Synlogic Publishes Papers in Nature Journals Demonstrating Proof-of-Mechanism and Potential of Synthetic Biotic Platform for the Treatment of Phenylketonuria (PKU)

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- Data show dose-responsive, non-saturated increases in gastrointestinal consumption of Phe in humans by SYNB1618 -
- SYNB1618 Phase 2 study in patients with PKU ongoing with proof-of-concept readout anticipated in 2H 2021 -
- Phase 1 study of SYNB1934, an evolved strain of SYNB1618 in the PKU portfolio, initiated -

CAMBRIDGE, Mass., July 22, 2021 /PRNewswire/ -- Synlogic, Inc. (Nasdaq: SYBX), a clinical stage company bringing the transformative potential of synthetic biology to medicine, announced today the publication of two papers in the journals Nature Metabolism and Communications Biology. The publications detail findings from a first-in-human study of investigational Synthetic Biotic™ medicine SYNB1618 and the development of a mechanistic model to predict the function of an engineered bacterial therapeutic in healthy volunteers and Phenylketonuria (PKU) patients. These data add to the growing body of scientific research demonstrating the therapeutic potential of Synthetic Biotic™ medicines for the treatment of PKU.

"Our orally administered Synthetic Biotic medicines are intended to address the needs of PKU patients of all ages and disease types through the consumption of phenylalanine (Phe) in the gastrointestinal tract. With two Phe-consuming strains now in the clinic, and a proof-of-concept readout in SYNB1618 anticipated in the second half of 2021, we look forward to advancing our PKU pipeline and developing a meaningful treatment for those living with PKU," said Aoife Brennan, M.B. Ch.B., Synlogic's President and Chief Executive Officer.

Key findings from the Nature Metabolism paper entitled, "Safety and pharmacodynamics of an engineered E. coli Nissle for the treatment of phenylketonuria: a first-in-human Phase 1/2a study":

- In this first-in-human study of a frozen liquid formulation of SYNB1618 in healthy volunteers and patients with PKU, SYNB1618 was safe and well tolerated, with no systemic toxicity and no evidence of colonization. SYNB1618 was cleared within four days of the last dose.
- Dose-responsive increases in strain-specific Phe metabolites in plasma and urine were observed, demonstrating SYNB1618 is able to consume Phe and convert it to non-toxic metabolites in the GI tract of both healthy volunteers and patients with PKU.
- These data demonstrate the potential to use engineered bacteria in the treatment of rare metabolic disorders through the consumption of toxic substances in the GI tract.

Concurrently, the development of a mechanistic model predicting the potential for Phe-lowering efficacy in PKU patients was published today in Communications Biology. The paper, entitled, "Development of a Mechanistic Model to Predict Synthetic Biotic Activity in Healthy Volunteers and Patients with Phenylketonuria," used findings from the Phase 1/2a study to inform a mechanistic model of strain activity in PKU patients.

Key findings include:

- Construction of a mechanistic model that predicts SYNB1618 function in non-human primates and healthy subjects is feasible by combining in vitro simulations and prior knowledge of human physiology.
- The model can be extended using plasma Phe kinetics to PKU patients, informing clinical development of potential treatments for PKU.
- Increases in Phe removal from the GI tract are predicted to correlate strongly with reduction of Phe in the blood.
- The results of this dose-response model suggest Phe-consuming Synthetic Biotic medicines such as SYNB1618 may have potential to achieve clinically meaningful reduction of blood phenylalanine levels in patients with PKU.

Data on the solid oral formulation of SYNB1618 was presented at the American College of Medical Genetics meeting in April 2021. Data on the development of SYNB1934, an evolved strain of SYNB1618, was presented at the Synthetic Biology: Engineering, Evolution & Design (SEED) conference in June 2021.

SYNB1618 continues to advance in a proof-of-concept Phase 2 clinical trial in adults with PKU, SynPheny-1 study (NCT04534842), with data expected in the second half of 2021. Learn more by visiting https://pkuresearchstudy.com. Information about Synlogic's programs and pipeline can be found at https://www.synlogictx.com.

About PKU
Phenylketonuria (PKU) is an inherited metabolic disease that manifests at birth and is marked by an inability to break down phenylalanine (Phe), an amino acid that is commonly found in many foods. Left untreated, high levels of Phe become toxic and can lead to serious neurological and neuropsychological problems affecting the way a person thinks, feels, and acts. Due to the seriousness of these symptoms, infants are screened at birth in many countries to ensure early diagnosis and treatment to avoid intellectual disability and other complications.

About SYNB1618 and SYNB1934
SYNB1618 and SYNB1934 are investigational oral drugs for the treatment of Phenylketonuria (PKU) composed of an engineered Synthetic Biotic designed to lower plasma phenylalanine (Phe) levels by consuming Phe in the GI tract. A solid oral lyophilized formulation of SYNB1618 was found to

be safe and well-tolerated, and consume Phe in the GI tract of healthy volunteers. Synlogic has initiated a Phase 2 study of SYNB1618 in PKU patients (NCT04534842) and a Phase 1 study of SYNB1934 in healthy volunteers.

About Synlogic
Synlogic™ is bringing the transformative potential of synthetic biology to medicine. With a premiere synthetic biology platform that leverages a reproducible, modular approach to microbial engineering, Synlogic designs Synthetic Biotic™ medicines that target validated underlying biology to treat disease in new ways. Synlogic's proprietary pipeline includes Synthetic Biotics for the treatment of metabolic disorders including Phenylketonuria (PKU) and Enteric Hyperoxaluria. The company is also building a portfolio of partner-able assets in immunology and oncology.

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, clinical development plans, 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, and inflammatory and immune disorders; our expectations about sufficiency of our existing cash balance; 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 of SYNB1618 and availability of clinical trial data including Phase 2 data of SYNB1618 for the treatment of PKU. 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 clinical and 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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