Loxo Oncology Announces Larotrectinib Clinical Update in Patients with TRK Fusion Cancers at the European Society for Medical Oncology 2018 Congress

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- Median Duration of Response Not Reached With One Year of Additional Follow-up -

- 67 Newly Reported TRK Fusion Patients Exhibit 81% ORR -

STAMFORD, Conn., Oct. 21, 2018 (GLOBE NEWSWIRE) -- Loxo Oncology, Inc. (Nasdaq: LOXO), a biopharmaceutical company developing highly selective medicines for patients with genomically defined cancers, and Bayer AG, Germany, today announced updated clinical data for larotrectinib, an investigational oral, selective, and CNS-active TRK inhibitor, in adult and pediatric patients with TRK fusion cancers. The update included approximately one year of additional follow-up for the 55 patients described in the larotrectinib *New England Journal of Medicine* publication from February 2018. In addition, the update included data for an additional 67 patients who were subsequently enrolled across the larotrectinib development program. As of a data cut-off date of July 30, 2018, median duration of response (DOR) had not been reached in either dataset. These data are being presented today at the European Society for Medical Oncology (ESMO) 2018 Congress.

“It is exciting to see larotrectinib deliver durable responses to patients in these studies with TRK fusion cancer, regardless of age, tumor site of origin, or CNS involvement,” said Ulrik Lassen, M.D., Ph.D., Department of Oncology, Rigshospitalet, Copenhagen. “The sixty-seven new patients have nearly the same overall response rate as the first fifty-five, and duration of response has actually improved with longer patient follow-up. It is interesting to note that once again, depth of response, indicated by a complete response or deep partial response, is a good predictor of duration of response. Additionally, we observed a safety profile with larotrectinib that is conducive to such chronic therapy. The larotrectinib experience provides strong clinical evidence supporting the development of single-purpose drugs against oncogenic driver targets, and underscores the importance of tumor genomic profiling capable of identifying NTRK gene fusions alongside other activating alterations."

Loxo Oncology and Bayer are engaged in a collaboration for the development and commercialization of larotrectinib. The U.S. Food and Drug Administration (FDA) has accepted the New Drug Application (NDA) submitted by Loxo Oncology , and granted Priority Review for larotrectinib for the treatment of adult and pediatric patients with locally advanced or metastatic solid tumors harboring a neurotrophic tyrosine receptor kinase (NTRK) gene fusion. The FDA has set a target action date of November 26, 2018, under the Prescription Drug User Fee Act (PDUFA). Bayer has submitted a Marketing Authorization Application (MAA) in the European Union (EU) and additional filings in other markets are underway.

Key Data Presented

The ESMO presentation included additional follow-up for the first 55 consecutively enrolled adult and pediatric patients with TRK fusion cancers treated across Loxo Oncology’s Phase 1 adult trial, Phase 2 trial (NAVIGATE), and Phase 1/2 pediatric trial (SCOUT). These patients were the subject of the *New England Journal of Medicine* publication from February 2018, and constitute the primary analysis population supporting larotrectinib’s NDA filing. The presentation also included data for the 67 TRK fusion patients subsequently enrolled. Presented data were based on a July 30, 2018 data cut-off

date, providing approximately one year of additional follow up for the primary analysis population.

The datasets adhered to the intent to treat (ITT) principle and included patients with RECIST-evaluable disease enrolled to the three clinical trials, regardless of prior therapy or tumor tissue diagnostic method used to establish their TRK fusion diagnosis. In the ESMO presentation, response evaluations were based on investigator assessment.

The 122-patient integrated dataset included both adult and pediatric patients, who ranged in age from one month to 80 years and carried 24 unique TRK fusion-positive tumor diagnoses. Tumor types included 10 distinct soft tissue sarcomas, salivary gland, infantile fibrosarcoma, thyroid, lung, melanoma, colon, gastrointestinal stromal tumor (GIST), breast, bone sarcoma, cholangiocarcinoma, carcinoma of unknown primary, congenital mesoblastic nephroma, appendiceal, and pancreas cancers.

In the primary dataset, the overall response rate (ORR) was 80% (44/55) (95% CI: 67-90%), with a 62% partial response rate and an 18% complete response rate. In the supplementary dataset, the ORR was 81% (44/54) (95% CI: 69-91%), with a 65% partial response rate and a 17% complete response rate. Across both datasets, the ORR was 81% (88/109) (95% CI: 72-88%), with a 63% partial response rate and 17% complete response rate. The ORR analyses for the supplementary and integrated datasets included nine patients with unconfirmed partial responses awaiting confirmatory response assessments, but did not include 13 patients who were awaiting an initial response assessment and continuing on study.

