Cogent Biosciences Announces Positive Initial Data from Phase 2 SUMMIT Trial Evaluating Bezuclastinib in Patients with Nonadvanced Systemic Mastocytosis (NonAdvSM)

December 9, 2023

Rapid and ongoing improvement in patient symptoms, with 57% median best improvement on MC-QoL and 78% of patients reporting ≥1 point improvement on PGIS by week 20

100% of bezuclastinib treated patients achieved at least 50% improvement across all relevant biomarker measures, including serum tryptase, KIT D816V VAF, and mast cell burden;

Placebo patients, after cross-over to bezuclastinib, also demonstrated rapid symptomatic improvement, with 75% median best improvement on MC-QoL, and 67% of patients reporting ≥1 point improvement on PGIS

Bezuclastinib safety and tolerability profile supports potential for chronic dosing with no related serious adverse events and no bleeding or cognitive events

Cogent to host investor webcast on Monday, December 11 at 8:00 a.m. ET

WALTHAM, Mass. and BOULDER, Colo., Dec. 09, 2023 (GLOBE NEWSWIRE) -- Cogent Biosciences, Inc. (Nasdaq: COGT), a biotechnology company focused on developing precision therapies for genetically defined diseases, today reported positive initial data from the Company's ongoing Phase 2 SUMMIT trial evaluating bezuclastinib in patients with nonadvanced systemic mastocytosis (NonAdvSM) at the 65th American Society of Hematology (ASH 2023) Annual Meeting & Exposition taking place December 9-12, 2023 in San Diego, CA.

"Nonadvanced systemic mastocytosis is a chronic hematologic disorder that significantly impacts patients' quality of life," said principal investigator, Prithviraj Bose, M.D., professor, Department of Leukemia at The University of Texas MD Anderson Cancer Center. "Significant unmet need remains for these patients and the availability of a well-tolerated, efficacious therapy with rapid symptom improvement could represent an important advancement in treatment."

"The initial data presented today from the SUMMIT trial represent an important step forward in the development of a novel treatment for NonAdvSM patients," said PD Dr. Frank Siebenhaar, M.D., Head University Outpatient Clinic, Institute of Allergology, Charité - Universitätsmedizin Berlin. "Effectively targeting the underlying driver mutation of this disease is critical, and the impressive outcomes generated with bezuclastinib treatment in these patients is very encouraging."

"We are very pleased with the emerging profile bezuclastinib is demonstrating in the NonAdvSM patient population," said Andrew Robbins, Cogent's President and Chief Executive Officer. "Matching the benefit of a selective KIT inhibitor that can potently target overactive and proliferative mast cells, with a safety profile that may support chronic treatment has been elusive up until this point. We are excited to rapidly advance into Part 2 of SUMMIT, a registration-directed, global, randomized placebo-controlled trial, and look forward to presenting additional data from SUMMIT in the first quarter of 2024."

Patient Demographics

SUMMIT is a randomized, double-blind, placebo-controlled, global, multicenter, Phase 2 clinical trial of bezuclastinib in patients with NonAdvSM. Twenty patients in Part 1a were treated with either bezuclastinib or placebo plus best supportive care for all arms. The median age of patients at study entry was 50.5 years (ranging from 38-75 years). Patients were enrolled with the following sub-types: 18 patients with indolent systemic mastocytosis (ISM) and two patients with smoldering systemic mastocytosis (SSM). One patient had received prior avapritinib.

Safety Data

Bezuclastinib demonstrated an encouraging safety and tolerability profile for patients dosed at both 100 mg and 200 mg QD. The majority of treatment emergent adverse events were low grade and reversible with no related serious adverse events, bleeding or cognitive impairment events reported. There were two dose reductions for fatigue and one patient discontinued treatment due to increased ALT. One patient with SSM was enrolled at a 400mg dose and following Grade 4 neutropenia was dose reduced to 200mg. Following completion of Part 1a patients received a median duration of treatment in the open label extension (OLE) of 16 weeks. A consistent safety and tolerability profile was observed for patients starting bezuclastinib treatment following placebo.

Pharmacodynamic Data

Twenty patients enrolled in SUMMIT Part 1a were evaluated for signs of clinical activity within the first 12 weeks, including

well-accepted biomarkers of disease burden.

- 100% of bezuclastinib patients achieved ≥50% reduction in serum tryptase levels vs. 0% of placebo patients
  - 90% (9/10) of bezuclastinib patients with elevated baseline serum tryptase (>20 ng/ml) achieved reduction below 20 ng/ml within 12 weeks
  - 67% (8/12) of patients with abnormal baseline serum tryptase (≥11.4ng/mL) achieved a normal tryptase value (<11.4ng/mL) after 12 weeks of bezuclastinib
- 100% of bezuclastinib patients with detectable baseline variant allele fraction (VAF) achieved ≥50% reduction in KIT D816V VAF vs. 0% of placebo patients
- 100% of bezuclastinib patients with measurable baseline mast cell aggregates achieved ≥50% reduction in bone marrow mast cell burden vs. 14% of placebo patients

Patient Reported Outcomes (PRO) Data

Twenty patients enrolled in SUMMIT Part 1a were evaluated for signs of clinical activity within the first 12 weeks across quality-of-life and/or symptomatic severity scales including Mast Cell Quality-of-Life (MC-QoL), Mastocytosis Activity Scale (MAS), Patient Global Impression of Severity (PGIS) and Patient Global Impression of Change (PGIC). Additional patient assessments were made during the open-label extension using MC-QoL, PGIS and PGIC. In patients with completed questionnaires:

