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

December 11, 2022

- *89% ORR in TKI-therapy naïve patients; 73% ORR in all evaluable patients with 27-week median follow-up*
- *Rapid and deep responses seen including first confirmed CR at 20 weeks; 77% of patients with at least 2 cycles of treatment had complete clearance of bone marrow mast cell aggregates*
- *Favorable safety and tolerability profile with no related cognitive effects or reported intracranial bleeding events*
- *Cogent to host investor webcast Monday, December 12 at 8:00 a.m. ET*

WALTHAM, Mass. and BOULDER, Colo., Dec. 11, 2022 (GLOBE NEWSWIRE) -- Cogent Biosciences, Inc. (Nasdaq: COGT), a biotechnology company focused on developing precision therapies for genetically defined diseases, today announced positive updated clinical data from its ongoing Phase 2 APEX clinical trial evaluating the selective KIT D816V inhibitor bezuclastinib in patients with advanced systemic mastocytosis (AdvSM). The data are being presented in an oral presentation at the 64th American Society of Hematology (ASH) Annual Meeting in New Orleans, LA.

“Advanced systemic mastocytosis is a rare and life-threatening disease,” said Daniel J. DeAngelo, M.D., Ph.D., Chief of the Division of Leukemia at the Dana-Farber Cancer Institute and APEX clinical trial investigator. “Updated results from the APEX trial demonstrate rapid and deep responses with bezuclastinib while maintaining an impressive safety and tolerability profile.”

“We are very encouraged by the clinical profile that bezuclastinib has shown to date,” said Andrew Robbins, President and Chief Executive Officer at Cogent Biosciences. “We are especially excited that a growing body of data supports bezuclastinib’s differentiated safety and tolerability profile enabling therapeutic exposures that could support key differentiation for both AdvSM patients and non-advanced systemic mastocytosis patients.”

Updated Data from Ongoing Phase 2 APEX Clinical Trial

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 October 26, 2022, 16 patients had been 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 69 years (ranging from 33-87 years). Patients were enrolled with the following sub-types: three patients with aggressive systemic mastocytosis (ASM), 12 patients with systemic mastocytosis with associated hematologic neo-plasm (SM-AHN), and one patient with mast cell leukemia (MCL). Three patients had received prior avapritinib and midostaurin treatment.

Updated Safety Data

As of the cutoff date October 26, 2022, bezuclastinib was generally well-tolerated at all doses. The majority of adverse events were Grade 1/2 and occurred in no more than one patient. Grade 3 events reported as at least possibly related to bezuclastinib were neutropenia (2 patients), thrombocytopenia (1 patient), anemia (1 patient) and hypersensitivity/mediator flare (1 patient). Importantly, there were no related cases of cognitive impairment and no reported intracranial bleeding events, which have been associated with other KIT inhibitors. Limited low-grade edema was observed, and analysis of platelet counts in bezuclastinib-treated patients showed no trend in platelet reduction at any dose.

Updated Clinical Activity Data

As of the cutoff date of October 26, 2022, 11 patients were evaluable for response per the modified IWG-MRT-ECNM criteria, and 12 patients were evaluable for response using pure pathological response (PPR) criteria. Reported ORR per mIWG-MRT-ECNM criteria includes centrally adjudicated confirmed and unconfirmed CR, CRh, PR, and CI.

- 89% ORR in TKI therapy naïve patients, including 67% of patients achieving CR, CRh or PR, and 22% of patients achieving CR or CRh
  - 73% ORR in all patients, regardless of prior treatment
- 75% ORR in all patients by PPR criteria, regardless of prior treatment

Additionally, results of key markers of clinical activity were reported from 16 patients.

- 14/16 patients achieved ≥ 50% reduction in serum tryptase levels by central assessment
  - 85% median reduction in serum tryptase
  - Eight of these patients achieved reduction to <20 ng/mL
- 13/13 patients with ≥2 cycles of treatment achieved ≥50% reduction in bone marrow mast cells by central review
  - 10 of these patients achieved complete clearance of bone marrow mast cell aggregates
- 11/12 patients with baseline D816V mutation and ≥2 cycles of treatment achieved ≥50% reduction in KIT D816V variant allele fraction (VAF) by droplet digital polymerase chain reaction (ddPCR)

Bezuclastinib Clinical Development

Based on the continued favorable safety and tolerability profile and clinical activity observed to date in the Phase 2 APEX clinical trial with

bezuclastinib for patients with AdvSM, Cogent will continue enrolling patients in Part 1 of APEX to determine a recommended dose for use in Part 2 of the trial.

In addition, Cogent continues to actively enroll patients in SUMMIT, a Phase 2 clinical trial with bezuclastinib for patients with non-advanced systemic mastocytosis (NonAdvSM), and PEAK, a registrational randomized, open-label, global, Phase 3 clinical trial in patients with imatinib-resistant Gastrointestinal Stromal Tumors (GIST). Cogent plans to present initial clinical efficacy results from the PEAK lead-in study during the first half of 2023 and present initial clinical data from SUMMIT in the second half of 2023.

Webcast Information & ASH Poster

Cogent will host a webcast on December 12, 2022 at 8:00 a.m. ET (7:00 a.m. CT) to discuss today's updated clinical data from the ongoing APEX trial. The live event can be accessed on the Investor 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 poster is available to registered conference attendees as well as on 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 FGFR2 and ErbB2. 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: Twitter and LinkedIn. Information that may be important to investors will be routinely posted on our website and Twitter.

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 become a best-in-class treatment option for patients with AdvSM, the potential for bezuclastinib to achieve therapeutic exposures that could support key differentiation for patients with both AdvSM and NonAdvSM, Cogent's plans to continue enrolling patients in Part 1 of APEX to determine a recommended dose for use in Part 2 of the trial, Cogent's plan to present initial clinical efficacy results from the PEAK lead-in study during the first half of 2023, and Cogent's plan to present initial clinical data from SUMMIT in the second half of 2023. 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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