Synlogic Announces Data Presentations at the Society for Inherited Metabolic Disorders (SIMD) 44th Annual Meeting

March 20, 2023

Presentations included full data from both the Phase 2 Synpheny-1 Study in phenylketonuria and Phase 1 Study for SYNB1353 as a potential treatment for homocystinuria

CAMBRIDGE, Mass., March 20, 2023 (GLOBE NEWSWIRE) -- Synlogic, Inc. (Nasdaq: SYBX), the leading company advancing therapeutics based on synthetic biology, announced that positive data from the company's Phase 2 Synpheny-1 study for phenylketonuria (PKU) were presented in a podium presentation yesterday during the Society for Inherited Metabolic Disorders (SIMD) 44th Annual Meeting in Salt Lake City, Utah. In separate poster presentations, the company also presented clinical data and preclinical data related to its homocystinuria (HCU) program.

These findings build on positive top-line data from Synpheny-1 presented by Synlogic in October 2022, confirming proof-of-concept in PKU patients for SYNB1934, as well as positive top-line Phase 1 data from the HCU program announced in November 2022, demonstrating proof of mechanism for SYNB1353.

"We were delighted to review these encouraging findings from our two rare metabolic disease programs among the expert metabolic clinicians who attend the SIMD meeting," said Dave Hava, Chief Scientific Officer and Head of Research and Development at Synlogic. "The favorable results from our PKU study have brought interest and momentum to the program as we prepare to begin our Phase 3 trial in the first half of this year. These data reinforce the potential of Synlogic's Synthetic Biotic platform to advance a novel class of therapeutics to address diseases in need of new treatment options."

Highlights from the Synpheny-1 PKU Phase 2 Study Results

The Synpheny-1 results were presented by Dr. Jerry Vockley, MD, PhD, Director, Center for Rare Disease Therapy, Chief, Medical Genetics, at UPMC Children's Hospital of Pittsburgh, Professor of Pediatrics and Human Genetics at University of Pittsburgh, and lead investigator in the Synpheny-1 study.

Synpheny-1 included 20 patients with PKU. Results presented included successfully meeting the primary endpoint (change in area under the curve of D5-Phe following a meal challenge) with D5-Phe reductions of –33.8% and –42.9% for SYNB1618 and SYNB1934, respectively. The study also confirmed greater activity in PKU patients for SYNB1934, the next-generation Synthetic Biotic designed to consume Phe, as compared to first-generation candidate SYNB1618.

Highlights from results for SYNB1934 in the presentation include:

- Evidence of Phe metabolism by SYNB1934 in all patients, based on production of strain specific biomarkers (D5-TCA and D5-HA);
- Plasma Phe reduction of -53% among responders (defined as >20% reduction in Phe from baseline); response rate was 60% (3 of 5 patients);
- Data included one patient who was taking Kuvan at baseline; this patient achieved an additional reduction in plasma Phe of -80% compared to baseline; and
- Adverse events (AEs) were either mild or moderate in severity and mostly gastrointestinal in nature, consistent with those of a probiotic

"As the lead investigator for Synlogic's PKU Phase 2 Synpheny-1 study, I was pleased to see the significant levels of interest in the additional results from the study presented during the SIMD meeting," said Dr. Vockley. "We have now seen consistently across the program the potential to quite meaningfully reduce Phe levels in patients with PKU. I very much look forward to assessing this more broadly in the Phase 3 study, given the significant need for new treatment options for those living with PKU."

Highlights from Data Presented from the HCU Program

The company also shared additional clinical and preclinical data for SYNB1353 at the SIMD Annual Meeting. Clinical data presented included positive data from the Phase 1 study evaluating SYNB1353 in healthy volunteers using a dietary model of HCU. SYNB1353 is a Synthetic Biotic designed to consume methionine (Met), a precursor to homocysteine (HCy), as a potential treatment for HCU. A Met-restricted diet is a standard means of reducing total homocysteine (tHcy) levels, and associated risk of life-threatening complications, in patients with HCU. Study findings demonstrated proof of mechanism through the lowering of plasma Met levels and mechanistic support through the assessment of strain biomarkers of activity. Preclinical data include evidence of Met enterorecirculation and significant blunting of plasma D4-Met and plasma D4-tHCy with SYNB1353 in a mouse model of cystathionine beta-synthase (CBS) deficiency.

