Cogent Biosciences Presents New Preclinical Data Demonstrating Bezuclastinib as a Differentiated KIT Inhibitor with Minimal Brain Penetration

October 7, 2021

Currently enrolling APEX, a Phase 2 clinical study of bezuclastinib (CGT9486) for patients with Advanced Systemic Mastocytosis (AdvSM)

On track to initiate clinical trials of bezuclastinib for patients with Non-Advanced Systemic Mastocytosis (NonAdvSM) and Gastrointestinal Stromal Tumors (GIST) in 2021

CAMBRIDGE, Mass. and BOULDER, Colo., Oct. 7, 2021 /PRNewswire/ -- Cogent Biosciences, Inc. (Nasdaq: COGT), a biotechnology company focused on developing precision therapies for genetically defined diseases, today announced preclinical data providing further evidence of bezuclastinib as a differentiated, potent, and selective KIT inhibitor. The data were presented in a virtual poster at the 2021 AACR-NCI-EORTC Virtual International Conference on Molecular Targets and Cancer Therapeutics.

"Today Cogent presented new preclinical data that reinforces bezuclastinib's selectivity for targeting KIT mutations while demonstrating minimal brain penetration," said Andrew Robbins, President and CEO of Cogent Biosciences. "We are excited with bezuclastinib's differentiated profile among KIT inhibitors and continue to work quickly to have three clinical trials for AdvSM, NonAdvSM and GIST patients open for enrollment in 2021."

Preclinical studies evaluated the selectivity of bezuclastinib, and other KIT mutant inhibitors, against closely related kinases including PDGFRα, PDGFRβ, and CSF1R. Inhibition of these kinases has been linked to off-target toxicities such as edema and pleural effusions. Comparative screening was performed against a broad spectrum of 71 ion channels, transporters, enzymes, and cell based models, confirming prior evidence that bezuclastinib is a potent and unique inhibitor of KIT A-loop mutations (exon 17/18). In head-to-head studies comparing KIT mutant inhibitors, bezuclastinib demonstrated no activity against closely related kinases, in contrast to other KIT mutant inhibitors with demonstrated potency against PDGFRα and PDGFRβ.

In a nonclinical safety pharmacology study in rodents, bezuclastinib and another KIT A-loop mutant inhibitor were evaluated at doses which closely correlate with clinical exposures previously shown in clinical studies of GIST patients. After three days, bezuclastinib demonstrated minimal brain penetration with a low brain to plasma ratio. These data are supported by a separate neurobehavioral study of bezuclastinib in rodents in which no CNS-related effects were observed. The absence of brain penetration is a preferred feature for a KIT mutant inhibitor as CNS-related adverse events have been observed clinically with some commercially available mutant KIT inhibitors.

Poster Presentation Details for Bezuclastinib:
Title: Preclinical data identifies bezuclastinib as a differentiated KIT inhibitor with unique selectivity to KIT D816V and minimal evidence of brain penetration
Virtual Poster Number: P257
Date/Time: All poster presentations are made available by the conference at the opening of the meeting on October 7, 2021, at 9:00 am ET.

The presentation is available on the Cogent Biosciences website at: https://investors.cogentbio.com/posters-and-publications.

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 newly formed Cogent Research team is developing a portfolio of novel targeted therapies to help patients fighting serious, genetically driven diseases. 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: discussion of the company's business and operations; clinical development plans and timelines including for its lead program, bezuclastinib; the expectation to initiate two additional clinical trials with bezuclastinib before the end of 2021; and the anticipated contributions of the Cogent Research Team. 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 Cogents' 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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