May 14, 2024

Codexis Presents Groundbreaking Enzymatic Synthesis Data at TIDES USA Annual Meeting

REDWOOD CITY, Calif., May 14, 2024 (GLOBE NEWSWIRE) -- Codexis, Inc. (NASDAQ: CDXS), a leading enzyme engineering company, today announced it has successfully synthesized an oligonucleotide via an enzymatic route to support RNA-based therapeutics manufacturing. Data highlighting this historic manufacturing milestone are being presented today in a Spotlight Presentation at the TIDES USA annual meeting taking place in Boston, MA, and virtually May 14 – 17, 2024.

“The data presented today by Codexis are truly unprecedented—I believe this is the first enzymatic synthesis of a full-length oligonucleotide from starting material through the attachment of a conjugation moiety. This milestone provides meaningful proof of process to industry that there are alternative manufacturing methods available as the demand for RNAi therapeutics increases. The ECO Synthesis™ manufacturing platform has the potential to be a scalable and sustainable way to manufacture this important and growing new class of medicines,” said John Maraganore, PhD, Founder and Former Chief Executive Officer at Alnylam Pharmaceuticals and member of Codexis’ Strategic Advisory Board.

Codexis Enzymatically Synthesizes Fully Modified RNA Oligonucleotide

During the presentation, Codexis will showcase data on the enzymatic synthesis of a known siRNA oligonucleotide that incorporates the nucleotide modifications most frequently found in approved therapeutic assets today. This includes the synthesis of siRNA compounds using the Company’s Enzyme Catalyzed Oligonucleotide (ECO) Synthesis™ manufacturing platform from a starter oligonucleotide to the inclusion of a conjugation moiety. This final step primes the oligonucleotide for the attachment of a customer’s proprietary targeting moiety to enable direct delivery of the therapeutic agent to the desired cells. Key data from the presentation noted that the ECO Synthesis™ manufacturing platform:

- Incorporated RNA bases with common modifications used in current siRNA therapeutic assets
- Achieved coupling efficiency greater than 98%
- Executed the enzymatic addition of a conjugation moiety
- Confirmed lack of notable impurities typically observed in phosphoramidite chemistry synthesis

Now that Codexis has successfully achieved this important technical milestone, the Company is continuing process development to optimize yield, purity and quality with the goal of providing customers with siRNA material of comparable or better quality to phosphoramidite chemistry for preclinical testing.

Codexis Launches RNA Ligase Screening and Optimization Services

Codexis also today announced the launch of its RNA Ligase Screening and Optimization Services. An overview of this new offering will be highlighted during a TIDES Talk session on Thursday, May 16, 2024.

During phosphoramidite chemical synthesis of RNA, each nucleotide added to the growing oligonucleotide amplifies inherent coupling errors, leading to a decrease in the yield of the desired full-length RNA construct. By utilizing a ligation approach, multiple short, single-stranded RNA (ssRNA) fragments can be synthesized, via phosphoramidite chemistry or the ECO Synthesis™ manufacturing platform, then duplexed and ligated together with an ecoRNA™ double-stranded ligase to form the desired double-stranded RNA (dsRNA) construct. This method provides the potential for higher purity and yield, which allows for increased scalability and reduced manufacturing costs.

As part of Codexis' Center of Excellence for Enzymatic RNA Synthesis, the Company provides RNA ligase screening and optimization services, which include the custom evolution of dsRNA ligase enzyme variants, screening and protocol optimization for manufacturing and use of the dsRNA ligase, and research-grade RNA production, which can be used for future preclinical studies. More information on Codexis' new RNA Ligase Screening and Optimization Services can be found in the Products & Services section of its corporate website.

"This week's presentations clearly demonstrate our ability to make full-length oligonucleotides enzymatically. We are thrilled at the rapid progress that we've made on enzyme evolution, incorporation of modified nucleotides, and attachment of conjugation moieties since first unveiling the ECO Synthesis™ platform at the TIDES USA conference one year ago. Supplementing that with the launch of our RNA ligase screening and optimization program enables us to ultimately offer sequential enzymatic synthesis—potentially in combination with ligation—to deliver full-length siRNA constructs," said Stephen Dilly, MBBS, PhD, Chief Executive Officer at Codexis. "We are hearing great excitement at these developments from our potential customers, partners and collaborators, and our team has dozens of meetings already scheduled this week to further discuss both the ECO Synthesis™ platform and our RNA ligase program with prospective CDMOs and drug developer customers."

