Cogent Biosciences Presents Preclinical Data at AACR Annual Meeting Highlighting Precision Therapy Pipeline and Announces Initiation of Part 2 of the Registration-Enabling APEX Trial with Bezuclastinib in Advanced Systemic Mastocytosis

April 17, 2023

Preclinical data describes a novel EGFR-sparing, brain-penetrant ErbB2 inhibitor active against key oncogenic ErbB2 mutations

In vivo characterization shows a novel, selective, reversible FGFR2 inhibitor has potency against molecular brake mutations and potential advantages over covalent approaches

APEX Part 2 underway in AdvSM patients at once-daily 150 mg optimized dose of bezuclastinib

WALTHAM, Mass. and BOULDER, Colo., April 17, 2023 (GLOBE NEWSWIRE) -- Cogent Biosciences, Inc. (Nasdaq: COGT), a biotechnology company focused on developing precision therapies for genetically defined diseases, today announced updated preclinical data from the Company's pipeline programs, including its novel EGFR-sparing brain-penetrant ErbB2 inhibitor and its next-generation selective fibroblast growth factor receptor 2 (FGFR2) program. The data are being presented today in poster sessions at the American Association for Cancer Research (AACR) 2023 Annual Meeting. Cogent also announced the initiation of Part 2 of the Company's ongoing APEX trial with bezuclastinib in Advanced Systemic Mastocytosis (AdvSM).

"We are pleased to share our progress highlighting the Cogent Research Team in their ongoing effort to discover and advance potential best-in-class novel therapies for rare disease populations with high unmet medical need," said Andrew Robbins, Cogent's President and Chief Executive Officer. "Separately, based on bezuclastinib's impressive and consistent clinical activity, safety and tolerability, we are also excited to announce the initiation of Part 2 of the APEX trial in AdvSM at a once-daily dose of 150 mg. We remain on track to provide clinical updates in the second half of 2023 from both APEX and SUMMIT, our trial of bezuclastinib in NonAdvSM patients, as well as updated clinical results from the PEAK lead-in trial in GIST patients this quarter."

AACR Poster Details

Title: Identification of a novel EGFR sparing brain penetrant ErbB2 inhibitor with activity against oncogenic ErbB2 mutations
Session Category: Molecular/Cellular Biology and Genetics
Session Title: Cell Cycle Progression, Checkpoint, and Telomeres
Session Date and Time: Monday Apr 17, 2023 9:00 AM - 12:30 PM ET
Location: Poster Section 10
Poster Board Number: 21
Published Abstract Number: 1440

Cogent is developing a potential best-in-class EGFR-sparing, brain-penetrant ErbB2 inhibitor that includes coverage of key mutations (YVMA, S310F, V842I, L755S) inadequately addressed by currently approved therapies. Activating mutations in the ErbB2 gene have been identified in multiple cancers and demonstrate a tumorigenic role similar to that of ErbB2 amplification. The poster presented today describes a series of novel compounds which potently inhibit several key ErbB2 mutations, including YVMA insertions, while sparing inhibition of EGFR. An exemplar compound from these series demonstrates advantages versus tucatinib, an approved benchmark compound, on tumor growth inhibition in a peripheral ErbB2 L755S driven mutant model, as well as in an ErbB2 driven intracranial model. Recent program advances with a novel chemotype have further improved ErbB2 mutational potency and selectivity, increased estimated brain penetrance to 40% and improved human whole blood stability to nearly 24 hours, suggesting a favorable profile for optimal clinical efficacy.

Title: *In vivo* characterization of a selective FGFR2 inhibitor with potency against gatekeeper and molecular brake mutations
Session Category: Molecular/Cellular Biology and Genetics
Session Title: Cell Cycle Progression, Checkpoint, and Telomeres
Session Date and Time: Monday Apr 17, 2023, 9:00 AM - 12:30 PM ET
Location: Poster Section 10
Poster Board Number: 20
Published Abstract Number: 1439

FGFR inhibitors are well-established oncogenic drivers in multiple diseases, but approved medicines fail to capture the full landscape of FGFR altered tumor types, with FGFR1-mediated hyperphosphatemia serving as the most common dose-limiting toxicity for pan-FGFR inhibitors. The poster presented today provides the first published evidence of a reversible, selective FGFR2

inhibitor with coverage of activating and emerging resistance mutations that spares inhibition of FGFR1. Preclinical data demonstrate a profile that delivers equipotent coverage across both key gatekeeper and molecular brake mutations (V564X, N549X) in FGFR2, while avoiding any evidence of FGFR1-linked hyperphosphatemia at efficacious plasma concentrations. In addition, as a reversible inhibitor, the Cogent program retains enzymatic potency against potential cysteine 491 mutations which are known to emerge as key resistance mutations in patients treated with covalent inhibitors.

APEX Part 2 Design Highlights

APEX is an ongoing Phase 2 trial evaluating bezuclastinib in patients with AdvSM. Part 2 will enroll approximately 65 patients treated at a once-daily 150 mg optimized dose and if successful, is designed to support regulatory submission. Enrollment is expected to be complete by the end of 2024. Several additional patient cohorts are anticipated during Part 2 of the APEX trial designed to demonstrate the breadth of AdvSM patients who may benefit from bezuclastinib, including:

- Up to 20 patients with systemic mastocytosis with an associated hematologic neoplasm (SM-AHN) treated concomitantly with bezuclastinib and AHN directed therapies, including azacitidine.
- Up to 15 patients with inevaluable mIWG disease without C-findings.
- Approximately 10 patients at a dose of 300 mg once-daily to explore the effect of exceeding IC90 KIT D816V engagement in AdvSM patients.

The predicted clinical exposure of the optimized 150 mg formulation of bezuclastinib is expected to surpass that of the previous formulation of bezuclastinib dosed at 100 mg twice-daily in APEX Part 1. Clinical data from approximately 30 patients from APEX Part 1 will be included in a presentation at a scientific meeting in the second half of 2023. Currently, clinical activity, safety and tolerability of patients dosed in APEX Part 1 remains consistent with results presented at the 64th American Society of Hematology (ASH) meeting in December 2022.

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 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 advantages of the Company's preclinical ErbB2 and FGFR programs, the Company's plans to present clinical data from its Phase 3 PEAK lead-in study in GIST patients in the second quarter of 2023, the Company's plans to present clinical data from its SUMMIT trial in NonAdvSM patients in the second half of 2023, the Company's plans to present updated clinical data from Part 1 of its APEX trial in AdvSM patients in the second half of 2023, and clinical development plans and timelines for the Company's APEX trial, including anticipated enrollment, additional patient cohorts, and the anticipated clinical exposure of the optimized 150 mg formulation of bezuclastinib. 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.

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