Synlogic Doses First Subject in Phase 1/2a Trial of SYNB1618 for Treatment of Phenylketonuria

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– Second Synthetic Biotic™ program to move into clinical studies in 2018 –
– SAD/MAD study will include healthy volunteers and expansion cohorts of adult patients with PKU –
– Interim data expected in 2018; full data in 2019 –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 18, 2018-- Synlogic (Nasdaq: SYBX), a clinical-stage company applying synthetic biology to probiotic bacteria to develop novel living medicines, announced that it has dosed the first subject in its Phase 1/2a clinical trial of SYNB1618. SYNB1618 is a Synthetic Biotic medicine being developed for the treatment of phenylketonuria (PKU), a genetic disorder that results in decreased metabolism and accumulation of the amino acid phenylalanine (Phe), which can lead to seizures and cognitive impairment if not appropriately managed. Patients living with PKU currently have limited treatment options and endure a very restrictive diet that is low in protein, the source of dietary Phe.

"We believe that SYNB1618 has the potential to provide PKU patients with an orally administered therapeutic option to help them maintain their blood Phe levels within the range recommended to prevent long-term complications," said Aoife Brennan, M.B., B.Ch., Synlogic's chief medical officer. "Our preclinical studies in mouse models of disease and healthy non-human primates demonstrate that, acting from the gut, SYNB1618 can metabolize Phe from the diet and the blood to lower overall blood Phe. These preclinical studies have provided quantitative biomarkers and have been used to design the Phase 1/2a trial."

"SYNB1618 is the second Synthetic Biotic medicine to enter clinical studies during the last year. This is a significant milestone for our therapeutic platform and supports our vision of developing a robust pipeline of novel therapeutics," said JC Gutiérrez-Ramos, Ph.D., Synlogic's president and chief executive officer. "Applying genetic control and metabolic engineering elements of our proprietary synthetic biology platform to a well characterized single probiotic strain has enabled us to develop Synthetic Biotic medicines with pharmacological potency and predictable biomarkers that allow us to establish dose responses, as well as reproducible manufacturing processes."

Synlogic's Synthetic Biotic medicines for the treatment of inborn errors of metabolism, such as PKU, are designed to function in the gastrointestinal tract to convert metabolites that can build up to toxic levels in the blood into harmless metabolites that can be excreted from the body. Elevated Phe levels are toxic to the brain and can have severe consequences. SYNB1618 is designed to consume Phe and convert it into metabolites, including trans-cinnamic acid in the blood which can be further metabolized in the liver and excreted as hippurate in the urine, providing potentially important biomarkers of SYNB1618's activity.

About Synlogic's Phase 1/2a Trial of SYNB1618 in Healthy Volunteers and Patients with PKU
This clinical trial is a single and multiple dose-escalation, randomized, double-blind, placebo-controlled study of orally administered SYNB1618 in healthy adult volunteers and adult subjects with PKU, designed to evaluate safety, tolerability, kinetics, and pharmacodynamics as well as exploratory end-points associated with the ability of SYNB1618 to metabolize Phe.

The study will evaluate SYNB1618 as follows:

Part 1: A single-ascending dose (SAD) study will be conducted in an inpatient setting over four days in healthy volunteers (HV) who will be evaluated in up to six dose cohorts (3 treated :1 placebo) to identify the maximum tolerated dose (MTD) within the single dose range studied. Up to 24 healthy subjects may be enrolled in this part of the study.

Following attainment of the MTD in HV, a SAD cohort of up to four subjects, previously diagnosed with PKU (≥18 years old with elevated Phe at baseline) will be enrolled and treated (3 treated:1 placebo).

Part 2: A multiple-ascending dose (MAD) study will be conducted in an inpatient setting over 10 days in HV evaluated in up to four cohorts (6 treated:2 placebo) and treated at doses that will not exceed the MTD from the SAD part of the study. This will identify the MTD of SYNB1618 within the multiple-dose range. Up to 32 healthy subjects may be enrolled in this part of the study. Once the highest MAD cohort and the SAD PKU cohort have been completed, a multiple-dose cohort of subjects previously diagnosed with PKU (≥18 years old with elevated Phe at baseline) will be evaluated. Up to 20 subjects with PKU may be enrolled and treated (12 treated:8 placebo) in the MAD PKU cohort.

Synlogic expects to report interim data from the SAD (Part 1) portion of this trial in 2018 and the full data in 2019. More information on this study will be posted on https://clinicaltrials.gov.

About Phenylketonuria
PKU is caused by a defect in the gene encoding phenylalanine hydroxylase (PAH), a liver enzyme that metabolizes Phe. Phe is an essential amino acid that enters the body as a component of dietary protein and can be toxic if it accumulates in the blood and brain. Current disease management of PKU involves strict dietary protein restriction with the consumption of Phe-free protein supplements. The only currently approved medication, Kuvan®, is indicated for a subgroup of patients and does not eliminate the need for ongoing dietary management. Life-long Phe control is challenging due to the highly restrictive nature of the diet and patients typically experience worsening neurological function depending on the severity of their genetic mutation and their treatment compliance. PKU is diagnosed at birth, and the National PKU Alliance estimates that there are currently 16,500 people living with the disorder in the U.S.

About Synthetic Biotic Medicines
Synlogic's innovative new class of Synthetic Biotic medicines leverages the tools and principles of synthetic biology to genetically engineer probiotic microbes to perform or deliver critical functions missing or damaged due to disease. The company's two lead programs, SYNB1020 and SYNB1618, target hyperammonemia as a result of liver damage or genetic disease, and phenylketonuria, respectively. Patients with these diseases are unable to break down commonly occurring by-products of digestion that then accumulate to toxic levels and cause serious health consequences. When delivered orally, Synthetic Biotic medicines can act from the gut to compensate for the dysfunctional metabolic pathway and have a systemic effect, with the potential to significantly improve symptoms of disease for affected patients. Synlogic has earlier-stage programs that apply the broad potential of its Synthetic Biotic platform in other disease areas, from inflammatory and immune disorders to cancer.

About Synlogic
Synlogic is pioneering the development of a novel class of living medicines, Synthetic Biotic medicines, based on its proprietary drug development platform. Synlogic's initial pipeline includes Synthetic Biotic medicines for the treatment of rare genetic diseases, such as urea cycle disorders (UCD) and phenylketonuria (PKU). In addition, the company is leveraging the broad potential of its platform to create Synthetic Biotic medicines for the treatment of more common diseases, including liver disease, inflammatory and immune disorders, and cancer. Synlogic is collaborating with AbbVie to develop Synthetic Biotic-based treatments for inflammatory bowel disease (IBD). For more information, please 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, 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 PKU, urea cycle disorders and other inborn errors of metabolism, hyperammonemia and other liver disorders, cancer, and inflammatory and immune disorders; the ability of SYNB1618 to lower blood phenylalanine in patients; the progress of clinical trials and the timing of data availability; the future clinical development of Synthetic Biotic medicines; the approach Synlogic is taking to discover and develop novel therapeutics using synthetic biology; the potential of Synlogic's technology to treat phenylketonuria and urea cycle disorders; and the advancement of our collaborations. 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 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 SEC. 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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