- By week 12, bezuclastinib patients showed a median best improvement of 37% on MC-QoL vs. 24% for placebo patients.
  - By week 20, bezuclastinib patients increased median best improvement to 57% on MC-QoL
  - Patients who crossed over from placebo to bezuclastinib, showed median best improvement on MC-QoL of 75% by week 8 of active treatment
- At week 12, bezuclastinib patients showed a 35% change from baseline on MAS vs. a 28% change from baseline for placebo
  - For bezuclastinib patients treated at 100 mg QD, the MAS improvement from baseline at week 12 was 49%
- At week 12, 63% of bezculastinib patients showed a ≥1 point improvement on PGIS (5 point scale) compared with 0% of placebo patients
  - At week 20, this increased to 78% of bezuclastinib patients reporting ≥1 point improvement
  - 67% of patients who crossed over from placebo to bezuclastinib showed ≥1 point improvement on PGIS by week 8 of active treatment
- At week 12, 63% of bezuclastinib patients reported overall symptoms were “much better” to “very much better” on PGIC vs. 0% of placebo patients
  - At week 20, this increased to 78% of bezuclastinib patients
  - 43% of patients who crossed over from placebo to bezuclastinib reported symptoms were “much better” to “very much better” by week 8 of active treatment
  - By week 20, 100% of patients treated with bezuclastinib reported improved Dermatological and Pain symptoms, 75% of patients reported improvement in Fatigue, and 67% of patients reported improvement in Gastrointestinal symptoms

Bezuclastinib Clinical Development

Cogent completed enrollment in SUMMIT Part 1 and plans to initiate SUMMIT Part 2, a registration-directed, global, randomized placebo-controlled trial in the first half of 2024. In addition, Cogent plans to present data from the completed SUMMIT Part 1 trial (1a and 1b), including all 54 patients enrolled across Part 1a and Part 1b, in the first quarter of 2024.

Data from Part 1 of the Phase 2 APEX clinical trial evaluating bezuclastinib in patients with advanced systemic mastocytosis (AdvSM) will be presented in a poster session at ASH on Monday, December 11, 2023 at ASH. Cogent continues to actively enroll Part 2 of the APEX trial which is expected to include approximately 65 AdvSM patients and is on-track to complete enrollment by the end of 2024.

In Gastrointestinal Stromal Tumors (GIST), Cogent continues to actively enroll patients in Part 2 of the Phase 3 registration-enabling PEAK trial and remains on track to complete enrollment by the end of 2024, with over 100 active sites globally.

Webcast Information and ASH Presentation

Cogent will host a webcast on Monday, December 11, 2023 at 8:00 a.m. ET (5:00 a.m. PT) to discuss the Part 1a data presented today at ASH and the APEX data being presented on Monday. The live event will be available on the Investors & Media page of Cogent’s website at investors.cogentbio.com. A replay of the webcast will be available approximately two hours after the completion of the event and will be archived for up to 30 days. The ASH presentation is available to registered conference attendees and is also in the Posters and Publications section of Cogent’s website at www.cogentbio.com/research.

About Cogent Biosciences, Inc.

Cogent Biosciences is a biotechnology company focused on developing precision therapies for genetically defined diseases. The most advanced clinical program, bezuclastinib, is a selective tyrosine kinase inhibitor that is designed to potently inhibit the KIT D816V mutation as well as other mutations in KIT exon 17. KIT D816V is responsible for driving systemic mastocytosis, a serious disease caused by unchecked proliferation of mast cells. Exon 17 mutations are also found in patients with advanced gastrointestinal stromal tumors (GIST), a type of cancer with strong dependence on oncogenic KIT signaling. In addition to bezuclastinib, the Cogent Research Team is developing a portfolio of novel targeted therapies to help patients fighting serious, genetically driven diseases initially targeting mutations in FGFR2, ErbB2 and PI3Kα (genes/pathways). Cogent Biosciences is based in Waltham, MA and Boulder, CO. Visit our website for more information at www.cogentbio.com. Follow Cogent Biosciences

on social media: X (formerly known as Twitter) and LinkedIn. Information that may be important to investors will be routinely posted on our website and X.

Forward Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding: the potential for bezuclastinib's safety and tolerability profile to support chronic dosing; plans for the company to rapidly initiate Part 2 of SUMMIT in the first half of 2024 and present data from the completed SUMMIT Part 1 trial (1a and 1b), including all 54 patients enrolled across Part 1a and Part 1b, in the first quarter of 2024; plans to complete enrollment of approximately 65 patients in Part 2 of APEX by the end of 2024; and plans to complete enrollment in PEAK by the end of 2024 with over 100 active sites globally. The use of words such as, but not limited to, "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "will," or "would" and similar words expressions are intended to identify forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our clinical results, the rate of enrollment in our clinical trials and other future conditions. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. We may not actually achieve the forecasts or milestones disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Such forward-looking statements are subject to a number of material risks and uncertainties including but not limited to those set forth under the caption "Risk Factors" in Cogent's most recent Quarterly Report on Form 10-Q filed with the SEC. Any forward-looking statement speaks only as of the date on which it was made. Neither we, nor our affiliates, advisors or representatives, undertake any obligation to publicly update or revise any forward-looking statement, whether as result of new information, future events or otherwise, except as required by law. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date hereof.

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