’s website at www.kuraoncology.com, and will be archived there for 30 days.

About Peripheral T-Cell Lymphoma

PTCL is a rare and diverse group of aggressive lymphomas that develop from white blood cells called NK/T-cells that grow abnormally. The term PTCL is sometimes used to describe a heterogeneous group of T-cell lymphomas. The most common types of PTCL are PTCL-NOS and AITL. Significant advances in the genetic landscape of T-cell and NK-cell neoplasms as the result of genomic studies, as well as the introduction of more powerful diagnostic technologies have led to revisions in the classification and introduction of new entities. Many of the same genetic changes observed in AITL are also observed in cases of PTCL-NOS that manifest a T follicular helper (TFH) phenotype. This common genotype/phenotype has led to follicular T-cell lymphoma (FTCL) and AITL being unified under a common heading. Cases of nodal PTCL with TFH phenotype are now included in the same grouping as well. As a result, patients with the PTCL-NOS phenotype are increasingly being characterized as having AITL and/or related tumors.

Recently, the U.S. Food and Drug Administration (FDA) approved ADCETRIS® (brentuximab vedotin) in combination with chemotherapy for previously untreated systemic ALCL or other CD30-expressing PTCL, including AITL and PTCL-NOS. This was the first FDA-approved frontline treatment for PTCL. Previously approved therapies in relapsed or refractory PTCL were based on single-arm clinical trials of 130 patients or fewer with response rates in the range of 25-27% and limited duration of clinical benefit in unselected populations.

About CXCL12

CXCL12 is a stroma-derived chemokine that promotes the progression of lymphoma as well as other hematological and solid tumors carrying the CXCR4 receptor. Results from ancillary studies show that high CXCL12 expression is a negative prognostic factor for standard-of-care PTCL therapy. Approximately 50% of the AITL patients and 35% of the non-AITL patients in Kura’s Phase 2 trial of tipifarnib in PTCL overexpressed CXCL12.

About Tipifarnib

Kura Oncology’s lead drug candidate, tipifarnib, is a potent, selective and orally bioavailable inhibitor of farnesyl transferase in-licensed from Janssen in December 2014. Previously, tipifarnib was 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 been determined that could explain its clinical activity across a range of solid tumor and hematologic indications. 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, following an end of Phase 2 meeting with the FDA, Kura initiated its first registration-directed trial of tipifarnib in patients with recurrent or metastatic HRAS mutant head and neck squamous cell carcinoma (HNSCC).

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

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 is conducting 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, which is anticipated to enter into a Phase 1 clinical trial in mid-2019. For additional information about Kura, 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 Kura's product candidate tipifarnib, and progress and expected timing of Kura's drug development programs and clinical trials. 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 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," "anticipates," "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 assumes no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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