Synlogic Presents Clinical and Preclinical Data from Synthetic Biotic™ Medicine Programs for Treatment of Inborn Errors of Metabolism at Annual Meeting of The Society for Inherited Metabolic Disorders

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– Expanded clinical data set from Phase 1 study confirms proof of mechanism and supports continued development of SYNB1020 for treatment of hyperammonemia –

– A Phase 1b / 2a clinical trial to further evaluate SYNB1020 is open and screening patients –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 12, 2018-- Synlogic (Nasdaq:SYBX), a clinical-stage company applying synthetic biology to probiotic bacteria to develop novel living medicines, announced the presentation of the expanded clinical data set from its first-in-human Phase 1 study of SYNB1020, a Synthetic Biotic medicine being developed for the treatment of hyperammonemia associated with urea cycle disorders (UCDs) and cirrhosis. In addition, new preclinical data from this program and from a second Synthetic Biotic medicine, SYNB1618, being developed for the treatment of phenylketonuria (PKU), were presented at the 40th Annual Meeting of the Society for Inherited Metabolic Disorders (SIMD) which is being held in San Diego from March 11 to 14, 2018.

"Our first clinical trial was a major milestone for Synlogic, providing proof-of-mechanism of a new modality of cell-based therapies which uses engineered probiotic bacteria to treat disease," said J.C. Gutiérrez-Ramos, Ph.D., Synlogic's president and chief executive officer. "In contrast to other cell-based therapies, we are developing our Synthetic Biotic medicines to have predictable drug qualities, with engineered potency and dose-dependent activity. The data presented at SIMD demonstrate we have established these standards in our lead programs and we look forward to continuing to evaluate the broad potential of our Synthetic Biotic platform."

In its initial programs, Synlogic is developing Synthetic Biotic medicines for the treatment of inborn errors of metabolism (IEMs) such as UCDs and PKU. These therapies are designed to function in the gastrointestinal (GI) tract to convert metabolites such as ammonia and phenylalanine (Phe) that build up to toxic levels in the blood of patients with UCD and PKU, respectively, to harmless metabolites that can be excreted from the body. Synlogic has initiated a Phase 1b/2a clinical trial of SYNB1020, in patients with cirrhosis and elevated ammonia, designed to evaluate safety and tolerability as well as lowering of blood ammonia levels, an important endpoint in this patient population.

"Clinical data presented at SIMD demonstrate that SYNB1020 is well-tolerated, rapidly cleared following discontinuation of dosing, and functions as designed in humans, supporting its continued development for the treatment of patients with hyperammonemia," said Aoife Brennan, M.B., B.Ch., Synlogic's chief medical officer. "Additionally, we are pleased to report our Phase 1b / 2a study designed to evaluate safety and tolerability as well as lowering of blood ammonia in patients with liver cirrhosis, is now open and screening subjects. In the first half of this year, we also expect to initiate a clinical trial of SYNB1618 for the treatment of PKU, based on preclinical data presented at SIMD, and anticipate we will have data from both clinical studies by the end of 2018."

Summary of Data from the Phase 1 Study of SYNB1020 in Healthy Volunteers
Data from Synlogic's Phase 1 study in healthy volunteers were presented at SMID and demonstrated that SYNB1020, a probiotic engineered to convert ammonia into an essential amino acid arginine (Arg), was safe and well tolerated in 52 healthy volunteers up to a maximum tolerated daily dose of $1.5x10^{12}$ CFU for 14 days. There were no serious adverse events (SAEs), AEs observed at higher doses in the single ascending dose stage of the study designed to establish the maximum tolerated dose, were mild to moderate nausea and vomiting which resolved rapidly. As designed, the bacteria did not colonize and all subjects cleared SYNB1020 from their systems within two weeks of the final dose. Blood ammonia levels were in the normal range at baseline and, as expected in healthy individuals who maintain tight control over ammonia levels, there was no change in this end-point over the course of the study. In the MAD component of the Phase 1 study, a tracer study was undertaken using orally administered ^{15}N ammonium chloride, a substrate for SYNB1020. This revealed a dose-dependent relationship between administration of SYNB1020 and change in plasma and urinary nitrate, a terminal product of Arg degradation, compared to baseline that was statistically significant in the highest dose cohort compared to placebo. In addition, a dose dependent relationship was observed in total urinary nitrate. These mechanistic data demonstrate that the strain was functioning as designed in humans.