Posters presented at the SIMD meeting are posted on the Publications page of the Synlogic website.

About the PKU Program & Phase 2 Synpheny-1 Study

Synlogic's PKU program has included four clinical trials and dosing experience in 240 individuals and more than 30 PKU patients to date. The Phase 2

Synpheny-1 study was a Phase 2, open-label, 28-day study to assess safety, tolerability and efficacy of two Synthetic Biotics designed to metabolize Phe: the first-generation SYNB1618 and the next-generation SYNB1934. Synpheny-1 enrolled 20 adult patients with PKU, 11 in the SYNB1618 arm and nine in the SYNB1934 arm. The study's objective was to confirm metabolism of Phe in PKU patients via the primary endpoint of a change in area under the curve (AUC) of plasma levels of labeled D5-phenylalanine (D5-Phe) after a meal challenge before and after the treatment period, a specific indicator of the ability of each investigational therapy to consume Phe. Dietary intake of Phe was carefully managed during the study to match patients' usual protein and Phe intake.

About Synlogic

Synlogic is the leading company advancing therapeutics based on synthetic biology. Synlogic's pipeline includes its lead program in phenylketonuria (PKU), which has demonstrated proof of concept with plans to start a pivotal, Phase 3 study in the first half of 2023, and additional novel drug candidates designed to treat homocystinuria (HCU), enteric hyperoxaluria and gout. The rapid advancement of these potential biotherapeutics, called Synthetic Biotics, has been enabled by Synlogic's reproducible, target-specific drug design. Synlogic uses programmable, precision genetic engineering of well-characterized probiotics to exert localized activity for therapeutic benefit, with a focus on metabolic and immunological diseases. In addition to its clinical programs, Synlogic has a research collaboration with Roche on the discovery of a novel Synthetic Biotic for the treatment of inflammatory bowel disease (IBD). Synlogic has also developed two drug candidates through a research collaboration with Ginkgo Bioworks: SYNB1353, designed to consume methionine for the potential treatment of HCU, and SYNB2081, designed to lower uric acid for the potential treatment of gout. For additional information visit www.synlogictx.com.

Forward-Looking Statements

This press release contains "forward-looking statements" that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, included in this press release regarding strategy, future operations, clinical development plans, future financial position, future revenue, projected expenses, prospects, plans and objectives of management are forward-looking statements. In addition, when or if used in this press release, the words "may," "could," "should," "anticipate," "believe," "look forward, " "estimate," "expect," "intend," "on track, " "plan," "predict" and similar expressions and their variants, as they relate to Synlogic, may identify forward-looking statements. Examples of forward-looking statements, include, but are not limited to, statements regarding the potential of Synlogic's approach to Synthetic Biotics to develop therapeutics to address a wide range of diseases including: inborn errors of metabolism and inflammatory and immune disorders; our expectations about sufficiency of our existing cash balance; the future clinical development of Synthetic Biotics; the approach Synlogic is taking to discover and develop novel therapeutics using synthetic biology; and the expected timing of Synlogic's clinical trials of SYNB1934, SYNB1353, SYNB8802 and SYNB2081 and availability of clinical trial data. Actual results could differ materially from those contained in any forward-looking statements as a result of various factors, including: the uncertainties inherent in the clinical and preclinical development process; the ability of Synlogic to protect its intellectual property rights; and legislative, regulatory, political and economic developments, as well as those risks identified under the heading "Risk Factors" in Synlogic's filings with the U.S. Securities and Exchange Commission. The forward-looking statements contained in this press release reflect Synlogic's current views with respect to future events. Synlogic anticipates that subsequent events and developments will cause its views to change. However, while Synlogic may elect to update these forward-looking statements in the future, Synlogic specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Synlogic's view as of any date subsequent to the date hereof.

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