Synlogic Doses First Patient in Phase 1b/2a Trial of SYNB1020 for Treatment of Hyperammonemia in Patients with Cirrhosis

April 2, 2018

– First clinical trial of a Synthetic Biotic ™Medicine in patients –

– Randomized, double-blind, placebo-controlled study evaluating safety and tolerability of SYNB1020 as primary endpoint; ammonia-lowering as secondary endpoint –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 2, 2018-- Synlogic (Nasdaq:SYBX), a clinical-stage company applying synthetic biology to probiotic bacteria to develop novel living medicines, announced that the first patient was dosed in its Phase 1b/2a clinical trial of SYNB1020. SYNB1020 is a Synthetic Biotic medicine being developed for the treatment of hyperammonemia, associated with cirrhosis and urea cycle disorders (UCDs), which can result in severe and life-threatening consequences for patients. This randomized, double-blind, placebo-controlled study is designed to evaluate the safety and tolerability of SYNB1020, as well as its ability to lower blood-ammonia levels in patients with cirrhosis and elevated blood ammonia.

"Our recently reported Phase 1 trial of SYNB1020 demonstrated that this Synthetic Biotic medicine was well tolerated and provided a dose-dependent proof of mechanism, functioning as designed in healthy volunteers. We look forward to evaluating the safety, tolerability and therapeutic potential of SYNB1020 in patients with liver disease who have developed cirrhosis," said Aoife Brennan, M.B., B.Ch., Synlogic's chief medical officer. "There is unmet medical need for additional treatment options for patients with chronic liver disease and we are excited by the potential of SYNB1020 in this indication."

Synthetic Biotic therapies 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 blood ammonia levels are toxic to the brain and can have severe consequences, including neurologic crises requiring hospitalization and resulting in irreversible cognitive damage and death. SYNB1020 is designed to consume ammonia and convert it to arginine, an amino acid.

About Synlogic's Phase 1b/2a Trial of SYNB1020 in Patients with Cirrhosis

This Phase 1b/2a study has two parts:

First, an initial sentinel open-label cohort of subjects with cirrhosis and a Model for End-Stage Liver Disease (MELD) score < 12 will receive orally administered SYNB1020 (5×10^{11} CFU TID) for six days. Subjects will be admitted to an inpatient facility for a run-in diet, baseline assessments, safety monitoring, and collection of blood, urine, and fecal samples for the evaluation of safety, tolerability, pharmacokinetics and pharmacodynamics of treatment. Once safety and tolerability have been established in these subjects, enrollment will be opened to subjects in Part 2.

Part 2 of the trial comprises a randomized, double-blinded, placebo-controlled study in patients with cirrhosis and hyperammonemia. Eligible subjects will be admitted to an inpatient facility for a run-in diet and 24-hour ammonia profile, and those with an elevated ammonia level will proceed with randomization and receive either placebo or orally administered SYNB1020 (5×10^{11} CFU TID) for six days. The primary endpoint of the study is safety and tolerability. In addition, the study will evaluate the effect of SYNB1020 administration on plasma ammonia levels as well as other exploratory endpoints.

Synlogic expects to report top-line data from this trial by year-end 2018. More information on this study can be found at https://clinicaltrials.gov under the study ID NCT03447730.

About Hyperammonemia

Hyperammonemia is a metabolic condition characterized by an excess of ammonia in the blood. In healthy individuals, ammonia is primarily produced in the intestine as a byproduct of protein metabolism and microbial degradation of nitrogen-containing compounds. Ammonia is then converted to urea in the liver and is excreted in urine. However, if the liver's ability to convert ammonia to urea is compromised, either due to a genetic defect such as UCDs or acquired liver disease that leads to cirrhosis, ammonia accumulates in the blood. Elevated blood ammonia levels are toxic to the brain and can have severe consequences, including neurologic crises requiring hospitalization, irreversible cognitive damage and death.

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 hyperammonemia and other liver disorders, inborn errors of metabolism, cancer, and inflammatory and immune disorders; the ability of SYNB1020 to lower ammonia 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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