Synlogic Announces Positive Phase 2 Data Demonstrating Reduction in Plasma Phenylalanine Levels in Patients with Phenylketonuria

September 20, 2021

-- SYNB1618 demonstrated proof of concept with meaningful reduction of plasma phenylalanine (Phe) levels in an interim analysis of the Phase 2 SynPheny-1 Study --

-- SYNB1934, an optimized strain of SYNB1618, demonstrated two-fold increase in biomarkers of Phe metabolism compared to SYNB1618 --

-- Phase 2 SynPheny-1 study will incorporate SYNB1934. Company to prepare to start Phase 3 program with the most promising strain in Phenylketonuria (PKU) in 2022 --

-- Conference call and webcast to discuss results at 8:30 AM --

CAMBRIDGE, Mass., Sept. 20, 2021 /PRNewswire/ -- Synlogic, Inc. (Nasdaq: SYBX), a clinical stage company bringing the transformative potential of synthetic biology to medicine, today announced positive data from clinical studies evaluating both SYNB1618 and SYNB1934, investigational Synthetic Biotic™ medicines for the treatment of phenylketonuria (PKU).

SYNB1618 demonstrated clinically meaningful reductions of phenylalanine (Phe) at several dose levels, across multiple time points, in an interim analysis of the Phase 2 SynPheny-1 study. SYNB1934, an optimized strain evolved from SYNB1618, demonstrated two-fold higher activity than SYNB1618 in a head-to-head Phase 1 study in healthy volunteers, as measured by biomarkers of Phe metabolism.

Synlogic intends to incorporate SYNB1934 into an arm of the Phase 2 SynPheny-1 trial with final results expected in the first half of 2022. Based on the favorable clinical data from the SYNB1618 and SYNB1934 programs available to date, the Company intends to initiate planning for a pivotal Phase 3 study for the most promising strain.

"The PKU program demonstrated clear proof of concept in this analysis, with SYNB1618 achieving a clinically meaningful reduction of phenylalanine in patients across multiple endpoints and time points," said Aoife Brennan, M.B. Ch.B., Synlogic's President and Chief Executive Officer. "Additionally, our second PKU candidate SYNB1934 provides greater potency, which will allow us to optimize the clinical profile to address the profound needs of patients with PKU."

"Together, these data provide strong support for the ability of Synthetic Biotic medicines to make a meaningful difference to patients. These events mark a major milestone for Synlogic's Synthetic Biotic platform. We look forward to completing our Phase 2 SynPheny-1 study and advancing the PKU program into a pivotal study," continued Dr. Brennan.

"In addition to our strong clinical results, we're highly encouraged by the predictive validity of our prospective biomarker driven modeling of therapeutic effect," said David Hava, Ph.D., Chief Scientific Officer. "Patient clinical data observed to date was consistent with our preclinical predictions of Phe metabolism by the strains. The ability to translationally model clinical activity enables rapid and effective strain optimization, which we have applied both to PKU and other inherited and acquired metabolic disorders."

Interim SYNB1618 Synpheny-1 Phase 2 Results

Synpheny-1 (NCT04534842) is an open-label, single arm Phase 2 study in patients with PKU. The study evaluated a dose-ramp regimen consisting of four dose levels of SYNB1618 over 15 days of treatment. The primary endpoint was reduction of the area under the curve (AUC) for plasma D5-phenylalanine (D5-Phe) after a meal challenge. Secondary endpoints include changes from baseline in fasting levels of plasma Phe at multiple timepoints, and incidence of treatment-emergent adverse events (TEAEs). Dietary intake of Phe was carefully managed during the study through individualized diet management plans.

The interim analysis included 8 patients. Clinical results demonstrated meaningful reductions of Phe, consistent with prospective biomarker-driven modeling. These results included:

- 20% reduction in fasting plasma Phe after 14 days of dosing, at a dose of 1e12 live cells;
  - Fasting plasma Phe level began to trend down after seven days of dose titration, at a dose up to 3e11 live cells, and was statistically significant at the 1e12 dose at day 14
- 40% reduction in labeled plasma D5-Phe after meal challenge at day 15, at a dose of 2e12 live cells; and
- Rebound of plasma Phe levels following cessation of dosing, confirming therapeutic effect

Safety and tolerability were consistent with prior studies, with no serious adverse events or systemic events of any kind. AEs were primarily GI related and mild to moderate in nature. There were no treatment drug related discontinuations.

