# Synlogic Publishes Preclinical Data Supporting Development of SYNB1618, a Synthetic Biotic™ Medicine as a Potential Treatment for Phenylketonuria

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*– Preclinical studies published in Nature Biotechnology identify key biomarkers of SYNB1618 activity in healthy animals and disease models –*

*– Clinical data expected in 2018 from healthy volunteer cohorts of ongoing Phase 1/ 2a study of SYNB1618; data from patients with phenylketonuria (PKU) in 2019 –*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 13, 2018-- Synlogic, Inc., (Nasdaq: SYBX) a clinical stage company applying synthetic biology to probiotics to develop novel, living medicines, today announced the publication of data from preclinical studies of SYNB1618, the Company's Synthetic Biotic development program targeting PKU, in *Nature Biotechnology*.The data demonstrate that oral administration of SYNB1618 significantly reduced blood phenylalanine (Phe) levels, the key metabolite associated with PKU, in mouse models of PKU and resulted in dose-dependent pharmacodynamics in healthy non-human primates (NHPs).

The paper titled "Development of a synthetic live bacterial therapeutic for the human metabolic disease phenylketonuria" appears as an Advance Online Publication on *Nature Biotechnology's* website.

"These preclinical studies highlight the potential of our engineered Synthetic Biotic medicines to act with potency within the gut to normalize systemic levels of a toxic metabolite. In addition, in two species, we demonstrate dose-dependent production of biomarkers of activity for SYNB1618, which will be very useful in evaluating its efficacy in our ongoing clinical study in healthy volunteers and patients with PKU," said Paul Miller, Ph.D., Synlogic's chief scientific officer. "These data provide compelling evidence to support the continued development of our orally administered Synthetic Biotic medicine, SYNB1618, for the potential treatment of PKU."

Synlogic's Synthetic Biotic platform leverages the tools and principles of synthetic biology to engineer a strain of probiotic bacteria ( *E. coli* Nissle) to perform or deliver specific functions lost or damaged due to disease. SYNB1618 is designed to metabolize Phe and was engineered by inserting specific genetic circuits including a bacterial gene that encodes phenylalanine ammonia lyase (PAL). PAL is an enzyme that breaks down Phe to generate trans-cinnamic acid (TCA), which is converted to hippuric acid (HA) in the liver and excreted in urine. Thus, plasma TCA and urinary HA levels can serve as biomarkers of PAL and, therefore, of SYNB1618 activity *in vivo*.

The publication describes the engineering and characterization of SYNB1618, as well as preclinical studies of SYNB1618 in both a mouse model of PKU (*Pah* $^{enu2/enu2}$) and healthy NHPs that have a metabolism and gastrointestinal (GI) physiology more similar to humans. Synlogic scientists confirmed previously reported observations in rodents that Phe is abundant in the small intestine and derived from two sources, the diet and the blood. In both species, Phe re-enters the GI tract in the form of enzymes and secretions via a process known as enterorecirculation, supporting the feasibility of a GI-based approach for Phe consumption.

To monitor SYNB1618 activity *in vivo,* Synlogic scientists investigated the production of major SYNB1618-derived metabolites, including TCA and HA. Studies demonstrated that orally administered SYNB1618 resulted in a significant decrease in blood Phe levels independent of dietary protein intake in the PKU mouse model, and inhibited increases in serum Phe after an oral Phe challenge in healthy NHPs. In both species, SYNB1618 exhibited dose-responsive pharmacokinetics, as determined by production of urinary HA.

Synlogic is currently evaluating SYNB1618 in a Phase 1/2a clinical trial for the management of PKU and expects to report interim data from healthy volunteers in 2018 and full data, including cohorts of patients with PKU, in 2019. More information about Synlogic's Phase 1/2a clinical trial in healthy adult volunteers and patients with PKU can be found at https://clinicaltrials.gov under the study ID NCT03516487.

**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 and approved therapies of PKU involve strict dietary protein restriction with the consumption of Phe-free protein supplements, representing a significant need for additional treatments. 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 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, SYNB1020 and SYNB1618, 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. 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 and phenylketonuria; 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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Source: Synlogic, Inc.

Synlogic, Inc.
**MEDIA CONTACT:**
Courtney Heath, 617-872-2462
courtney@scientpr.com
or
**INVESTOR CONTACT:**
Elizabeth Wolffe, Ph.D., 617-207-5509
liz@synlogictx.com