Synlogic Presents Data from Phase 1/2a Study of SYNB1618 at the Annual Symposium of the Society for the Study of Inborn Errors of Metabolism (SSIEM)

September 4, 2019

– Advancing clinical development of SYNB1618 as a novel therapy to potentially serve all patients with phenylketonuria –

– Synlogic has initiated a bridging study of a new solid formulation of SYNB1618 to inform dosing in future efficacy study –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 4, 2019-- Synlogic, Inc., (Nasdaq: SYBX), a clinical stage company applying synthetic biology to beneficial microbes to develop novel, living medicines, today announced presentation of the full clinical data set from healthy volunteers and patient cohorts of a randomized, double-blind, placebo-controlled Phase 1/2a study of SYNB1618, which is being developed as an oral therapy for the treatment of phenylketonuria (PKU). The data were presented by Jerry Vockley, M.D. Ph.D., Professor of Pediatrics and Chief of Medical Genetics, University of Pittsburgh, on September 4, 2019 at the annual symposium of the Society for the Study of Inborn Errors of Metabolism (SSIEM) in Rotterdam.

“Lifetime dietary management of PKU is effective but challenging for patients and there remains a significant unmet need for this population,” said Dr. Vockley, who was a principal investigator on Synlogic’s study. “Physicians, patients and families welcome the development of novel therapies like SYNB1618 that have the potential to impact the lives of all PKU patients.”

The study’s primary objectives were to evaluate safety and tolerability of an early liquid formulation of SYNB1618, as well as clearance of SYNB1618 from the gastrointestinal (GI) tract after cessation of dosing. Exploratory outcomes were related to the assessment of the pharmacodynamic effects of SYNB1618, including measurement of previously identified biomarkers related to SYNB1618’s engineered ability to consume phenylalanine (Phe).

“With this study, we have taken another step towards our goal of delivering a safe, oral therapy option for all patients with PKU regardless of age or disease type,” said Aoife Brennan, M.B., B.Ch., Synlogic’s president and chief executive officer. “These important data have informed advancement of SYNB1618 and, more broadly, have demonstrated the potential of our Synthetic Biotic development platform to deliver novel medicines designed to perform a therapeutic function.”

Synlogic’s Synthetic Biotic platform leverages the tools and principles of synthetic biology to engineer a non-pathogenic strain of *E. coli* (Nissle) to perform or deliver specific functions lost or damaged due to disease. SYNB1618, designed to function in the GI tract, has been engineered with two different mechanisms to consume Phe, an essential amino acid that can accumulate to harmful levels in patients with PKU with severe consequences. SYNB1618 is designed to metabolize Phe to harmless compounds including *trans*-cinnamic acid (TCA) in the blood which is further metabolized in the liver and excreted as hippurate (HA) in the urine. TCA and HA represent specific quantitative biomarkers of SYNB1618 activity as demonstrated by Synlogic’s preclinical data that were published in *Nature Biotechnology* and in data from healthy volunteers from the first part of this Phase 1/2a study. SYNB1618 is also designed to metabolize Phe to phenylpyruvate (PP) via a second enzyme mechanism, L-amino acid transaminase (LAAD). One of the downstream metabolites of LAAD activity is phenyl-lactic acid (PLA) which can be measured in the urine.

In summary:

- A statistically significant increase in biomarkers of SYNB1618 activity (TCA and HA) was observed in both healthy volunteers and PKU patients treated with SYNB1618, but not in subjects treated with placebo, indicating that SYNB1618 was able to carry out its designed function and consume Phe in the human GI tract.
- Equivalent biomarker production and tolerability were observed in both patients and healthy volunteers at a dose of 7 x 10^{10} colony forming units (CFU) supporting the evaluation of a solid oral formulation of SYNB1618 in a bridging study in healthy volunteers to inform dosing in a subsequent efficacy study in patients.
- Evidence of activity in the human GI tract of the second Phe-consuming function engineered into SYNB1618 (LAAD) was provided by data from healthy volunteers.
- There were no treatment-related serious adverse events (SAEs), treatment-emergent AEs were either mild or moderate in severity. Most were GI-related, mild and reversible.
- All subjects cleared the bacteria in the expected time frame. There was no evidence of colonization, and no subject required antibiotics.
- Blood Phe levels were measured in all PKU patients over the course of the study. However, the study was not designed or powered to demonstrate Phe lowering.

In addition to the presentation highlighting results of the Phase 1/2a study of SYNB1618, Synlogic presented a poster describing a mathematical model for the relationship of blood Phe lowering with decreasing Phe levels in the GI tract as a result of reduced dietary Phe intake. The model can be used to estimate the potential effects of Phe consumption by SYNB1618 on blood Phe lowering in PKU patients.

SYNB1618 Clinical Development Plans and Upcoming Milestones
Synlogic has developed a robust and reproducible process and manufactured a new solid formulation of SYNB1618 that maintains strain viability and activity. Synlogic is currently evaluating this new formulation in an ongoing bridging study in healthy volunteers. A solid oral formulation of SYNB1618 with improved quality attributes may enable dosing to higher activity in a larger out-patient efficacy study in patients. Synlogic expects to initiate the

SYNB1618 efficacy study in the first half of 2020.

About Phenylketonuria (PKU)
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. 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 approximately 16,500 people living with the disorder in the U.S.

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 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 lead program, SYNB1618, targets PKU. 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. 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 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, including statements regarding Synlogic's plans and expectations for the development of SYNB1618. 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: cancer, inborn errors of metabolism, 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; and 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 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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