About Synlogic's Phase 1b / 2a Study of SYNB1020 in Patients with Cirrhosis
Synlogic has recently initiated a Phase 1b/2a clinical study in patients with cirrhosis and elevated blood ammonia that is designed to evaluate safety and tolerability as well as ammonia lowering, an end-point that has been closely related to clinical outcome in prior studies in this patient population.

The study has two parts: an initial sentinel open-label cohort of subjects with cirrhosis and a MELD (Model for End-Stage Liver Disease) 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 evaluation of safety, tolerability, and pharmacokinetic and pharmacodynamic evaluations 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-blind, 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 24-hour ammonia AUC 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. More information on this study can be found at www.clinicaltrials.gov under the study ID NCT03447730.

Summary of Preclinical Data Supporting the SYNB1020 Program
SYNB1020 is an engineered probiotic designed to function in the GI tract to convert toxic ammonia into arginine, an essential amino acid. Data presented at SMID demonstrated that in a mouse model of chronic hyperammonemia a dose-dependent lowering of plasma ammonia was observed in SYNB1020 treated mice that corresponded to improved survival in animals that were made hyperammonemic on a high protein diet.

SYNB1020 activity was also demonstrated using a modified version of the Synthetic Biotic strain that had been engineered to further convert L-arginine into D-arginine, a related but distinct form of the amino acid that cannot be metabolized in mammalian cells and is excreted in the urine. This allows the duration of strain activity to be followed *in vivo*. D-arginine was measured in urine and plasma in non-human primates (NHPs). The data demonstrated that the Synthetic Biotic medicine was active over the six-hour sampling period in both NHPs and mice. As seen in the Phase I human study, an elevation in urinary nitrate was observed in NHPs dosed with SYNB1020. Clearance of SYNB1020 was assessed in both mouse and NHP. SYNB1020 was detectable in feces of both species during dosing and was rapidly cleared (within 7 days) following cessation of dosing, consistent with a non-colonizing probiotic strain.

Summary of Preclinical Data Supporting the SYNB1618 Program
SYNB1618 is an engineered probiotic designed to function in the GI tract to convert Phe into trans-cinnamic acid (TCA), a harmless metabolite that can be further metabolized in the liver to generate hippuric acid (HA) which is excreted in the urine. Levels of plasma TCA and urinary HA provide useful biomarkers for the activity of SYNB1618. The data presented at SIMD demonstrate that in a mouse model of PKU, administration of SYNB1618 resulted in a decrease in blood Phe concentration compared to mice receiving a control strain. SYNB1618 was effective at lowering blood Phe from both the diet and from systemic Phe that is actively recirculated into the GI tract. Blood Phe lowering correlated with HA production in the urine of SYNB1618-treated mice. SYNB1618 also inhibited elevation of blood Phe in healthy NHPs following an oral Phe dietary challenge and demonstrated drug-like dose response properties. This work supports the future development of SYNB1618 as a treatment for patients with PKU.

About Hyperammonemia
Hyperammonemia is a metabolic condition characterized by an excess of ammonia in the blood, which can result in severe and life-threatening consequences for patients. In healthy individuals, ammonia is primarily produced in the intestine as a byproduct of protein digestion 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, 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 Phenylketonuria (PKU)
PKU is a rare IEM caused by a genetic defect in phenylalanine hydroxylase ("PAH"), the enzyme used to break down Phe leading to accumulation of Phe in the blood and brain, where it is neurotoxic and can lead to neurological deficits and even death. Despite recommendations supporting life-long control of Phe levels, compliance is challenging due to the highly restrictive nature of the diet, putting patients at risk for cognitive and psychiatric disease and supporting the need for novel treatment approaches.

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 target a group of rare metabolic diseases – inborn errors of metabolism (IEM). Patients with these diseases are born with a faulty gene, inhibiting the body's ability to break down commonly occurring by-products of digestion that then accumulate to toxic levels and cause serious health consequences. When delivered orally, these medicines can act from the gut to compensate for the dysfunctional metabolic pathway and have a systemic effect. Synthetic Biotic medicines are designed to reduce toxic metabolites associated with specific metabolic diseases and have the potential to significantly improve symptoms of disease for affected patients.

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 current 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: inborn errors of metabolism, hyperammonemia and other liver disorders, cancer, 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 potential of Synlogic's technology to treat urea cycle disorders and phenylketonuria; 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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