Cogent Biosciences Announces Positive Part 1b Data from SUMMIT Trial Evaluating Bezuclastinib in Patients with Nonadvanced Systemic Mastocytosis

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Registration-enabling SUMMIT Part 2 initiated and actively enrolling at 40 sites globally; RP2D selected at 100 mg once-daily optimized formulation based on:

- *51% week 12 mean change in Total Symptom Score (TSS), including 70% of patients achieving ≥50% reduction in TSS at week 12*
- *49% week 12 mean improvement in quality-of-life (McQoL)*
- *Safety and tolerability profile generally similar to placebo with no grade 3/4 events; no bleeding, edema or cognitive events; no dose reductions and no discontinuations*

Cogent to host investor webcast tomorrow, February 23 at 8:00 a.m. ET

WALTHAM, Mass. and BOULDER, Colo., Feb. 22, 2024 (GLOBE NEWSWIRE) -- Cogent Biosciences, Inc. (Nasdaq: COGT), a biotechnology company focused on developing precision therapies for genetically defined diseases, today reported positive Part 1b data from the Company's ongoing SUMMIT trial evaluating bezuclastinib in patients with nonadvanced systemic mastocytosis (NonAdvSM) at the 2024 American Academy of Allergy Asthma & Immunology Annual Meeting (AAAAI) meeting taking place February 23-26, 2024 in Washington, D.C.

"The results from SUMMIT Part 1b show that bezuclastinib has the potential to provide NonAdvSM patients with a potent and well-tolerated KIT inhibitor that can drive rapid and clinically meaningful impact across a multitude of symptoms resulting in an impressive improvement in overall quality of life," said PD Dr. Frank Siebenhaar, M.D., Head University Outpatient Clinic, Institute of Allergology, Charité - Universitätsmedizin Berlin.

"We are pleased to announce these positive results from our SUMMIT Part 1b trial, the specifics of our new MS2D2 symptomatic severity PRO measure, and the news that we have initiated SUMMIT Part 2, with extremely positive support from the NonAdvSM community," said Andrew Robbins, Cogent's President and Chief Executive Officer. "The magnitude and speed of symptomatic reductions, along with corresponding improvements in quality-of-life, reported by patients in SUMMIT Part 1b has not been seen previously with other treatment options in this patient population. We are fully dedicated to our three actively enrolling, registration-directed clinical trials and see a clear path to establishing bezuclastinib as the best-in-class KIT mutant inhibitor for patients fighting systemic mastocytosis and gastrointestinal stromal tumors."

Patient Demographics
SUMMIT is a randomized, double-blind, placebo-controlled, global, multicenter, Phase 2 clinical trial of bezuclastinib in patients with NonAdvSM. Thirty-four patients in Part 1b were treated with either bezuclastinib or placebo plus best supportive care. The median age of patients at study entry was 52 years (ranging from 27-76 years). Patients were enrolled with the following sub-types: 33 patients with indolent systemic mastocytosis (ISM) and one patient with smoldering systemic mastocytosis (SSM). One patient had received prior avapritinib.

Safety Data
The majority of treatment emergent adverse events were low grade and reversible with no bleeding or cognitive impairment events reported across cohorts. There were no dose reductions in the 100 mg cohort and two dose reductions in the 150 mg cohort (Grade 1 ALT and Grade 2 abdominal pain). Only one serious adverse event (SAE) was reported in the 150mg cohort in which a patient experienced ALT/AST increase that led to discontinuation.

Pharmacodynamic Data
Thirty-four patients enrolled in SUMMIT Part 1b were evaluated for signs of clinical activity over 12 weeks, including well-accepted biomarkers of disease burden. At the recommended phase 2 dose (RP2D) of 100 mg once daily bezuclastinib, results showed:

- 100% of patients with baseline tryptase ≥20ng/mL achieved <20ng/mL at week 12 versus 0% of placebo patients
- 100% of patients with detectable baseline variant allele fraction (VAF) achieved ≥50% reduction in KIT D816V VAF at week 12 versus 0% of placebo patients
- 86% of patients with evaluable bone marrow samples achieved ≥50% reduction in bone marrow mast cell burden at week 12 versus 40% of placebo patients

Patient Reported Outcomes (PRO) Data
Thirty-four patients enrolled in SUMMIT Part 1b were evaluated for signs of clinical activity over 12 weeks using multiple PRO measures, including Cogent's novel Mastocytosis Symptom Severity Daily Diary (MS2D2) and the Mast Cell Quality-of-Life (MC-QoL) scale. At the RP2D 100 mg dose, patients reported:

- 51% week 12 mean change in MS2D2 TSS (improvement in overall symptom severity from baseline) versus

18% improvement for placebo
    - Statistically significant reduction in total symptom severity after 12 weeks when compared to placebo (-23.78 vs. -9.03; p=0.0003)
    - 70% of patients achieved ≥50% reduction in MS2D2 TSS at Week 12 vs. 8% placebo patients
- 49% week 12 mean improvement in quality of life (MC-QoL) versus 24% for placebo
    - Statistically significant improvement in quality of life after 12 weeks when compared to placebo (–24.86 vs. -12.39, p=0.046)

Bezuclastinib Clinical Development

Based on the complete SUMMIT Part 1 data, along with the recommendation from an Independent Data Monitoring Committee, Cogent has initiated SUMMIT Part 2, a registration-directed, global, randomized placebo-controlled trial utilizing the 100 mg once daily dose of bezuclastinib. SUMMIT Part 2 is expected to include 159 patients and complete enrollment in Q2 2025, with estimated top-line results by the end of 2025.

Patient enrollment continues on the registration-directed APEX trial which is expected to include approximately 65 AdvSM patients and remains on-track to complete enrollment by the end of 2024, with top-line results expected in mid-2025.

In second-line Gastrointestinal Stromal Tumors (GIST) patients, Cogent continues to actively enroll the global Phase 3 PEAK trial and expects to complete enrollment by the end of 2024, with top-line results expected by the end of 2025.

Webcast Information and AAAAI Poster

Cogent will host a webcast tomorrow Friday, February 23, 2024 at 8:00 a.m. ET to discuss the SUMMIT Part 1b data. 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 AAAAI poster 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 PI3Ka. 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 to provide NonAdvSM patients with a potent and well-tolerated KIT inhibitor that can drive rapid and clinically meaningful impact across a multitude of symptoms resulting in an impressive improvement in overall quality of life; the potential for bezuclastinib to become the best-in-class KIT mutant inhibitor for patients fighting systemic mastocytosis and GIST; the expectation for SUMMIT to enroll 159 patients in Q2 2025 and to deliver top-line results by the end of 2025; the expectation for APEX to enroll approximately 65 AdvSM patients by the end of 2024 and to deliver top-line results by the end of 2025; and the expectation for PEAK to complete enrollment by the end of 2024 and to deliver top-line results by the end of 2025. 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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