



# Loxo Oncology Announces LOXO-292 Durability Update in Patients with RET-Mutant Medullary Thyroid Cancer and RET Fusion-Positive Thyroid Cancer from LIBRETTO-001 at the 88th Annual Meeting of the American Thyroid Association

October 6, 2018

*- 16/17 (94%) Responding RET-Mutant Medullary Thyroid Cancer Patients Remain on Therapy, With Median Follow-Up of 8.4 Months -*

*- 7/7 (100%) Responding RET Fusion-Positive Thyroid Cancer Patients Remain on Therapy, With Median Follow-Up of 8.5 Months -*

STAMFORD, Conn., Oct. 06, 2018 (GLOBE NEWSWIRE) -- Loxo Oncology, Inc. (Nasdaq: LOXO), a biopharmaceutical company developing highly selective medicines for patients with genomically defined cancers, today announced updated interim clinical data for LOXO-292 from the global Phase 1/2 LIBRETTO-001 trial in patients with RET-mutant medullary thyroid cancer (MTC) and RET fusion-positive thyroid cancer who were initially included in the LOXO-292 presentation at the 2018 ASCO Annual Meeting. In these 38 patients, approximately 3.5 months of additional patient follow-up were available, as were first follow-up scans for the nine patients most recently enrolled. Sixteen of 17 (94%) responding RET-mutant MTC patients remained on therapy, with median follow-up of 8.4 months. Seven of seven (100%) responding RET fusion-positive thyroid cancer patients remained on therapy, with median follow-up of 8.5 months. Inclusion of new restaging data for the most recently enrolled patients resulted in a 59% overall response rate (56% confirmed overall response rate) in the presented subset of RET-mutant MTC patients, and a 78% confirmed overall response rate in the presented subset of RET fusion-positive thyroid cancer patients. These data are being presented today at the 88th Annual Meeting of the American Thyroid Association.

"I am very pleased to present the latest LOXO-292 clinical data to colleagues at ATA, demonstrating the activity and safety profile of this promising new agent for RET-altered thyroid cancers," said Lori J. Wirth, M.D., associate professor of medicine at Harvard Medical School and Massachusetts General Hospital. "In the months since ASCO we continue to see encouraging early evidence that LOXO-292 has the potential to provide durable responses in heavily pre-treated patients with RET-driven cancers, with a promising safety profile at the Phase 2 dose of 160 mg BID. RET has been a known oncogene in thyroid cancer for many years and I am hopeful that these LOXO-292 data can further increase the awareness of this important target and, with Breakthrough Therapy Designation in hand, that the clinical program will quickly advance to reach our patients in need. "

## **Trial Background**

LIBRETTO-001 is a Phase 1/2 trial of LOXO-292 in advanced cancer patients who primarily have activating RET alterations. LIBRETTO-001 contains a Phase 1 dose escalation phase and a Phase 2 dose expansion phase. The primary endpoint of the Phase 1 is the determination of the maximum tolerated dose (MTD) or recommended dose for further



study. Secondary endpoints include safety, overall response rate (by RECIST 1.1) and duration of response. Initial clinical data were first reported at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

### **Key Data Presented**

The data presented today were based on a July 19, 2018 data cut-off date and included the 29 patients with RET-mutant MTC and the nine patients with RET fusion-positive thyroid cancer who were initially included in the LOXO-292 presentation at the 2018 ASCO Annual Meeting.

Patients were heavily pretreated, having received a median of three prior systemic treatment regimens. Of the patients with RET-mutant MTC, 79% had previously received cabozantinib or vandetanib and 45% had received prior treatment with both agents. Of the patients with RET fusion-positive thyroid cancer, 78% had previously received radioactive iodine and 78% had previously received sorafenib or lenvatinib.

With 3.5 months of additional follow-up since the 2018 ASCO Annual Meeting presentation, LOXO-292 demonstrated encouraging, early evidence of durable activity. Sixteen of 17 (94%) responding RET-mutant MTC patients remained on therapy and in response (median follow-up of 7.6 months for all 29 patients; median follow-up of 8.4 months for responding patients). Seven of seven (100%) responding RET fusion-positive thyroid remained on therapy and in response (median follow-up of 7.6 months for all nine patients; median follow-up of 8.5 months for responding patients). The longest treated patient was the first RET-mutant MTC patient enrolled, who had been on therapy for more than 13 months as of the data cut-off date.

