



# Loxo Oncology Announces Positive Interim Clinical Data from LOXO-292 Dose Escalation Trial in RET-Altered Cancers Presented at the American Society of Clinical Oncology Annual Meeting

June 2, 2018

*– 77% Overall Response Rate in RET Fusion Cancers and 45% Overall Response Rate in RET Mutated Medullary Thyroid Cancer (MTC) –*

*– Activity Observed Independent of RET Alteration, Tumor Type (Lung, Thyroid, Pancreas), or Prior Multikinase Inhibitor (MKI) Treatment –*

*– Expansion Cohorts of Phase 1 Trial are Now Open and Enrolling –*

*– Company to Host Conference Call and Webcast Today at 4:00 p.m. CT –*

STAMFORD, Conn., June 02, 2018 (GLOBE NEWSWIRE) -- Loxo Oncology, Inc. (Nasdaq:LOXO), a biopharmaceutical company developing highly selective medicines for patients with genomically defined cancers, today announced interim clinical data from the LOXO-292 global Phase 1 LIBRETTO-001 (LOXO-292 Investigated to Block RET-altered Tumors) dose escalation trial. LOXO-292 is an investigational, highly potent and selective RET inhibitor. These data are being presented today at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago (abstract 102).

"The LOXO-292 Phase 1 data are striking," said Alexander Drilon, M.D., clinical director in the Early Drug Development Service at Memorial Sloan Kettering Cancer Center and presenting author. "The activity we reported is impressive and I am thrilled to see this promising efficacy with limited adverse events, especially in this heavily pre-treated patient population of RET fusion cancers, including those with brain metastases, and RET mutated MTC."

"We are very excited to share the initial LOXO-292 clinical experience with the oncology community at ASCO," said Josh Bilenker, M.D., chief executive officer of Loxo Oncology. "We have long believed that patients with RET fusion cancers and RET mutated MTC needed a purpose-built medicine tailored to their tumors. We hope that LOXO-292 continues to deliver on that premise. Thank you to the patients, investigators and clinical trial teams who made possible today's presentation."

## **Trial Background**

The LIBRETTO-001 Phase 1 trial contains a dose escalation phase and a dose expansion phase. The dose escalation phase follows a "3+3" design. LOXO-292 is dosed orally in 28-day cycles. As dose cohorts are cleared, additional patients can enroll in these cleared cohorts. Intra-patient dose escalation is also permitted as dose cohorts are cleared. The primary endpoint of the trial 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. The dose expansion phase is designed to further characterize the overall response rate, durability of response, and safety of LOXO-292 in predefined groups of patients with activating RET alterations.

## Key Data Presented at ASCO

The data presented at ASCO were based on an April 2, 2018 data cut-off date. Eighty-two total patients had been enrolled to eight dose escalation cohorts: 20 mg QD (n=6), 20 mg BID (n=10), 40 mg BID (n=16), 60 mg BID (n=10), 80 mg BID (n=18), 120 mg BID (n=4), 160 mg BID (n=12) and 240 mg BID (n=6). RET alterations were identified by local laboratories either in tumor or plasma and included the following primary diagnoses:

- 38 patients with RET fusion-positive non-small cell lung cancer (NSCLC) (21 with prior MKI treatment, 17 without)
- 9 patients with RET fusion-positive thyroid cancer (8 with prior MKI treatment, 1 without)
- 2 patients with RET fusion-positive pancreatic cancer (1 with prior MKI treatment, 1 without)
- 29 patients with RET-mutated medullary thyroid cancer (MTC) (23 with prior MKI treatment, 6 without)
- 4 patients with no known activating RET alterations

In addition to many patients with prior MKI treatment, 46% of patients had received prior chemotherapy and 24% had received prior immunotherapy (47% of those with NSCLC).

Pharmacokinetic analyses during the dose escalation demonstrated dose-dependent increases in LOXO-292 exposure with increasing dose. Starting at the 40 mg BID dose and the 80 mg BID dose, respectively, LOXO-292 delivered sustained >IC90 RET fusion and >IC90 RET M918T-mutant target coverage, based on cell-based potencies.

The data presented at ASCO, summarized below, are based on response assessments performed by each respective clinical trial site (local, investigator-assessed radiology).

	RET Fusion-Positive Cancers			RET-Mutated MTC	No Known Activating RET Alteration
	All	NSCLC	Other <sup>1</sup>		
Enrolled	49	38	11	29	4
Eligible for response evaluation <sup>2</sup>	39	30	9	22	3
<b>Overall response rate (95% CI)<sup>3</sup></b>	<b>77% (61%-89%)</b>	<b>77% (58%-90%)</b>	<b>78% (40%-97%)</b>	<b>45% (24%-68%)</b>	<b>0% (0%-71%)</b>
Confirmed overall response rate <sup>3,4</sup>	74%	74%	71%	33%	0%
CR	--	--	--	1	--
uCR <sup>5</sup>	--	--	--	1	--
PR	25	20	5	5	--
uPR <sup>5</sup>	5	3	2	3	--
SD	6	4	2	9	2
PD	--	--	--	2	1
Not evaluable <sup>6</sup>	3	3	--	1	--

1. Patients eligible for response evaluation include thyroid cancer (n=7), pancreatic cancer (n=2).

2. Excludes patients recently enrolled that remain on treatment, but have not had a first post-baseline response assessment.