SYNB1934 Phase 1 Results

SYNB1934 was evolved from SYNB1618 to potentially provide increased Phe lowering activity for patients living with PKU. Clinical studies of SYNB1934 were initiated following preclinical *in vivo* and *in vitro* studies demonstrating an approximately two-fold improvement in the ability of SYNB1934 to break down Phe compared to SYNB1618.

The Phase 1 multiple ascending dose study of SYNB1934 (NCT04984525) evaluated the safety, tolerability and Phe consumption activity of SYNB1934, including a head-to-head comparison with SYNB1618 in healthy volunteers using biomarkers of Phe consumption such as trans-cinnamic acid (TCA). Results included:

- Dose dependent increase in plasma TCA area under the curve;
- Two-fold higher activity level than SYNB1618 in a head-to-head comparison based on biomarkers of Phe consumption
- Safety and tolerability in cohorts 1 – 3 were similar to other Synthetic Biotic medicines, including SYNB1618, at equivalent doses. The most common adverse events were GI-related, mild to moderate in severity, and some events led to discontinuation of dosing
- Dosing continues in the dose escalation portion of the study and the maximum tolerated dose has not been reached

SYNB1934 clinical results were consistent with preclinical data and previously presented prospective biomarker driven modeling. The Company believes that the increased activity of SYNB1934, relative to SYNB1618, could provide the opportunity to optimize the clinical profile based on individual patient needs.

Next Steps

Synlogic intends to complete the SynPheny-1 study with a cohort of patients receiving SYNB1934 and anticipates final SynPheny-1 results in the first half of 2022.

Based on the clinical data from the SYNB1618 and SYNB1934 programs available to date, the Company intends to initiate planning for a pivotal Phase 3 study of the most promising strain.

Synlogic continues to evaluate Synthetic Biotic medicines for other metabolic diseases such as Enteric Hyperoxaluria, including development of predictive efficacy models. Preclinical and Phase 1A data suggest SYNB8802 has the potential to consume clinically meaningful levels of dietary oxalate in patients with disease. The Company is continuing to enroll Part B of the Phase 1 study of SYNB8802 and due to ongoing challenges presented by the COVID-19 pandemic, anticipates study data will be available in the first half of 2022.

Synlogic continues to advance preclinical programs targeting additional inherited and acquired metabolic indications. The company expects to file an IND for an additional metabolic indication in 2022.

Patients can learn more about the SynPheny-1 study (NCT04534842) by visiting https://pkuresearchstudy.com. More information about Synlogic's programs and pipeline can be found at https://www.synlogictx.com.

Conference Call & Webcast Information

Synlogic will host a conference call and live webcast at 8:30 a.m. ET today, Monday, September 20, 2021. To access the live webcast, please visit the "Event Calendar" page within the Investors and Media section of the Synlogic website. Investors may listen to the call by dialing +1 (844) 815-2882 from locations in the United States or +1 (213) 660-0926 from outside the United States. The conference ID number is 1154745. A replay will be available for 30 days on the Investors and Media section of the Synlogic website.

About Phenylketonuria

Phenylketonuria (PKU) is an inherited metabolic disease that manifests at birth and is marked by an inability to break down Phe, an amino acid commonly found in many foods. Left untreated, high levels of Phe become toxic and can lead to serious neurological and neuropsychological problems affecting the way a person thinks, feels, and acts. Due to the seriousness of these symptoms, infants are screened at birth in many countries to ensure early diagnosis and treatment to avoid intellectual disability and other complications.

About Synlogic

Synlogic™ is bringing the transformative potential of synthetic biology to medicine. With a premiere synthetic biology platform that leverages a reproducible, modular approach to microbial engineering, Synlogic designs Synthetic Biotic medicines that target validated underlying biology to treat disease in new ways. Synlogic's proprietary pipeline includes Synthetic Biotics for the treatment of metabolic disorders including Phenylketonuria (PKU) and Enteric Hyperoxaluria. The company is also building a portfolio of partner-able assets in immunology and oncology.

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," "estimate," "expect," "intend," "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 platform to develop therapeutics to address a wide range of diseases including: cancer, inborn errors of metabolism, metabolic diseases, and inflammatory and immune disorders; the future clinical development of Synthetic Biotic medicines; the approach Synlogic is taking to discover and develop novel therapeutics using synthetic biology; the expected timing of Synlogic's clinical trials and availability of clinical trial data. Actual results could differ materially from those contained in any forward-looking statement 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 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 could 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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