The new data cutoff date allowed for the inclusion of first follow-up scans for nine patients (seven with RET-mutant MTC and two with RET fusion-positive thyroid cancer) who had not had any post-baseline response assessment as of the ASCO presentation. Of 29 patients with RET-mutant MTC, 17 demonstrated an objective response by RECIST 1.1 (two complete responses and 15 partial responses, including two patients with unconfirmed partial responses awaiting confirmatory response assessments) and seven additional patients demonstrated evidence of tumor regression (-12% to -26%). The overall response rate was 59% (17/29) (95% CI: 39%-77%) and the confirmed overall response rate was 56% (15/27) (95% CI: 35%-75%). Included in this analysis are two patients with non-measurable disease at baseline (1 confirmed complete response, 1 stable disease). Of nine patients with RET fusion-positive thyroid cancer, seven demonstrated an objective response by RECIST 1.1 (all partial responses) and one additional patient demonstrated evidence of tumor regression (-21%). The confirmed overall response rate was 78% (7/9) (95% CI: 40%-97%). Included in the analysis is one patient with non-measurable disease at baseline (stable disease). Response assessments were performed by the local clinical trial sites.

Anti-tumor activity was observed regardless of RET mutation, RET fusion partner, and prior multikinase inhibitor treatment. One patient, with RET fusion-positive thyroid cancer, had RECIST target lesions in the central nervous system (CNS) and exhibited an intracranial partial response by RECIST 1.1, pending confirmation.

Of the 82 patients in the safety analysis, most treatment-emergent adverse events were Grade 1 in severity and judged by the investigator as not related to LOXO-292. The treatment-emergent adverse events observed in ~10% of patients, regardless of relationship to LOXO-292, were diarrhea (15% Grade 1, 7% Grade 2, 1% Grade 3), fatigue (9% Grade 1, 13% Grade 2, 0% ?Grade 3), dry mouth (21% Grade 1, 0% ?Grade 2), constipation (17% Grade 1, 2% Grade 2, 0% ?Grade 3), hypomagnesemia (12% Grade 1, 1% Grade 2, 0% ?Grade 3), cough (11% Grade 1, 1% Grade 2, 0% ?Grade 3), headache (10% Grade 1, 1% Grade 2, 1% Grade 3) and nausea (9% Grade 1, 4% Grade 2, 0% ?Grade 3). Four patients experienced adverse events ?Grade 3 that were attributed to LOXO-292 (all Grade 3): tumor lysis syndrome, increased ALT/AST, diarrhea, and thrombocytopenia. All resolved with dose interruption. 160mg BID has been advanced as the Phase 2 dose, with dose exploration at 200mg BID ongoing to further characterize LOXO-292 safety and efficacy.

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

### **About LOXO-292**

LOXO-292 is an oral and selective investigational new drug in clinical development for the treatment of patients with cancers that harbor abnormalities in the rearranged during transfection (RET) kinase. RET fusions and mutations occur across multiple tumor types with varying frequency. LOXO-292 was designed to inhibit native RET signaling as well as



anticipated acquired resistance mechanisms that could otherwise limit the activity of this therapeutic approach. LOXO-292 has been granted Breakthrough Therapy Designation by the U.S. FDA.

LOXO-292 is currently being studied in the global [LIBRETTO-001 Phase 1/2 trial](#). For additional information about the LOXO-292 clinical trial, please refer to [www.clinicaltrials.gov](http://www.clinicaltrials.gov). Interested patients and physicians can contact the Loxo Oncology Physician and Patient RET Clinical Trial Hotline at 1-855-RET-4-292 or email [clinicaltrials@loxooncology.com](mailto:clinicaltrials@loxooncology.com).

### **About RET-Altered Cancers**

Genomic alterations in RET kinase, which include fusions and activating point mutations, lead to overactive RET signaling and uncontrolled cell growth. RET fusions have been identified in approximately 2% of non-small cell lung cancer, 10-20% of papillary and other thyroid cancers, and a subset of other cancers. Activating RET point mutations account for approximately 60% of medullary thyroid cancer (MTC). Both RET fusion cancers and RET-mutant MTC are primarily dependent on this single activated kinase for their proliferation and survival. This dependency, often referred to as "oncogene addiction," renders such tumors highly susceptible to small molecule inhibitors targeting RET.

### **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](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, statements we make regarding the timing and success of our clinical trials, the potential therapeutic benefits and economic value of LOXO-292 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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