

Codexis Presents Pre-Clinical Data Highlighting its Programs in Homocystinuria and Maple Syrup Urine Disease at ICIEM 2021

REDWOOD CITY, Calif., Nov. 22, 2021 (GLOBE NEWSWIRE) -- Codexis, Inc. (NASDAQ: CDXS), a leading enzyme engineering company enabling the promise of synthetic biology, today announced that two of the Company's wholly owned biotherapeutic programs, CDX-6512 for the treatment of homocystinuria (HCU) and enzymes for the treatment of maple syrup urine disease (MSUD), were the subject of oral presentations at the [14th International Congress of Inborn Errors of Metabolism \(ICIEM\) 2021](#) held in Sydney, Australia from November 21-24, 2021. The enzyme candidates are gastrointestinal (GI)-stable enzymes specifically engineered to be highly resistant to both the acidic conditions of the stomach and to proteases of the upper intestines, to effectively degrade methionine and leucine that is liberated from protein digestion. Elevated levels of these amino acids and their metabolites can lead to the variety of clinical manifestations of HCU and MSUD respectively.

"Our engineered enzymes have demonstrated the potential to be first-in-class oral enzyme therapeutics for patients with homocystinuria and maple syrup urine disease, who currently have limited therapeutic options and must adhere to a life-long, protein restricted diet," said John Nicols, Codexis President and CEO. "As we have demonstrated with our Phase 1 Phenylketonuria and Exocrine Pancreatic Insufficiency programs, and now through our HCU and MSUD programs, food constituent degrading enzymes designed to be stable to the conditions in the GI-tract hold exciting potential as treatments for inborn errors of metabolism and gastrointestinal conditions. We look forward to driving the clinical development of these programs and continuing to push the boundaries of what our enzymes can do to address patients' unmet needs."

Kristen Skvorak, PhD, Translational Scientist and Patient Ambassador at Codexis, presented 'Discovery of CDX-6512, a gastrointestinal-stable methionine-gamma-lyase as a potential orally-administered enzyme therapy for homocystinuria,' which demonstrated up to a 45% suppression in serum total homocysteine ($p < 0.001$), at 4 hours post protein challenge in HCU mice treated with a single dose of CDX-6512, compared to vehicle. Similarly, a statistically significant, dose-dependent reduction in plasma methionine was observed following administration of CDX-6512 in healthy non-human primates receiving a peptone meal.

Dr. Skvorak also presented 'Discovery of a gastrointestinal-stable bacterial leucine decarboxylase as a potential orally-administered enzyme therapy for maple syrup urine disease,' which demonstrated an up to 45% suppression in blood leucine levels, measured as incremental area under the curve (iAUC), in whey-fed iMSUD mice with a single dose of leucine decarboxylase compared to vehicle ($p < 0.01$). A dose-dependent reduction in the plasma leucine iAUC was also observed in healthy non-human primates receiving the

engineered enzyme. This pivotal preclinical work has led to Codexis' elevation of our lead candidate, CDX-6210, for MSUD.

About Homocystinuria (HCU)

Homocystinuria is a rare inborn error of metabolism most commonly due to cystathionine beta-synthase (CBS) deficiency and is characterized by elevated levels of homocysteine in blood and urine that when left untreated may lead to learning and intellectual disabilities, cardiovascular disease, osteoporosis, and stroke. Homocysteine is a metabolite derived from methionine, an essential amino acid that enters the body as part of dietary protein. Strict, life-long adherence to a methionine-restricted diet, often paired with vitamin supplementation (e.g., pyridoxine, folate, vitamin B12, betaine), is currently the only available therapy. According to the Genetic and Rare Disease Information Center (GARD), it is thought that world-wide about 1 in 150,000 people has HCU due to either a CBS or an MTHFR gene mutation. HCU is listed on the Recommended Uniform Screening Panel of disorders recommended by the Secretary of the Department of Health and Human Services for states to screen as part of their universal newborn screening programs.

About Maple Syrup Urine Disease (MSUD)

Maple syrup urine disease is an inborn error of metabolism related to the branched-chain amino acids and is characterized by accumulation of leucine and its metabolites in the brain, blood, and urine that can lead to intellectual and developmental disabilities. A life-long leucine-restricted diet can promote proper development and prevent severe consequences, however compliance remains a significant challenge. Orthotopic liver transplantation is an effective, yet highly invasive and risky, investigational therapy. Episodes of metabolic crisis require swift medical interventions, such as dialysis, and are not meant for long-term treatment. According to the Genetic and Rare Disease Information Center (GARD), about 1 in 150,000-185,000 people is born with MSUD. MSUD is listed on the Recommended Uniform Screening Panel of disorders recommended by the Secretary of the Department of Health and Human Services for states to screen as part of their universal newborn screening programs.

About Codexis

Codexis is a leading enzyme engineering company leveraging its proprietary CodeEvolver® platform to discover and develop novel, high performance enzymes and novel biotherapeutics. Codexis enzymes have applications in the sustainable manufacturing of pharmaceuticals, food, and industrial products; in the creation of the next generation of life science tools; and as gene therapy and biologic therapeutics. The Company's unique performance enzymes drive improvements such as: reduced energy usage, waste generation and capital requirements; higher yields; higher fidelity diagnostics; and more efficacious therapeutics. Codexis enzymes enable the promise of synthetic biology to improve the health of people and the planet. For more information, visit www.codexis.com.

Forward-Looking Statements

To the extent that statements contained in this press release are not descriptions of historical facts regarding Codexis, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. You should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties

and other factors that are, in some cases, beyond Codexis' control and that could materially affect actual results. Factors that could materially affect actual results include, among others: our biotherapeutic programs are early stage, highly regulated and expensive; our ability to obtain additional development partners for the programs, to advance our product candidates to clinical trials and to ultimately receive regulatory approvals is highly uncertain ; the regulatory approval processes of the U.S. Food and Drug Administration and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are unable to obtain or maintain regulatory approval for our products and product candidates, our business will be substantially harmed; results of preclinical studies and early clinical trials of product candidates may not be predictive of results of later studies or trials; our product candidates may not have favorable results in later clinical trials, if any, or receive regulatory approval; if any of our product candidates do not work as intended or cause undesirable side effects, it could hinder or prevent receipt of regulatory approval or realization of commercial potential for them or our other product candidates and could substantially harm our business; and even if we obtain regulatory approval for any products that we develop alone or with collaborators, such products will remain subject to ongoing regulatory requirements, which may result in significant additional expense. Additional information about factors that could materially affect actual results can be found in Codexis' Annual Report on Form 10-K filed with the Securities and Exchange Commission ("SEC") on March 1, 2021, and in Codexis' Quarterly Report on Form 10-Q filed with the SEC on November 5, 2021, including under the caption "Risk Factors," and in Codexis' other periodic reports filed with the SEC. Codexis expressly disclaims any intent or obligation to update these forward-looking statements, except as required by law.

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