Cogent Biosciences Announces Positive Data from Ongoing Phase 2 APEX Trial Evaluating Bezuclastinib in Patients with Advanced Systemic Mastocytosis (AdvSM)

December 11, 2023

56% ORR in TKI-naïve patients, including 86% ORR by PPR criteria and 100% ORR in APEX patients treated at 100 mg BID with exposures consistent with go-forward dose

Nearly all patients achieved at least 50% improvement in key biomarkers of disease burden: serum tryptase reduction (94%), KIT D816V VAF reduction (93%), and bone marrow mast cell burden (97%)

Encouraging safety and tolerability profile with no related cognitive impairment or bleeding events reported

Cogent to host investor webcast today at 8:00 a.m. ET

WALTHAM, Mass. and BOULDER, Colo., Dec. 11, 2023 (GLOBE NEWSWIRE) -- Cogent Biosciences, Inc. (Nasdaq: COGT), a biotechnology company focused on developing precision therapies for genetically defined diseases, today reported positive data from Part 1 of the Company's ongoing Phase 2 APEX clinical trial evaluating bezuclastinib in patients with advanced systemic mastocytosis (AdvSM) at the 65th American Society of Hematology (ASH 2023) Annual Meeting & Exposition taking place December 9-12, 2023 in San Diego, CA.

"Advanced systemic mastocytosis is a serious and life-threatening disease," said Pankit Vachhani, M.D., Associate Professor of Medicine, Division of Hematology and Oncology, University of Alabama at Birmingham. "The data presented today from the APEX trial demonstrate the potential of bezuclastinib to become a new treatment option for these patients given its combination of rapid and deep clinical activity with an impressive safety profile."

"We are pleased that today's data reinforce bezuclastinib's differentiated safety and tolerability profile while still delivering impactful clinical outcomes," said Andrew Robbins, Cogent's President and Chief Executive Officer. "Delivering high rates of clinical response with a well-tolerated profile is important for AdvSM patients given that available therapies have significant safety and tolerability challenges. Enrollment in Part 2 of the registration enabling portion of APEX is on track and we expect to complete enrollment by the end of 2024."

Patient Demographics

APEX is a global, open-label, multi-center, two-part Phase 2 clinical trial in patients with AdvSM evaluating the safety, efficacy, pharmacokinetic, and pharmacodynamic profiles of bezuclastinib. As of the data cutoff date of September 25, 2023, 32 patients were treated in Part 1 at one of four dose levels (50 mg BID, 100 mg BID, 200 mg BID or 400 mg QD). The median age of patients at study entry was 68 years (ranging from 33-87 years). Patients were enrolled with the following sub-types: seven patients with aggressive systemic mastocytosis (ASM), 23 patients with systemic mastocytosis with associated hematologic neoplasm (SM-AHN), and two patients with mast cell leukemia (MCL). Five patients had received prior avapritinib and 10 patients had received prior midostaurin treatment.

Safety Data

As of the data cutoff date of September 25, 2023, bezuclastinib continues to demonstrate a differentiated safety and tolerability profile across doses. The majority of adverse events were low grade and reversible and there were no related cognitive impairment or bleeding events reported. Related serious adverse events were reported in four patients including Grade 4 thrombocytopenia, Grade 3 hypersensitivity (mediator flare), Grade 3 leishmaniasis, and Grade 3 drug induced liver injury in a patient who was subsequently found to have biliary tract outflow obstruction. Nine patients required dose reduction due to adverse events, six of whom were at the 400mg dose, and three patients discontinued due to adverse events.

Clinical Activity Data

As of the data cutoff date of September 25, 2023, 32 patients enrolled were evaluated for signs of clinical activity, 27 of whom were mIWG-MRT-ECNM evaluable. Patients without post baseline biomarker data were excluded from relevant analyses.

- 52% ORR (CR+CRh+PR) per mIWG-MRT-ECNM criteria, including 56% ORR for TKI-treatment-naïve patients
  - 100% of patients treated with 100 mg BID achieved PR or better and all remain on study
    - 150 mg QD optimized formulation dose selected for APEX Part 2 is expected to deliver patient exposures consistent with this cohort
- 75% ORR (CR+PR) per pure pathological response (PPR) criteria, including 86% ORR for TKI-treatment-naïve patients
- Nearly all patients demonstrated a significant improvement in biomarkers associated with disease burden
  - 94% of patients achieved ≥50% reduction in serum tryptase levels
    - 100% of patients receiving ≥2 cycles achieved ≥50% reduction
    - 53% of patients achieved reduction of serum tryptase below 20 ng/mL
  - 93% of KITD816V-positive patients achieved ≥50% reduction in KIT D816V variant allele fraction (VAF)
  - 97% of patients achieved a ≥50% reduction in bone marrow mast cell burden
    - 79% achieved complete clearance of mast cell aggregates by central review

Bezuclastinib Clinical Development

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.

Cogent reported positive initial Part 1a data on December 9, 2023 from SUMMIT, a Phase 2 clinical trial of bezuclastinib in patients with nonadvanced systemic mastocytosis (NonAdvSM), showing rapid improvement in patient symptoms and improvement across all biomarkers with a safety and tolerability profile that supports the potential for chronic dosing. Cogent completed enrollment in SUMMIT Part 1 and plans to initiate SUMMIT Part 2 in the first half of 2024. In addition, Cogent plans to present data from the completed SUMMIT Part 1 trial (1a and 1b) in the first quarter of 2024.

In Gastrointestinal Stromal Tumors (GIST), Cogent is actively enrolling 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 Poster

Cogent will host a webcast today, Monday, December 11, 2023, at 8:00 a.m. ET (5:00 a.m. PT) to discuss today's APEX data and the SUMMIT data in NonAdvSM released on December 9. 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 APEX poster to be presented will be available in the Posters and Publications section of the Cogent website. Details of the poster are as follows.

- **Poster Title:** Safety and Efficacy of Bezuclastinib (CGT9486), a Novel, Highly Selective, Potent KIT D816V Tyrosine Kinase Inhibitor, in Patients with Advanced Systemic Mastocytosis (AdvSM): Results From Part 1 of the Phase 2 Apex Trial
  Date: Monday, December 11, 2023
  Time: 6:00 p.m. – 8:00 p.m. PT/9:00 p.m. – 11:00 p.m. ET
  Presenter: Dr. Pankit Vachhani, University of Alabama at Birmingham, Birmingham, AL

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 of bezuclastinib to become a new treatment option patients with AdvSM; the expectation for the company to complete enrollment of approximately 65 patients in Part 2 of APEX by the end of 2024; that the 150 mg QD optimized formulation dose selected for APEX Part 2 is expected to deliver patient exposures consistent with the 100 mg BID Part 1 cohort; plans to initiate SUMMIT Part 2 in the first half of 2024; plans to present data from the completed SUMMIT Part 1 trial (1a and 1b) in the first quarter 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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