3. Response status per RECIST 1.1. Overall response rate = CR+uCR+PR+uPR. Overall response rate, Confirmed overall response rate: all RET fusion-positive (30/39, 25/34), RET fusion-positive NSCLC (23/30, 20/27), RET fusion-positive other (7/9, 5/7), RET-mutant MTC (10/22, 6/18).

4. Excludes patients with unconfirmed CR/PR pending confirmation at time of data cut-off.

5. Unconfirmed responses in patients that remain on treatment awaiting a confirmatory response assessment.

6. Patients that discontinued treatment prior to a first post-baseline response assessment.

Anti-tumor activity was observed regardless of RET fusion partner (including KIF5B), RET mutation (including M918T and V804M gatekeeper mutations), and prior MKI treatment. Twelve patients with RET fusion cancers had central nervous system (CNS) metastases at enrollment and all remained on study without progression. Three of these patients had RECIST target lesions in the CNS, and all three exhibited intracranial partial responses. In patients with RET-mutant MTC, LOXO-292 treatment resulted in significant reductions in the serum tumor markers calcitonin and carcinoembryonic antigen



(CEA).

As of the data cutoff, LOXO-292 demonstrated early evidence of durable activity, with 90% of RET fusion-positive cancer patients and 93% of RET-mutant MTC patients remaining on therapy. All responding patients across all tumor types remained on therapy. The longest responding patient on therapy was the first RET fusion-positive NSCLC patient enrolled, who had been on therapy for more than ten months as of the data cut-off date.

Most treatment-emergent adverse events were Grade 1 in severity. The treatment-emergent adverse events observed in ~10% of patients, regardless of relationship to LOXO-292, were fatigue (12% Grade 1, 7% Grade 2, 0% ?Grade 3), diarrhea (10% Grade 1, 6% Grade 2, 0% ?Grade 3), constipation (13% Grade 1, 1% Grade 2, 0% ?Grade 3), dry mouth (12% Grade 1, 0% ?Grade 2), nausea (9% Grade 1, 4% Grade 2, 0% ?Grade 3), and dyspnea (7% Grade 1, 2% Grade 2, 1% ?Grade 3). Only two adverse events ?Grade 3 were attributed to LOXO-292 (Grade 3 tumor lysis syndrome, Grade 3 increased ALT). An MTD had not been reached. At the 240 mg BID dose level, one dose limiting toxicity (DLT) was reported (aforementioned Grade 3 tumor lysis syndrome).

LOXO-292 also demonstrated robust reduction and clearance of RET alterations as detected in patients' plasma cell free DNA (cfDNA). These data will be presented in a separate poster presentation on June 3, 2018.

### **LIBRETTO-001 Trial Update**

The expansion cohorts of the LIBRETTO-001 trial are now open and enrolling at the 160 mg BID dose. This dose was selected for initial expansion based on its promising activity and tolerability profile. Additional dose exploration above 160 mg BID is ongoing and patients enrolled to the expansion cohorts may dose escalate should a higher dose be advanced.

### **About the ASCO Presentations**

LOXO-292 data are being presented in two presentations at ASCO:

- **“A phase 1 study of LOXO-292, a potent and highly selective RET inhibitor, in patients with RET-altered cancers.”** This abstract is being presented in an oral presentation by Dr. Alexander Drilon, Memorial Sloan Kettering Cancer Center, during a Clinical Science Symposium session entitled, “Tumor Genomics: Finding the Target, Hitting the Target” from 8:00 – 9:30AM CT on Saturday, June 2, 2018 (Abstract 102).
- **“Detection and clearance of RET variants in plasma cell free DNA (cfDNA) from patients (pts) treated with LOXO-292.”** This abstract is being presented as a poster by Dr. Geoff Oxnard, Dana Farber Cancer Institute, during the Lung Cancer—Non-Small Cell Metastatic poster session from 8:00 – 11:30AM CT on Sunday, June 3, 2018 (Abstract 9048).

The presentations will be available online at <http://www.loxooncology.com/asco> at the time of their scheduled presentation at ASCO.

### **Conference Call and Webcast Information**

Loxo Oncology management will host a conference call and live webcast with slides and Q&A today at 4:00 p.m. CT to discuss the LOXO-292 data. To participate in the conference call, please dial (877) 930-8065 (domestic) or (253) 336-8041 (international) and refer to conference ID 3597058. A live webcast of the presentation will be available at <http://ir.loxooncology.com/>. A replay of the webcast will be available shortly after the conclusion of the call and archived on the company's website for 30 days following the call.

### **About LOXO-292**

LOXO-292 is a potent, 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 is currently being studied in the global [LIBRETTO-001 Phase 1 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 our lead product candidate 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.

### **Contacts for Loxo Oncology, Inc.**

Company:  
Lauren Cohen  
Director, Corporate Communications  
[lcohen@loxooncology.com](mailto:lcohen@loxooncology.com)

Investors:  
Peter Rahmer  
Endurance Advisors, LLC  
415-515-9763  
[prahmer@enduranceadvisors.com](mailto:prahmer@enduranceadvisors.com)

Media:  
Dan Budwick  
1AB Media  
973-271-6085  
[dan@1abmedia.com](mailto:dan@1abmedia.com)

[Primary Logo](#)

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