Median duration of response (DOR) had not been reached in either the primary dataset or supplementary dataset, with median follow-up of 17.6 months and 7.4 months, respectively. In the primary dataset, Kaplan-Meier landmark analyses improved since the July 2017 data cut-off date. At 6 months, 88% of responses were ongoing (83% based on the July 2017 data cut-off date). At 12 months, 75% of responses were ongoing (71% based on the July 2017 data cut-off date). Kaplan-Meier landmark analyses of the supplementary dataset were highly concordant with the primary dataset. At 6 months, 93% of responses were ongoing and at 12 months, 81% of responses were ongoing. Across the integrated dataset, as of the July 2018 data cut-off date, 84% of responding patients remained on treatment or had undergone surgery with curative intent. Of 8 TRK fusion patients treated in the Phase 1 trial, 6 remained in response and on therapy at 22, 30, 33, 34, 37, and 41 months of follow up. With median follow-up for progression-free survival (PFS) of 19.6 months in the primary dataset, median PFS had been reached, at 28.3 months (95% CI: 9.9 months – Not estimable). This estimate is not statistically stable due to a low number of progression events, as evidenced by the wide confidence interval.

The safety data presented at ESMO encompassed the entire larotrectinib safety database in cancer patients (n=207), which includes 70 patients without a TRK fusion diagnosis. Larotrectinib was well tolerated, with the majority of adverse events recorded as grade 1 or 2. No treatment-related grade 3 or 4 adverse events occurred in more than 5% of patients. Eleven patients (9%) required larotrectinib dose reductions. In all cases, patients whose doses were reduced maintained their best response at the lower dose. One patient (<1%) discontinued larotrectinib due to an adverse event.

The ESMO presentation will be available online at https://ir.loxooncology.com/events-presentations.

Larotrectinib Program Update

As of September 30, 2018, the larotrectinib program had treated 179 patients with TRK fusion cancer, which includes the 122 patients reported at ESMO, an additional 15 treated since the ESMO data cut-off date, 24 treated under expanded access protocols, and 18 who had either non-measurable disease or primary central nervous system tumors. By comparison, the program had treated 133 patients with TRK fusion cancer as of March 31, 2018 and 98 as of September 30, 2017.

About Larotrectinib

Larotrectinib is an oral, selective, and CNS-active investigational tropomyosin receptor kinase (TRK) inhibitor in clinical development for the treatment of patients with cancers that harbor a neurotrophic tyrosine receptor kinase (NTRK) gene fusion. Growing research suggests that the NTRK genes, which encode for TRKs, can become abnormally fused to other genes, resulting in growth signals that can lead to cancer in many sites of the body. In clinical trials, larotrectinib demonstrated anti-tumor activity in patients with tumors harboring NTRK gene fusions, regardless of patient age or tumor type. In an analysis of 55 RECIST-evaluable adult and pediatric patients with NTRK gene fusions, using a July 17, 2017 data cutoff, larotrectinib demonstrated a 75 percent centrally-assessed confirmed overall response rate (ORR) and an 80

percent investigator-assessed confirmed ORR, across many different types of solid tumors. The majority (93 percent) of all adverse events were grade 1 or 2.

Larotrectinib has been granted Priority Review, Breakthrough Therapy Designation, Rare Pediatric Disease Designation and Orphan Drug Designation by the U.S. FDA.

In November 2017, Loxo Oncology and Bayer entered into an exclusive global collaboration for the development and commercialization of larotrectinib and LOXO-195, a next-generation TRK inhibitor. Bayer and Loxo Oncology are jointly developing the two products with Loxo Oncology leading the ongoing clinical studies as well as the filing in the U.S., and Bayer leading ex-U.S. regulatory activities and worldwide commercial activities. In the U.S., Loxo Oncology and Bayer will co-promote the products.

For additional information about the larotrectinib clinical trials, please refer to www.clinicaltrials.gov. Interested patients and physicians can contact the Loxo Oncology Physician and Patient Clinical Trial Hotline at 1-855-NTRK-123 or visit www.loxooncologytrials.com/trk-trials.

About TRK Fusion Cancer
TRK fusion cancer occurs when a neurotrophic tyrosine receptor kinase (*NTRK)* gene fuses with another unrelated gene, producing an altered tropomyosin receptor kinase (TRK) protein. The altered protein, or TRK fusion protein, is constantly active, triggering a permanent signal cascade. These proteins become the primary driver of the spread and growth of tumors in patients with TRK fusion cancer. TRK fusion cancer is not limited to certain types of cells or tissues and can occur in any part of the body. NTRK gene fusions occur in various adult and pediatric solid tumors with varying prevalence, including appendiceal cancer, breast cancer, cholangiocarcinoma, colorectal cancer, GIST, infantile fibrosarcoma, lung cancer, mammary analogue secretory carcinoma of the salivary gland, melanoma, pancreatic cancer, thyroid cancer, and various sarcomas. Only sensitive and specific tests can reliably detect TRK fusion cancer. Next-generation sequencing (NGS) can provide a comprehensive view of genomic alterations across a large number of genes. Fluorescence in situ hybridization (FISH) can also be used to test for TRK fusion cancer, and immunohistochemistry (IHC) can be used to detect the presence of TRK protein.

About Loxo Oncology
Loxo Oncology is a biopharmaceutical company developing 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 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, statements we make regarding the timing and success of our clinical trials or collaborations, the potential therapeutic benefits and economic value of larotrectinib or other product candidates, and timing of future filings. 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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