Synlogic Announces Positive Top-Line Phase 2 Data for Phenylketonuria (PKU); SYNB1934 Advances to Phase 3

October 18, 2022

Positive results include clinically meaningful Phe reductions, with a 60% response rate and 42% reduction in plasma Phe among responders across the study population

Consistent, positive measures of activity across all assessed endpoints

Company confirms SYNB1934 as candidate for Phase 3 initiation expected in H1 2023

Synlogic to Host Webcast Today at 8:30 a.m. ET

CAMBRIDGE, Mass., Oct. 18, 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 positive top-line data from the Phase 2 Synpheny-1 study in phenylketonuria (PKU). The company also confirmed that based on the results, SYNB1934 will be the drug candidate progressing to the Phase 3 registrational study expected to begin in H1 2023.

Top-line Results:

- The Phase 2 study enrolled 20 patients with PKU; 11 were enrolled in the SYNB1618 arm and 9 patients were enrolled in the SYNB1934 arm.
- Both strains demonstrated clinically meaningful reductions in fasting plasma Phe. On an “all comers” basis, the day 14 mean change from baseline in fasting plasma Phe was -20% for SYNB1618 and -34% for SYNB1934.
- Results were consistent and positive across all measured indicators of activity for both drug candidates, including plasma D5-Phe, plasma D5-TCA and urinary D5-HA, with numerically greater changes observed for SYNB1934, consistent with previously shared results in healthy volunteers.
- Results from patients who were already taking sapropterin (Kuvan®) at baseline, and then received SYNB1618 and SYNB1934, were consistent with the overall efficacy profile, demonstrating the potential for adjunctive use.
- All adverse events were mild or moderate in severity and were predominantly gastrointestinal (GI) in nature. There were no serious adverse events (SAEs).

“PKU continues to be a very challenging disease for patients, with many in need of new treatment options,” said Dr. Jerry Vockley, Professor of Human Genetics at University of Pittsburgh and lead investigator on the Phase 2 Synpheny-1 study. “It is very promising to see these results and the potential benefits of a new, orally administered investigational product that can meaningfully lower Phe in patients with PKU.”

“We are tremendously excited to share these top-line data from our Phase 2 study showing consistent positive results across all endpoints in patients with PKU. In particular, the robust plasma Phe reduction demonstrated by SYNB1934 indicates that it has potential to be a transformative treatment for patients with PKU,” said Aoife Brennan, M.B. Ch.B., Synlogic President and Chief Executive Officer. “I would like to thank the patients, clinicians and staff of our investigational sites who made this study possible. We look forward to further collaboration as we initiate our Phase 3 pivotal study, with the goal of bringing this potentially life-changing innovation in the treatment of PKU to patients.”

The Phase 2 Synpheny-1 Study

The Phase 2 Synpheny-1 study is a Phase 2, open-label, 28-day study to assess safety, tolerability and efficacy of SYNB1618 and SYNB1934 in patients with PKU. The primary endpoint is the 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 each drug candidate’s ability to consume Phe as intended. The study included a dose-ramp regimen over 15 days of treatment, with days 7 through 14 at the constant dose of $1x10^{12}$ live cells. Additional endpoints include change from baseline in fasting levels of plasma Phe, and incidence of treatment-emergent adverse events (TEAEs), as well as the levels of additional strain-specific metabolites plasma D5-TCA and urinary D5-HA. Dietary intake of Phe was carefully managed during the study to match patients’ usual protein and Phe intake.

Synpheny-1 enrolled 20 adults with PKU who had a Phe level above 600 µmol/L at screening despite treatment with diet and/or sapropterin. Eleven patients were enrolled in the SYNB1618 arm and 9 were enrolled in the SYNB1934 arm. Ten patients have completed the SYNB1618 arm and 5 patients have completed Arm 2 with SYNB1934.

Results included achieving a reduction in plasma levels of labeled D5-phenylalanine (D5-Phe), and in fasting plasma Phe levels from baseline for both strains. On an “all comers” basis among patients who completed dosing, the day 14 mean change from baseline in fasting plasma Phe was -20% for

SYNB1618 and -34% for SYNB1934. Results included data from patients who were already taking sapropterin (Kuvan®) at baseline, and then received SYNB1618 and SYNB1934. In these patients, results were consistent with the overall efficacy profile, demonstrating the potential for adjunctive use.

Response was defined as >20% reduction in Phe at either day 7 or day 14. Overall, 60% of patients enrolled who completed dosing in the study met these criteria (six of the ten patients dosed with SYNB1618 and three of the five that have completed dosing with SYNB1934 met this criterion). Phe reduction for those responders in aggregate averaged -42%. The ranges for Phe reduction among responders by strain were -20% to -61% and -29% to -80% for SYNB1618 and SYNB1934, respectively.

Adverse events were all mild to moderate and predominantly GI in nature. Results were similar across SYNB1618 and SYNB1934. There were no serious adverse events (SAEs). Across the study, three patients discontinued due to GI-related adverse events, one withdrew consent, and one patient withdrew following an adverse event of facial flushing which was attributed to a possible allergic reaction.

Full data from the Phase 2 study are expected to be presented at upcoming medical meetings and submitted to peer-reviewed medical journals.

Next Steps

Based on data obtained across the PKU program, Synlogic has confirmed that SYNB1934 will be the drug candidate advancing to a Phase 3 pivotal study expected to begin in the first half of 2023.

Synlogic also confirmed the following anticipated milestones:

- Share data from the Phase 1 trial in healthy volunteers for SYNB1353 for homocystinuria (HCU) in H2 2022
- Share proof of concept data for SYNB8802 for enteric hyperoxaluria (EH) in H2 2022

Conference Call & Webcast Information

Synlogic will host a conference call and live webcast at 8:30 a.m. ET today, October 18, 2022. **To access the webcast, please register here. To access the call by phone** from the U.S. dial (800) 715-9871 (toll-free); for outside of the U.S. dial: (646) 307-1963. 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 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.

About SYNB1934 and SYNB1618

SYNB1934 and SYNB1618 are orally administered, non-systemically absorbed drug candidates being studied as potential treatments for phenylketonuria (PKU), a genetic disease caused by potentially neurotoxic levels of the amino acid phenylalanine (Phe). Treatment options for PKU are currently limited due to efficacy and safety, and many of those who are treated are in need of additional Phe-lowering. Synlogic designed drug candidates to reduce levels of Phe in people with PKU using precision genetic engineering of the well-characterized probiotic *E. coli* Nissle. SYNB1934 reflects additional optimization to further increase productivity of Phe consumption compared to SYNB1618. Findings to date support the potential for an efficacious, safe, convenient, and flexible treatment option for PKU. SYNB1618 has received both Orphan Drug and Fast Track designations by the US Food and Drug Administration (FDA) and orphan medicinal product designation by the European Medicines Agency. Following results of the Synpheny-1 Phase 2 study with both candidates, Synlogic confirmed that SYNB1934 would be advancing as the drug candidate for the pivotal Phase 3 study and expected commercialization.

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, including SYNB2081; 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 and SYNB8802 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.

MEDIA CONTACT:
Bill Berry
Berry & Company Public Relations
Phone: 212-253-8881
Email: bberry@berrypr.com

INVESTOR CONTACT:
Andrew Funderburk
Kendall Investor Relations
Phone: 617-401-9152
Email: afunderburk@kendallir.com

Source: Synlogic, Inc.