



Synlogic Reports Positive Top-line Data from Phase 1/2a Study of SYN1618 in Patients with Phenylketonuria and Guides to Next Phase of Development

July 15, 2019

– Data demonstrate statistically significant biomarker activity at well-tolerated dose in PKU patients –

– Plan to initiate bridging study with new oral solid formulation in Q3 2019 –

– Conference call and webcast today, July 15, at 8:00 a.m. ET –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jul. 15, 2019--

[Synlogic, Inc.](#) (Nasdaq: SYBX), a clinical stage company developing a novel class of Synthetic Biotic™ therapeutics, today announced positive top-line clinical data from patient cohorts of a randomized, double-blind, placebo-controlled Phase 1/2a study of SYN1618, which is being developed for the treatment of phenylketonuria (PKU). The study's primary objectives were to evaluate safety and tolerability of an early liquid formulation. Exploratory outcomes were related to the assessment of the pharmacodynamic effects of SYN1618, including measurement of previously identified biomarkers related to SYN1618's engineered ability to consume phenylalanine (Phe).

A statistically significant increase in biomarkers of SYN1618 activity was observed in SYN1618-treated subjects but not in those treated with placebo. The full data set from the Phase 1/2a study will be discussed in an oral presentation at the upcoming annual symposium of the Society for the Study of Inborn Errors of Metabolism (SSIEM) to be held in Rotterdam, September 3-6, 2019.

"These data in PKU patients demonstrate that SYN1618 was well-tolerated by patients and provide a clear path forward for the program. Together with the biomarker data from the healthy volunteer cohorts, we have built a dose-response model that demonstrates SYN1618's potential to achieve clinically meaningful reduction of blood phenylalanine levels in patients with PKU" said Aoife Brennan, M.B., B.Ch., Synlogic's president and chief executive officer. "This important milestone demonstrates the potential of our Synthetic Biotic development platform in patients and brings us a step closer to our goal of treating all PKU patients, regardless of age or disease type."

SYN1618 Clinical Development Plans and Upcoming Milestones

Synlogic has regulatory alignment for plans to initiate a randomized, double-blind, placebo controlled bridging study of a new solid oral formulation of SYN1618 in healthy volunteers. In this bridging study, Synlogic plans to select optimal doses of SYN1618 for an efficacy study in patients with PKU designed to evaluate blood Phe-lowering. Synlogic has developed a [robust and reproducible process](#) and manufactured a new solid formulation of SYN1618 that maintains strain viability and activity. The solid oral formulation with improved quality attributes may enable dosing to higher activity. In addition, the convenience of a solid SYN1618 formulation enables a larger out-patient efficacy study in patients. Synlogic expects to initiate the SYN1618 efficacy study in the first half of 2020.

About the Phase 1/2a Trial Design

Synlogic's Phase 1/2a trial was a randomized, double-blind, placebo-controlled study of an orally administered early liquid formulation of SYN1618. The study had two parts; the first evaluated ascending doses of SYN1618 or placebo administered on a single day and multiple ascending doses administered over seven days in healthy volunteers (HV). The second part evaluated SYN1618 as a single dose and as multiple doses in patients with PKU. The study's primary objectives were to evaluate safety and tolerability of SYN1618. Exploratory endpoints assessed the pharmacodynamic effects of SYN1618, including measurement of biomarkers related to SYN1618's engineered ability to consume Phe. The Phase 1/2a study was not designed or powered to measure Phe-lowering in SYN1618-treated subjects.

The results of the HV part of this study were reported in [September 2018](#). These data demonstrated that SYN1618 was safe and established a dose that was well-tolerated for evaluation in patients with PKU. The secondary objective was to characterize the microbial kinetics of SYN1618 in feces, as measured by qPCR. Exploratory outcomes were related to the assessment of the pharmacodynamic effects of SYN1618, including measurement of biomarkers related to SYN1618 activity and, importantly, confirming that both pathways engineered to consume Phe are operational within the human GI tract.

Conference Call & Webcast Information

Synlogic will host a conference call and live webcast at 8:00 a.m. ET on July 15, 2019. To access the live webcast, please visit the "[Event Calendar](#)" page within the Investors and Media section of the Synlogic website at <https://investor.synlogictx.com/>. Alternatively, investors may listen to the call by dialing +1 (844) 815-2882 from locations in the United States or +1 (213) 660-0926 from outside the United States. The conference ID number is 9037619. A replay of the webcast will be available on the Synlogic website for 90 days following the call.

About Phenylketonuria (PKU)

PKU is caused by a defect in the gene encoding phenylalanine hydroxylase (PAH), a liver enzyme that metabolizes Phe. Phe is an essential amino acid that enters the body as a component of dietary protein and can be toxic if it accumulates in the blood and brain. Current disease management of PKU involves strict dietary protein restriction with the consumption of Phe-free protein supplements. Life-long Phe control is challenging due to the

highly restrictive nature of the diet and patients typically experience worsening neurological function depending on the severity of their genetic mutation and their treatment compliance. PKU is diagnosed at birth, and the National PKU Alliance estimates that there are currently approximately 16,500 people living with the disorder in the U.S.

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 probiotic microbes to perform or deliver critical functions missing or damaged due to disease. The company's two lead programs, SYN1020 and SYN1618, target hyperammonemia as a result of liver damage or genetic disease, and PKU, respectively. 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. 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, including statements regarding Synlogic's plans and expectations for the development of SYN1618. 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, inborn errors of metabolism, 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; and the expected timing of Synlogic's clinical trials and availability of clinical trial data. 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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