Synlogic Announces Achievement of Proof of Concept for SYNB8802 in Enteric Hyperoxaluria Based on Urinary Oxalate Lowering in Phase 1b Study

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Results include -38% reduction in urinary oxalate compared to placebo in Roux-en-Y gastric bypass patients

Favorable safety and tolerability, with frequency and severity of adverse events similar across placebo and active arms

Synlogic to host webcast today at 8:30 am. ET with Dr. Kyle Wood, Associate Professor, Urology, University of Alabama at Birmingham

CAMBRIDGE, Mass., Dec. 15, 2022 (GLOBE NEWSWIRE) -- Synlogic, Inc. (Nasdaq: SYBX), a clinical-stage biotechnology company developing medicines for metabolic and immunological diseases through its proprietary approach to synthetic biology, today announced that SYNB8802 has demonstrated proof of concept through clinically significant lowering of urinary oxalate in a Phase 1b study in patients with a history of gastric bypass surgery.

Top-line Findings:

- In the Phase 1b SYNB8802-CP-002 study, SYNB8802 demonstrated a dose-related reduction in urinary oxalate.
- The -38% urinary oxalate reduction observed at the $3x10^{11}$ live cell dose three times a day exceeds the level of urinary oxalate reduction (-20%) that has been associated with reduced risk of kidney stones in analyses based on observational data.[1]
- SYNB8802 was generally well tolerated. There were no serious adverse events (SAEs). All GI-related adverse events (AEs) were mild, and their frequency and severity were similar in the active and placebo group.

“Given the profound need for a medical treatment for enteric hyperoxaluria, we are delighted to demonstrate meaningful reductions in urinary oxalate in the Roux-en-Y gastric bypass patient population,” said Aoife Brennan, M.B. Ch.B., Synlogic President and Chief Executive Officer. “In addition, this important milestone represents the third positive clinical data readout this year in three different diseases, following our positive Phase 2 results for SYNB1934 for phenylketonuria and positive Phase 1 results for SYNB1353 for homocystinuria.”

“A subset of enteric patients have repeated kidney stones and life-altering disease that is particularly challenging to manage,” said Kyle Wood, MD, Associate Professor of Urology at the University of Alabama at Birmingham. “A therapeutic approach that lowers urinary oxalate in patients with underlying GI malabsorption is badly needed. The innovative mechanism of SYNB8802 and the strength of the data generated to date support the potential for SYNB8802 to be a highly meaningful first-in-category biotherapeutic.”

The SYNB8802-CP-002 Study

This Phase 1b study was a double-blind, randomized, placebo-controlled, inpatient study evaluating the safety and tolerability of SYNB8802 in subjects with a history of Roux-en-Y gastric bypass surgery. The primary endpoint was safety and tolerability. After a three-day diet and placebo run in, patients were randomized to either placebo or SYNB8802 for a 12-day dosing period. The dosing period included a dose escalation plan with the first six days at the lower dose of 1×10^{11} live cells, followed by six days at the 3×10^{11} live cell dose. Each six-day treatment period included a stepwise increase in dose frequency. To enable a controlled assessment of SYNB8802’s effects on oxalate, patients consumed a controlled diet for the duration of the inpatient stay. Urine was also collected for a 24-hour sample for each patient, each day.

The study enrolled 11 patients; 7 received SYNB8802 and 4 received placebo. SYNB8802 was well tolerated, with no SAEs. The most common AEs were GI-related, mild, and transient. The GI-related AEs occurred at a similar frequency in active and placebo groups. One patient in the placebo group discontinued during dosing due to the need for antibiotics.

Dosing with SYNB8802 was associated with a dose-dependent reduction in urinary oxalate. In a pharmacometric analysis that takes into account all patients’ data, dose level and dose frequency, there was a -28% (-37.2, -18.2) change from baseline in urinary oxalate vs. placebo at the $1x10^{11}$ TID dose, and a -38% (-46.4, -28.7) change from baseline in urinary oxalate vs. placebo at the $3x10^{11}$ TID dose.

In addition to the completed SYNB8802-CP-002 study, SYNB8802 is also being evaluated in an ongoing, outpatient study (SYNB8802-CP-001). Full results from both studies will be presented at a future medical meeting.

Conference Call & Webcast

Synlogic will host a conference call and live webcast at 8:30 a.m. ET today, December 15, 2022. Joining will be Dr. Kyle Wood, a specialist in kidney stone-related disease in his role as Associate Professor, Urology, University of Alabama at Birmingham. **To access the webcast, please register here. To access the call by phone** please dial (646) 307-1963 or for a toll-free option in the U.S. and Canada dial (800) 715-9871. **The event ID is: 4065357.** You can also access this information on the “Events Calendar” section of the Investors & Media webpage. For those unable to participate in the conference call or webcast, a replay will be available for 30 days on the Synlogic website here.

About Enteric Hyperoxaluria and SYNB8802

Enteric hyperoxaluria (EH) is a metabolic disease and well-recognized cause of recurrent kidney stones, typically caused by a chronic underlying GI disorder associated with malabsorption, which predisposes patients to excessive absorption of oxalate. Elevated oxalate in the circulation leads to oxalate crystal formation in the kidney, causing excruciating pain and progressive renal damage. There is no FDA-approved treatment for enteric hyperoxaluria. SYNB8802 is a novel, orally administered, non-systemically absorbed drug candidate being developed for the treatment of enteric hyperoxaluria. SYNB8802 was designed using precision genetic engineering of the well-characterized probiotic E. coli Nissle to metabolize oxalate in GI tract, preventing its absorption and resultant crystal formation, lowering levels of urinary oxalate.

References

[1] D'Costa et al. *Nephrol Dial Transplant* (2020) 1–8.

About Synlogic

Synlogic is a clinical-stage biotechnology company developing medicines through its proprietary approach to 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 or 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 SYNB1618, 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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