Science Translational Medicine Publishes First-in-Human Clinical Data and Supporting Preclinical Data for SYNB1020, Synlogic's Synthetic Biotic™ Medicine in Development as a Potential Treatment for Hyperammonemia

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–Phase 1 clinical trial to evaluate safety and tolerability of SYNB1020 in healthy volunteers demonstrated safety, clearance and proof of mechanism–

– Data from ongoing Phase 1b/2a clinical trial in patients with cirrhosis and elevated ammonia expected mid-2019 –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 16, 2019-- Synlogic, Inc., (Nasdaq: SYBX) a clinical stage company applying synthetic biology to beneficial microbes to develop novel, living medicines, today announced the publication in *Science Translational Medicine* of clinical data from its Phase 1 clinical study in healthy volunteers and supporting preclinical data from its investigational Synthetic Biotic candidate, SYNB1020. The data support the continued development of SYNB1020 which is currently being evaluated in a Phase 1b/2a clinical trial in patients with cirrhosis and elevated blood ammonia.

"These data demonstrate that we can engineer bacteria to carry out a specific function, deliver them to humans and that they perform as designed," said Paul Miller, Ph.D., Synlogic's chief scientific officer. "Ongoing manufacturing and formulation development work at Synlogic gives us confidence we will be able to scale and formulate our Synthetic biotic medicines to meet multiple needs in the marketplace for living medicines. The compelling data in this publication encouraged us to advance SYNB1020 into additional clinical studies and we look forward to presenting data from our trial, designed to evaluate the potential of SYNB1020 to lower ammonia in patients with cirrhosis, in mid-2019."

Long-standing evidence supports the importance of the gastro-intestinal (GI) tract as the major source of ammonia in the systemic circulation. The current standard-of-care for conditions that result in hyperammonemia, including hepatic encephalopathy stemming from liver damage and urea cycle disorders (UCDs), which are genetic diseases, employ orally administered approaches such as antibiotics, laxatives and ammonia scavengers. However, each of these agents has limitations resulting in a need for additional therapies to manage hyperammonemia.

The publication titled, "An Engineered *E. coli* Nissle Improves Hyperammonemia and Survival in Mice and Shows Dose-dependent Exposure in Healthy Humans," describes the engineering and characterization of SYNB1020, preclinical studies of SYNB1020 in mouse models of hyperammonemia (OTC *spf*^{ash} and the TAA model), safety in healthy mice and non-human primates (NHPs) as well as clinical data from Synlogic's Phase 1 study of SYNB1020 in healthy volunteers.

Synlogic's Synthetic Biotic platform leverages the tools and principles of synthetic biology to engineer a strain of non-pathogenic bacteria (*E. coli* Nissle) to perform or deliver specific functions lost or damaged due to disease. Orally administered SYNB1020 has been designed to respond to the low oxygen environment of the large intestine to convert ammonia into arginine, an amino acid. In addition, Synthetic Biotic medicines are engineered to limit their replication after manufacturing so that they do not grow or colonize the GI tract.

The preclinical data demonstrate that orally administered SYNB1020 is well tolerated in mice and NHPs, clears rapidly from the GI tract following completion of dosing and is not found in tissues outside the GI tract. When OTC *spf*^{ash} mice, a model of a urea cycle disorder (UCD), were fed a high protein diet to increase their blood ammonia levels, those that were orally dosed with SYNB1020 demonstrated lower blood ammonia and increased survival compared to mice that received heat-killed, inactive SYNB1020. Similar data were obtained in a mouse model of liver damage (TAA model).

The clinical data from Synlogic's Phase 1 clinical study demonstrate that in healthy volunteers, orally administered SYNB1020 was safe, well tolerated, at daily doses up to 1.5 x10^{12} colony forming units, and cleared from the gastrointestinal tract within two weeks. In addition, dose-dependent elevation in plasma and urine of nitrate, a biomarker of SYNB1020 activity, was observed in healthy volunteers treated with SYNB1020 but not in those treated with placebo, demonstrating proof of mechanism.

Synlogic is currently evaluating SYNB1020 in a Phase 1b/2a clinical trial in patients with cirrhosis and elevated blood ammonia for the management of systemic ammonia levels and expects to report data in mid-2019. More information about Synlogic's Phase 1b/2a clinical trial 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. 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 a urea cycle disorder (UCD) 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 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 beneficial microbes to perform or deliver critical functions missing or damaged due to disease. Synthetic Biotic medicines are designed to act locally and have a systemic effect to address disease in

patients. Synlogic's two lead programs, SYNB1020 and SYNB1618, are orally administered and target hyperammonemia as a result of liver damage or genetic disease, and phenylketonuria, respectively. Synlogic is also developing SYNB1891 as an intratumorally-administered Synthetic Biotic medicine for the treatment of cancer. In addition, the company is leveraging the broad potential of its platform to create additional Synthetic Biotic medicines for the treatment of liver disease, as well as inflammatory and immune disorders including Synlogic's collaboration 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: cancer, rare metabolic diseases, liver disease, 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 cancer, hyperammonemia, and phenylketonuria. 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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