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

December 8, 2024

52% ORR per mIWG criteria, including 83% ORR for patients receiving 100 mg BID

88% ORR per PPR criteria, including 100% ORR for patients receiving 100 mg BID

Median time to response 2.2 months with median duration of response and median PFS not yet reached

Top-line data from APEX Part 2 on-track for mid-2025

Cogent to host investor webcast on Monday, December 9 at 8:00 a.m. ET

WALTHAM, Mass. and BOULDER, Colo., Dec. 08, 2024 (GLOBE NEWSWIRE) -- Cogent Biosciences, Inc. (Nasdaq: COGT), a biotechnology company focused on developing precision therapies for genetically defined diseases, today reported positive updated 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 66th American Society of Hematology (ASH 2024) Annual Meeting & Exposition taking place December 7-10, 2024 in San Diego, CA.

"Bezuclastinib has the potential to transform the treatment landscape for people living with advanced systemic mastocytosis," said Daniel J. DeAngelo, M.D., Ph.D., Chief of the Division of Leukemia at the Dana-Farber Cancer Institute and Professor of Medicine, Harvard Medical School. "The impressive clinical data presented today from APEX Part 1 demonstrates a combination of rapid and deep clinical responses, with a safety profile that avoids several of the most concerning side effects for AdvSM patients today."

"We are excited to share today the updated clinical data from APEX Part 1 studying bezuclastinib in patients with advanced systemic mastocytosis," said Andrew Robbins, Cogent's President and Chief Executive Officer. "These results show the enormous promise that a highly potent, highly selective, non-brain penetrant KIT inhibitor may provide to this patient population. We look forward to completing enrollment in APEX Part 2 and sharing the results from that study in mid-2025."

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. Thirty-two 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). Earlier this year, Cogent announced APEX Part 2 would be conducted at the optimized 150mg QD dose, which closely matches the exposure from 100 mg BID dose in APEX Part 1. 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.

Clinical Activity Data

As of the data cutoff date of October 11, 2024, 32 patients enrolled were evaluated for signs of clinical activity, 27 of whom were mIWG-MRT-ECNM evaluable. Clinical activity analyzed across dose levels and focused on 100 mg BID cohort showed:

- 52% ORR (CR+CRh+PR+CI) per mIWG-MRT-ECNM criteria, including 61% ORR for TKI-treatment-naïve patients
  - 83% ORR for patients treated at 100 mg BID dose cohort
- 88% ORR (CR+PR) per pure pathological response (PPR) criteria
  - 100% ORR for patients treated at 100 mg BID dose cohort
- Median time to achieve response was 2.2 months and median duration of response has not yet been reached
  - Median PFS was not yet reached at median follow-up of 20 months; PFS rate at 24 months was 82%

Pharmacodynamic Data

Nearly all patients demonstrated a significant improvement in biomarkers associated with disease burden. Patients without post baseline biomarker data were excluded from relevant analyses.

- 94% of patients achieved ≥50% reduction in serum tryptase levels
  - 100% of patients receiving ≥2 cycles achieved ≥50% reduction
  - 66% 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)

- 100% of evaluable patients achieved a ≥50% reduction in bone marrow mast cell burden
  - 83% achieved complete clearance of mast cell aggregates by central review

Safety Data
As of the data cutoff date of October 11, 2024, bezuclastinib continues to demonstrate a differentiated safety and tolerability profile across doses. The majority of hematological adverse events were low grade and reversible. There have been no new treatment related serious adverse events or discontinuations reported since ASH 2023. Due to confounding medical issues, one patient previously reported with DILI has been reassessed and reported as a Grade 4 gamma-glutamyl transferase (GGT) elevation case. Twelve patients required dose reduction, eight of whom were treated at a 400 mg daily dose.

Bezuclastinib in Systemic Mastocytosis
Cogent is actively enrolling patients into APEX Part 2 which is anticipated to complete enrollment in Q1 2025 with top-line results expected in mid-2025.

Cogent will present 24-week follow-up data from patients who participated in the Open Label Extension portion of the ongoing SUMMIT trial on Monday, December 9, 2024 at ASH. SUMMIT is a randomized, double-blind, placebo-controlled, global, multicenter Phase 2 trial evaluating bezuclastinib in patients with Nonadvanced Systemic Mastocytosis (NonAdvSM).

Webcast Information and ASH Posters
Cogent will host a webcast on Monday, December 9, 2024 at 8:00 a.m. ET to discuss updated clinical results from both the APEX and SUMMIT ASH presentations. 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 posters will be available to registered conference attendees and will also be 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, PI3Kα and KRAS. 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 expectation for the company to complete enrollment for APEX Part 2 in Q1 2025 and to have top-line data in mid-2025; the potential for bezuclastinib to transform the treatment landscape for people living with AdvSM; and the potential benefit that a highly potent, highly selective, non-brain penetrant KIT inhibitor may provide to patients with AdvSM. 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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