Cogent Biosciences Announces Pipeline Expansion into KRAS and Poster Presentations at the 2024 EORTC-NCI-AACR International Symposium on Molecular Targets and Cancer Therapeutics

October 23, 2024

Preclinical data highlight company's fourth discovery stage program, a novel potent and selective KRAS(ON) inhibitor

Updated preclinical data from CGT6297, Cogent's H1047R mutant-selective PI3Kα inhibitor demonstrates robust inhibition of downstream signaling and efficacy

WALTHAM, Mass. and BOULDER, Colo., Oct. 23, 2024 (GLOBE NEWSWIRE) -- Cogent Biosciences, Inc. (Nasdaq: COGT), a biotechnology company focused on developing precision therapies for genetically defined diseases, today announced the addition of a potent and selective KRAS inhibitor to its pipeline. Preclinical data from this program as well as its newly announced H1047R mutant-selective PI3Kα clinical candidate will be presented in two poster presentations at the 2024 EORTC-NCI-AACR International Symposium on Molecular Targets and Cancer Therapeutics taking place in Barcelona, Spain October 23-25, 2024.

"Our Research team continues to make amazing progress, and we are excited to announce our third clinical candidate and fourth preclinical program today," said Andrew Robbins, Cogent's President and Chief Executive Officer. "Building upon earlier data presentations and recent advancements in the field, our first poster describes the properties of CGT6297, which we believe has the potential to emerge as a best-in-class H1047R mutant-selective PI3Kα inhibitor. Separately, for the first time, we outline our progress toward developing a potential best-in-class KRAS(ON) inhibitor, which in addition to its mechanistic attributes, has pharmacological properties differentiated from existing compounds in the class. Each of these programs align with our long-term strategy of creating and developing best-in-class molecules with the potential to have a broad impact on patients with genetically defined diseases."

Poster Details
The posters can be accessed in the 'Posters and Publications' page of Cogent's website.

Title: Identification of a Pan KRAS(On) Inhibitor with Selectivity Over KRAS over H/NRAS and pM Activity Across Prevalent KRAS Mutations
Session Date and Time: Wednesday, October 23, 2024 – 12.00 - 19.00 CEST
Location: Exhibition Hall, Centre de convencions internacional Barcelona (CCIB), Barcelona, Spain
Poster Number: PB108
Abstract Number: 120

Mutations in KRAS are among the most prevalent mutations found in cancer, occurring most often in colorectal cancer, non-small cell lung cancer and pancreatic cancer. The poster presented today describes Cogent's internally-developed pan KRAS(ON) inhibitor with selectivity over HRAS and NRAS and picomolar (pM) activity across KRAS mutations without the potential liabilities of molecules in the class. Following oral administration, CGT6737 demonstrated robust PK/PD and tumor growth inhibition with 90% PD inhibition in mouse xenograft models. Lead optimization of CGT6737 is ongoing.

Title: Preclinical Characterization of a Novel PI3Kα H1047R Mutant Selective Inhibitor
Session Date and Time: Wednesday, October 23, 2024 – 12.00 - 19.00 CEST
Location: Exhibition Hall, Centre de convencions internacional Barcelona (CCIB) Barcelona, Spain
Poster Number: PB133
Abstract Number: 145

Cogent is also developing a potential best-in-class, wild-type-sparing, PI3Kα inhibitor that provides coverage for the H1047R mutation, which affects >55,000 cancer patients each year. The phosphoinositide 3-kinase (PI3K) pathway is a key cell cycle regulating pathway that has an established role in tumor growth and development. The approved agents for these patients often lead to dose limitations, resulting from activity against wild-type PI3Kα.

The poster presented today highlights Cogent's clinical candidate CGT6297, a potent allosteric inhibitor of PI3K, with 25-fold selectivity over PI3Kα WT. CGT6297 has high oral bioavailability and low clearance across species, providing robust inhibition of downstream signaling and efficacy in animal models. Importantly, when compared to a clinically relevant dose of a currently approved therapy in a mouse tumor model, CGT6297 demonstrated superior efficacy with no increase in insulin. IND-enabling studies are expected to be initiated in 2025.

Upcoming Investor Conference
Cogent will participate in the following upcoming investor conference:

Guggenheim Healthcare Innovation Conference - November 12, 2024 at 10:30 a.m. ET.

A live webcast of the fireside discussion will be available in the Investors & Media section of Cogent's website at investors.cogentbio.com/events. A replay of the event will be archived on Cogent's website for up to 30 days.

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 potential for CGT6297 to be a best-in-class H1047R mutant-selective PI3Kα inhibitor, the expectation that the company will initiate IND-enabling studies for CGT6297 in 2025, and the potential for the company's KRAS program to produce a best-in-class KRAS(ON) inhibitor with pharmacological properties differentiated from existing compounds in the class and without the potential liabilities of molecules in the class. 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.

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