Presentation Details

Title: Enzymatic Oligonucleotide Synthesis Process Flow and Substance Impurity Profile
Date: Tuesday, May 14, 2024
Time: 12:45 pm – 1:15 pm ET
Location: Spotlight Presentations, Luncheon 1
Presenter: Derek Gauntlett, MBA, Director, Bioprocess Chemistry at Codexis

Title: Two Enzymatic Approaches for Large-scale siRNA Synthesis
Date: Thursday, May 16, 2024
Time: 10:10 am – 10:20 am ET
Location: TIDES Talks, Exhibit Hall
Presenter: Mathew Miller, PhD, Director, Life Science and RNA Technology at Codexis

The slide decks from both presentations are now available on the Codexis corporate website, www.codexis.com. A recording of the presentations will be posted following the conference.

Attendees of the TIDES USA conference may visit Codexis at Booth #628, located in the Exhibit Hall, for more information on the ECO Synthesis™ manufacturing platform and the Company's RNA Ligase Screening and Optimization Services.

About the ECO Synthesis™ Manufacturing Platform

Ribonucleic acid (RNA) as a therapeutic modality has gained tremendous traction in recent years with the growing number of messenger RNA (mRNA) vaccines and small interfering RNA (siRNA) candidates advancing in clinical studies. However, large-scale production of RNA interference (RNAi) therapeutics using traditional chemical synthesis faces complex challenges in nucleic acid quality and quantity, as well as overall economics. With over 450 RNAi therapies currently in clinical development, including more than 40 assets in Phase 2 and Phase 3 clinical trials targeting disease indications impacting millions of patients, RNAi therapeutic demand is projected to outpace current production capabilities by the end of the decade. Codexis' proprietary ECO Synthesis™ manufacturing platform is being designed to address these scalability and cost limitations by potentially enabling the commercial-scale manufacture of RNAi therapeutics through an enzymatic route. The Company achieved gram-scale synthesis in December 2023, where it demonstrated the preparative-scale manufacture of an oligonucleotide, composed of the modified nucleotide building blocks typically used in RNAi therapeutics, under process-like conditions.

About Codexis

Codexis is a leading enzyme engineering company leveraging its proprietary CodeEvolver® technology platform to discover, develop and enhance novel, high-performance enzymes and other classes of proteins. Codexis enzymes solve for real-world challenges associated with small molecule pharmaceuticals manufacturing and nucleic acid synthesis. The Company is currently developing its proprietary ECO Synthesis™ manufacturing platform to enable the scaled manufacture of RNAi therapeutics through an enzymatic route. Codexis' unique enzymes can drive improvements such as higher yields, reduced energy usage and waste generation, improved efficiency in manufacturing and greater sensitivity in genomic and diagnostic applications. For more information, visit https://www.codexis.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "positioned," "potential," "predict," "seek," "should," "suggest," "target," "on track," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. To the extent that statements contained in this press release are not descriptions of historical facts, they are forward-looking statements reflecting the current beliefs and expectations of management, including, but not limited to, the ability of an enzymatic oligonucleotide synthesis process to complement or replace traditional chemical synthesis; the potential of the Company's ECO Synthesis™ platform and RNA Ligase Screening and Optimization Services to create value for Codexis and its customers by enabling the delivery of full-length siRNA constructs; other anticipated technical and commercial milestones related to the ECO Synthesis™ platform and the dsRNA ligase program, and public announcements related thereto; potential details and features of the ECO Synthesis™ platform such as it being scalable and able to reduce manufacturing costs, as well as having higher purity and yield than existing methods; and the future demand for RNAi therapeutics. 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: Codexis' dependence on its licensees and collaborators; Codexis' ability to successfully develop new technology such as its ECO Synthesis™ platform and dsRNA ligase program; if any of its collaborators terminate their development programs under their respective license agreements with Codexis; Codexis may need additional capital in the future in order to expand its business; Codexis' dependence on a limited number of products and customers, and potential adverse effects to Codexis' business if its customers' products are not received well in the markets; whether the end markets for Codexis' customers' products develop and remain viable; if competitors and potential competitors who have greater resources and experience than Codexis develop products and technologies that make Codexis' products and technologies obsolete; Codexis' ability to comply with debt covenants under its loan facility; and market and economic conditions may negatively impact Codexis business, financial condition and share price. 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 February 28, 2024 and in Codexis' Quarterly Report on Form 10-Q filed with the SEC on May 2, 2024, 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.

For More Information

Investor Contact
Carrie McKim
(336) 608-9706
ir@codexis.com

Media Contact
Lauren Musto
(781) 572-1147
media@codexis.com

CODEXIS®

Source: Codexis, Inc.