Loxo Oncology Announces Initiation of Phase 1/2 Clinical Trial for Highly Selective, Non-Covalent BTK Inhibitor, LOXO-305

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STAMFORD, Conn., Dec. 21, 2018 (GLOBE NEWSWIRE) -- Loxo Oncology, Inc. (Nasdaq:LOXO), a biopharmaceutical company focused on the development and commercialization of highly selective medicines for patients with genomically defined cancers, today announced that it has initiated a Phase 1/2 clinical trial of LOXO-305. LOXO-305 is an investigational, highly selective, non-covalent Bruton's tyrosine kinase (BTK) inhibitor specifically designed to address acquired resistance and intolerance in patients previously treated with FDA-approved BTK inhibitors.

"We are pleased to initiate the clinical trial for our fourth novel drug candidate," said Josh Bilenker, M.D., chief executive officer of Loxo Oncology. "FDA-approved BTK inhibitors, which all covalently (irreversibly) bind to their targets, have meaningfully improved the lives of patients with certain B-cell leukemias and lymphomas. However, we are now learning that many patients are discontinuing these therapies due to disease progression or intolerance. When disease progression is caused by a resistance mechanism known as a C481 mutation, we believe that LOXO-305 has the potential to re-induce a response in affected patients. We also believe that the selectivity profile of LOXO-305 has the potential to avoid certain side effects. We look forward to working with our clinical investigators to determine whether LOXO-305 can deliver against these exciting possibilities."

This first-in-human, global, multi-center Phase 1/2 trial will evaluate LOXO-305 as a single agent in patients with previously treated chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), or non-Hodgkin's lymphomas (NHL). The primary objective of the Phase 1 portion of the trial is to determine the maximum tolerated dose or recommended phase 2 dose. Key secondary objectives include measures of safety, pharmacokinetics, and anti-tumor activity (i.e. Overall Response Rate and Duration of Response, as determined by appropriate histology-specific response criteria). The trial includes a Phase 1 dose escalation phase and a Phase 2 dose expansion phase. The Phase 1 dose escalation employs an accelerated titration design, initially enrolling single patient dose cohorts for patients with CLL/SLL or NHL who have received at least two prior lines of therapy and have progressed or are intolerant to standard of care. Based on reported adverse events, the dose escalation may switch to a "3+3" design. In the Phase 2 dose expansion phase, six cohorts are planned to allow for the characterization of the preliminary anti-tumor activity of LOXO-305: 1) CLL/SLL failed prior BTK inhibitor with BTK C481 mutation; 2) CLL/SLL failed prior BTK inhibitor without BTK C481 mutation; 3) Waldenstrom's macroglobulinemia (WM), mantle cell lymphoma (MCL) or marginal zone lymphoma (MZL) failed prior BTK inhibitor with BTK C481 mutation; 4) WM, MCL or MZL failed prior BTK inhibitor without BTK C481 mutation; 5) CLL/SLL, WM, MCL or MZL intolerant to prior BTK inhibitor; 6) CLL/SLL, WM, MCL or MZL failed prior BTK inhibitor with unknown BTK C481 mutation status and other CLL/SLL, WM, CML, MZL or other NHL patients not meeting the definitions of Cohorts 1 through 5.

About LOXO-305

LOXO-305 is an investigational, novel, highly selective non-covalent Bruton's tyrosine kinase (BTK) inhibitor. BTK plays a key role in the B-cell antigen receptor signaling pathway, which is required for the development, activation and survival of normal white blood cells, known as B-cells, and malignant B-cells. BTK is a validated molecular target found across numerous B-cell leukemias and lymphomas including chronic lymphocytic leukemia, Waldenstrom's macroglobulinemia, mantle cell lymphoma and marginal zone lymphoma. Currently available BTK inhibitors irreversibly inhibit BTK and the long-term efficacy of these therapies has been limited by acquired resistance, most commonly through BTK C481

mutations, and intolerance, due to off target inhibition of other cellular targets. LOXO-305 was designed to reversibly bind BTK, preserve activity in the presence of the C481 acquired resistance mutations, and avoid off-target kinases that have complicated the development of both covalent and investigational non-covalent BTK inhibitors. Interested patients and physicians can contact the Loxo Oncology Physician and Patient BTK Clinical Trial Hotline at 1-855-LOXO-305 or email clinicaltrials@loxooncology.com.

About Loxo Oncology
Loxo Oncology is a biopharmaceutical company focused on the development and commercialization of highly selective medicines for patients with genomically defined cancers. Our pipeline focuses on cancers that are uniquely dependent on single gene abnormalities, such that a single drug has the potential to treat the cancer with dramatic effect. We believe that the most selective, purpose-built medicines have the highest probability of maximally inhibiting the intended target, with the intention of delivering best-in-class disease control and safety. Our management team seeks out experienced industry partners, world-class scientific advisors and innovative clinical-regulatory approaches to deliver new cancer therapies to patients as quickly and efficiently as possible. For more information, please visit the company's website at http://www.loxooncology.com.

Forward Looking Statements
This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as: "anticipate," "intend," "plan," "goal," "seek," "believe," "project," "estimate," "expect," "strategy," "future," "likely," "may," "should," "will" and similar references to future periods. These statements are subject to numerous risks and uncertainties that could cause actual results to differ materially from what we expect. Examples of forward-looking statements include, among others, the availability of funding, timing and success of our clinical trials, including our Phase 1/2 clinical trial for LOXO-305, success in our collaborations and the potential therapeutic benefits LOXO-305 or other product candidates. Further information on potential risk factors that could affect our business and its financial results are detailed in our most recent Quarterly Report on Form 10-Q, and other reports as filed from time to time with the Securities and Exchange Commission. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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