Synlogic Reports Positive Top-Line Phase 1 Data Demonstrating Safety and Tolerability and Proof of Mechanism in Healthy Volunteers for SYNB1020, a Synthetic BioticTM Medicine for the Treatment of Hyperammonemia

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- SYNB1020 Oral Treatment Resulted in a Significant Dose-Dependent Effect on a Plasma Nitrogen Endpoint Demonstrating Mechanistic Activity -

- Data Support Initiation of Two Phase 1b/2a Studies in 2018 -

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 8, 2017-- Synlogic, Inc.,(Nasdaq:SYBX) a clinical-stage drug discovery and development company applying synthetic biology to probiotics to develop novel Synthetic Biotic medicines, today announced positive top-line clinical data from its Phase 1 placebo-controlled single (SAD) and multiple ascending dose (MAD) clinical trial of SYNB1020 in healthy volunteers. The trial successfully met the primary objectives demonstrating safety and tolerability in healthy volunteers and identifying the maximum tolerated dose. Furthermore, proof of mechanism was demonstrated by a clear signal in a plasma nitrogen endpoint.

SYNB1020, is a novel, first-in-class, Synthetic Biotic medicine that is orally delivered and designed to treat elevated blood ammonia levels, or hyperammonemia, in genetic urea cycle disorders (UCD) or in chronic liver disease

"The positive data from our Phase 1 study in healthy volunteers, demonstrates that SYNB1020 was well-tolerated and had a statistically significant dose-dependent effect on the level of a nitrogen endpoint, providing evidence to support its mechanism of action," said Aoife Brennan, M.B., B.Ch., Synlogic's chief medical officer. "These data support the hypothesis that SYNB1020 treatment may provide clinical benefit in patients with UCDs or liver disease, and will inform dose selection in our planned Phase 1b/2a study of SYNB1020 in patients, which we expect to begin in the first half of 2018."

"This first-in-human study represents a significant milestone for our new class of Synthetic Biotic medicines and demonstrates that they can operate from the gastrointestinal tract to metabolize systemic toxins," said JC Gutiérrez-Ramos, Ph.D., Synlogic's president and chief executive officer. "We look forward to evaluating SYNB1020 in patients, and to moving our second program, SYNB1618 for the treatment of phenylketonuria into clinical trials in 2018.

SYNB1020 was safe and well tolerated in subjects in multiple ascending dose cohorts who received total daily doses of up to $1.5x10^{12}$ CFU for 14 days. There have been no serious adverse events (SAEs), and no cases of infection with the bacteria in this study. While the study is ongoing, there is no evidence of colonization by SYNB1020 as all subjects who have completed follow-up have cleared the bacteria from their systems within the expected timeframe.

In the MAD component of the Phase 1 study, daily dosing of SYNB1020 over 14 days in healthy volunteers enabled identification of a dose-response relationship between SYNB1020 oral administration and changes in a nitrogen endpoint in plasma which was found to be statistically significant in the highest dose cohort compared to placebo. In addition, viability and evidence of mechanistic activity of the Synthetic Biotic was demonstrated in feces of subjects who received SYNB1020, but not in control subjects. As expected, SYNB1020 did not lower blood ammonia levels in these healthy individuals who had normal blood ammonia levels at baseline. Collectively, the data support the hypothesis that SYNB1020 treatment may enable metabolism of potentially neurotoxic blood levels of ammonia in patients with hyperammonemia stemming from UCDs or liver damage.

About the SYNB1020 Phase 1 Study

The Phase 1 study was a randomized, double-blind, placebo-controlled trial of orally administered SYNB1020 evaluating ascending doses each administered on a single day and multiple ascending doses administered over 14 days. The primary objective of the studies was to assess safety and tolerability of SYNB1020 in healthy volunteers. Secondary objectives were to characterize the microbial kinetics of SYNB1020 in feces as measured by qPCR and gastrointestinal tolerability assessed by the Gastrointestinal Symptom Rating Scale. Exploratory endpoints were designed to evaluate the pharmacodynamic effects of SYNB1020, including measurements of blood ammonia levels and other related biomarkers.

The results are from 52 healthy volunteers who were dosed orally with either SYNB1020 or placebo (ratio three to one), which includes 28 from 7 cohorts of the SAD study and 24 subjects from 3 cohorts of the MAD study. Complete safety results from the SAD and MAD Phase 1 study demonstrate that SYNB1020 was well tolerated at total daily doses up to $1.5x10^{12}$ CFU for 14 days. Higher doses were associated with mild to moderate gastrointestinal symptoms, mainly nausea and vomiting. The observed dose-dependent changes in a plasma nitrogen end-point are consistent with SYNB1020's mechanism of activity. SYNB1020 is genetically programmed to convert ammonia, a product of protein degradation, which can be toxic at high levels, into arginine, a beneficial amino acid.

As expected, based on previous clinical observations with the un-engineered probiotic and preclinical studies, subjects cleared SYNB1020 within the expected timeframe. Eight subjects in the MAD portion of the study continue to be followed for clearance of SYNB1020.

SAD Phase 1 Results

In the SAD study, seven cohorts treated with total daily doses of SYNB1020 ranging from $2x10^{9}$ to $6x10^{12}$ CFU were tested against placebo in a three to one ratio in a total of 28 healthy volunteers. Subjects received a single dose or three doses on a single day. The maximum tolerated total daily dose was 1.5×10^{12}CFU. There were no SAEs reported, with all AEs being mild to moderate, the most common being nausea and vomiting at the highest doses. Three subjects at the highest dose cohorts discontinued dosing.

MAD Phase 1 Results

All three cohorts reported data from a total 24 healthy volunteers dosed three times per day with SYNB1020 at total daily doses of up to $1.5x10^{12}$ CFU for 14 days or with placebo (three to one ratio). No SAEs were reported, all AEs occurred during the first week of dosing, were mild, and nausea and vomiting were most

common. One subject at the highest dose cohort discontinued dosing. A dose-responsive nitrogen endpoint was identified in blood which was found to be statistically significant in the highest dose cohort compared to placebo. While enrollment and treatment have been completed, subjects enrolled in the highest dose cohort continue to be monitored for clearance of SYNB1020.

SYNB1020 Clinical Development Plans and Upcoming Milestones

Synlogic plans to initiate a Phase 1b/2a study of SYNB1020 in patients with liver cirrhosis and elevated ammonia in the first half of 2018 and a second Phase 1b/2a study in patients with UCDs. Dosing will be determined based on the findings from MAD portion of this Phase 1 study in healthy volunteers. The company expects to provide final data from this Phase 1 study at an appropriate clinical meeting in 2018.

About Synthetic Biotic Medicines and SYNB1020

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 clear toxic metabolites associated with specific metabolic diseases and have the potential to significantly improve symptoms of disease for affected patients. SYNB1020 is genetically programmed to convert ammonia, a product of protein degradation which can be toxic at high levels, into arginine, a beneficial amino acid.

About Synlogic

Synlogic is pioneering the development of a novel class of living 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: inborn errors of metabolism, liver disease, inflammatory and immune disorders, and cancer; 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 hyperammonemia; the expected timing of initiation of Synlogic's anticipated clinical trials and that data from additional studies will demonstrate efficacy of SYNB1020 for the treatment of hyperammonemia. 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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