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

June 10, 2022

All patients treated with bezuclastinib achieved ≥50% reduction in serum tryptase, with a median reduction of 89%, regardless of prior KIT D816V inhibitor treatment

All bone marrow biopsy-assessed patients achieved ≥50% bone marrow mast cell reduction and decreases in blood KIT D816V variant allele fraction (VAF)

Bezuclastinib demonstrates favorable initial safety and tolerability profile with no reported periorbital or peripheral edema, cognitive effects or intracranial bleeding events

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

CAMBRIDGE, Mass. and BOULDER, Colo., June 10, 2022 (GLOBE NEWSWIRE) -- Cogent Biosciences, Inc. (Nasdaq: COGT), a biotechnology company focused on developing precision therapies for genetically defined diseases, today announced positive initial 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 today in a poster presentation at the 2022 European Hematology Association (EHA) Congress in Vienna, Austria.

“Advanced systemic mastocytosis is a severe, debilitating hematologic disorder and physicians and patients remain in search of more effective and better tolerated treatment options to fight this disease,” said Daniel DeAngelo, M.D., Ph.D., Chief of the Division of Leukemia at the Dana-Farber Cancer Institute and APEX clinical trial investigator. “I am very impressed with the early, encouraging results presented today from the APEX study. If results like these can be shown in a larger set of patients with AdvSM, I believe bezuclastinib has the potential to help us take a big step forward in treating systemic mastocytosis patients.”

“We are very excited to present initial clinical data from the APEX study of bezuclastinib in advanced systemic mastocytosis,” said Andrew Robbins, Chief Executive Officer at Cogent Biosciences. “These results reinforce the hypothesis that a potent, selective KIT D816V inhibitor with limited CNS penetration has the potential to provide meaningful clinical activity to all systemic mastocytosis patients, without the tolerability challenges seen with other available treatment options. Based on these results, we expect to accelerate our timelines and investment and look forward to providing another APEX clinical update by the end of 2022, and to presenting SUMMIT clinical data in non-advanced systemic mastocytosis (NonAdvSM) patients in the first half of 2023.”

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 May 24, 2022, 11 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 70 years (ranging from 48-87 years). Patients were enrolled with the following sub-types: two patients with aggressive systemic mastocytosis (ASM), eight patients with systemic mastocytosis with associated hematologic neoplasm (SM-AHN), and one patient with mast cell leukemia (MCL). Two patients had received prior avapritinib and midostaurin treatment.

Initial Safety Data

As of the cutoff date, May 24, 2022, bezuclastinib was generally well-tolerated at all doses. The majority of adverse events were Grade 1/2 and seen in no more than one patient with one serious adverse event and no Grade 4 events reported. Grade 3 events reported as at least possibly related were anemia (1 patient), neutropenia (1 patient) and hypersensitivity/mediator flare (1 patient). There were no reported cases of periorbital/peripheral edema, cognitive effects or intracranial bleeding events, which have been associated with other KIT inhibitors. As of the cutoff date, all patients remained on study. Subsequently, one SM-AHN patient with chronic myelomonocytic leukemia (CMML) transformed to acute myeloid leukemia (AML) and discontinued participation in the trial.

Initial Clinical Activity Data

As of the data cutoff date of May 24, 2022, all 11 patients treated were evaluated for signs of clinical activity. Eight of 11 patients had been treated for at least two cycles, had available data from bone marrow biopsy, and were evaluated for additional endpoints Cycle 3 Day 1 (C3D1) evaluable.

- 11/11 patients achieved ≥50% reduction in serum tryptase levels by central assessment
  - 89% median reduction in serum tryptase
  - Six of these patients achieved reduction to <20 ng/mL
- 8/8 patients (C3D1 evaluable) achieved ≥50% reduction in bone marrow mast cells by central review
  - Six of these patients achieved complete clearance of bone marrow mast cell aggregates
- 8/8 patients (C3D1 evaluable) demonstrated decreases in KIT D816V variant allele fraction (VAF) by droplet digital

polymerase chain reaction (ddPCR)
- All patients remained on treatment with treatment duration ranging from 0.5 - 4.8 months

Two patients enrolled had previously received and discontinued avapritinib for toxicity reasons (intracranial hemorrhage, thrombocytopenia). Both patients have demonstrated clinical outcomes consistent with the avapritinib-naïve patients, including similar magnitude reductions in serum tryptase.

Bezuclastinib Clinical Development
Based on the favorable initial safety and tolerability profile and clinical activity observed to date in the Phase 2 APEX clinical trial with bezuclastinib for AdvSM, Cogent will continue enrolling patients in Part 1 of APEX to determine a recommended dose for use in Part 2 of the trial. A pre-planned interim analysis is scheduled once approximately 28 patients have received at least two cycles of study treatment in Part 1. Cogent plans to present additional data from APEX by the end of 2022. In addition, Cogent continues to actively enroll patients in SUMMIT, a Phase 2 clinical trial with bezuclastinib for 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 data from SUMMIT and lead-in data from PEAK in the first half 2023.

Conference Call Information & EHA poster
Cogent will host a webcast today at 8:00 am ET to discuss today's APEX results. The webcast will be accessible through the Investors and Media section of Cogent's website at https://investors.cogentbio.com/events. Following the live webcast, an archived replay will also be available.

Dial-in Number
U.S./Canada Dial-in Number: 844-686-3753
International Dial-in Number: 704-753-0395
Conference ID: 2951969

The APEX poster to be presented at EHA is available to registered conference attendees as well as on the Cogent Biosciences website in the Posters and Publications section of 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 Cambridge, 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 provide meaningful clinical activity to systemic mastocytosis patients without the tolerability challenges seen with other available treatment options, the expectation to accelerate timelines and investment and provide another APEX clinical update by the end of 2022, the expectation to present SUMMIT clinical data in NonAdvSM patients in the first half of 2023, the expectation to present PEAK clinical data in GIST patients in the first half of 2023, and the plan to continue enrolling patients in Part 1 of APEX to determine a recommended dose for use in Part 2 of the trial. 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 Annual Report on Form 10-K filed with the SEC, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings 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.

Contact:

Christi Waarich
Senior Director, Investor Relations
617-830-1653
christi.waarich@cogentbio.com