Synlogic™ Doses First Subject in Phase 1 Trial of Novel Class of Synthetic Biotic™ Medicines

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Healthy volunteers study initiated for SYNB1020, a Synthetic Biotic™ medicine for the treatment of hyperammonemia

Cambridge, Mass, June 19, 2017 – Synlogic™ has dosed the first subject in a Phase 1 healthy volunteers study designed to assess the safety and tolerability of its lead compound, SYNB1020. SYNB1020 is an investigational Synthetic Biotic™ medicine intended as an oral treatment for hyperammonemia in diseases such as urea cycle disorders (UCD) and hepatic encephalopathy (HE), which are both associated with serious health consequences. SYNB1020 is the first in a novel class of living medicines under development by Synlogic. Synthetic Biotic medicines are generated using the company's proprietary technology platform, leveraging synthetic biology to genetically reprogram probiotic bacteria to perform critical functions or deliver therapeutic factors that compensate for those missing or damaged due to disease.

"The dosing of our first subject with our lead Synthetic Biotic medicine, SYNB1020, represents a significant milestone, not only for the program, but for the advancement of an entirely new class of living medicines," said Jose Carlos Gutierrez-Ramos, Ph.D., president and chief executive officer of Synlogic. "SYNB1020 has been designed to deliver a complementary metabolic pathway in the gut with the intended consequence of removing excess ammonia in the blood, essentially 'replacing' what a patient cannot do with his or her liver. We believe this novel approach could change the treatment paradigm for patients suffering from these devastating conditions."

SYNB1020 is the first Synthetic Biotic candidate, developed using Synlogic's technology platform, to enter the clinic. The data obtained from the Phase 1 study will inform future clinical trials of SYNB1020 as well as other investigational candidates in the company's portfolio generated by the platform. Pending the success of this first study in healthy volunteers with SYNB1020, Synlogic plans to initiate two additional clinical trials with the investigational candidate, by mid-2018, in symptomatic patients with urea cycle disorders (UCD) and hepatic encephalopathy (HE), both diseases where patients experience elevated and toxic ammonia levels. In the first half of 2018, the company also plans to initiate a clinical trial with SYNB1618, a Synthetic Biotic medicine designed to treat phenylketonuria (PKU), which is caused by defective metabolism of the amino acid phenylalanine.

About the Phase 1 Healthy Volunteers Study:

This Phase 1, dose-escalating, randomized, double-blinded study will evaluate SYNB1020 in placebo-controlled cohorts, enrolling approximately 50 subjects across two study parts. The first part will investigate a single-ascending dose (SAD) in healthy volunteer male and female subjects evaluated in several dose cohorts to identify the maximum tolerated dose (MTD) within the single dose-range studied. Subsequently, multiple-ascending doses (MAD) will be studied in an inpatient setting in healthy volunteer male and female subjects evaluated in several dose cohorts at doses that were proven tolerable in the SAD part of the study.

The primary outcome measures will evaluate the safety and tolerability of SYNB1020 by assessing nature and frequency of adverse events (AEs), laboratory assessments, and electrocardiogram (ECG). Secondary measures will investigate the gastrointestinal (GI) tolerability and the kinetics of SYNB1020

More information about this study including inclusion and exclusion criteria can be found on clinicaltrials.gov(Study ID number: NCT03179878).

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 the body's metabolism of dietary protein. Ammonia is then converted to urea in the liver and is excreted in urine. However, in urea cycle disorders (UCDs) and hepatic encephalopathy (HE) patients, the liver's ability to convert ammonia is reduced, either due to a genetic defect or acquired liver cirrhosis, respectively. As a result, ammonia begins to accumulate to toxic levels and eventually reaches the brain, where it acts as a neurotoxin. This toxicity can cause a number of 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 reengineer beneficial, 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 clear toxic metabolites associated with specific metabolic diseases and promise to significantly improve the quality of life for affected patients.

About Synlogic™

Synlogic™ is pioneering the development of a novel class of living Synthetic Biotic™ medicines based on its proprietary drug discovery and development platform. Synlogic's initial pipeline includes Synthetic Biotic medicines for the treatment of rare genetic diseases, such as Urea Cycle Disorder (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 other diseases, such as 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 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, the future clinical development of SYNB1020 and its prospects as a potential treatment for hyperammonemia and the future development of other product candidates, such as SYNB1618. 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.

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