Synlogic Presents New Preclinical Data at International Congress of Inborn Errors of Metabolism

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Data support the lead clinical program in urea cycle disorders (UCD) and the further development of Synthetic Biotic™ candidates as potential treatments for phenylketonuria (PKU) and maple syrup urine disease (MSUD)

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 7, 2017-- Synlogic (NASDAQ: SYBX) announced the presentation of new preclinical data from programs investigating the company's novel Synthetic Biotic drug candidates at the 13 thInternational Congress of Inborn Errors of Metabolism (ICIEM), which is being held in Rio de Janeiro, Brazil, September 5-8, 2017.

The data, generated in mouse and non-human primates, demonstrate that Synlogic's Synthetic Biotic medicines are active in the gastrointestinal (GI) tract and are able to break down both dietary and systemic sources of metabolites that build to toxic levels in patients with UCD, PKU and MSUD.

"These data demonstrate that our Synthetic Biotic medicines can act from the GI tract to potentially reduce the build-up of toxic metabolites throughout the body in each of these disorders," said Aoife Brennan, M.B., B.Ch., Synlogic's chief medical officer. "There is a huge need for improved treatment options for many Inborn Errors of Metabolism (IEMs), and we believe that orally administered living Synthetic Biotic medicines could provide a promising option for patients."

Presentation Details
Development of Genetically Engineered E. coli Nissle Strains for the Treatment of Phenylketonuria and Maple Syrup Urine Disease – Oral Presentation, Abstract number 248.

- PKU, caused by a defect in phenylalanine hydroxylase (PAH) activity, is characterized by the accumulation of systemic phenylalanine (Phe), which can lead to severe neurological deficits unless patients are placed on a strict low-Phe diet. SYN-PKU is an investigational Synthetic Biotic medicine that can metabolize Phe into easily excreted compounds, including hippurate, which is then excreted in the urine and serves as a useful biomarker of SYN-PKU activity in mouse models and non-human primates (NHP). In a mouse model of PKU challenged with subcutaneous administration of Phe, oral dosing with SYN-PKU resulted in significant reduction of Phe plasma levels compared to controls. In studies in which NHPs were administered labeled Phe by feeding, the data demonstrate that oral administration of SYN-PKU enabled a significant decrease in blood Phe levels. Systemically delivering labeled Phe to NHPs resulted in excretion of labeled hippurate in the urine. These data suggest that systemic Phe recirculates in the GI tract and is metabolized by SYN-PKU. These data will be used to design the early phase clinical studies which are planned to start in 2018.
- Other studies were performed using SYN-MSUD, an investigational Synthetic Biotic candidate for the treatment of MSUD, a rare genetic disorder associated with the inability to break down certain branch chain amino acids (BCAAs). In a mouse model of MSUD challenged with a high-protein diet, oral delivery of SYN-MSUD resulted in significantly reduced plasma levels of the BCAA leucine. In addition, a reduction in physical symptoms of disease and reduced levels of leucine in the brains of these animals was observed with SYN-MSUD treatment as compared with controls.

A Genetically Engineered E. coli Nissle to Prevent Hyperammonemia in Urea Cycle Disorder (UCD) – Poster Presentation, Abstract number 377.

- Urea cycle disorders (UCDs) are a group of inherited diseases in which the inability to efficiently convert waste nitrogen into urea leads to the toxic accumulation of systemic ammonia. An *in vitro* study demonstrated that SYNB1010 and SYNB1020, investigational Synthetic Biotic candidates designed for the treatment of UCD, were able to consume ammonia and produce a beneficial metabolite, arginine.
- The systemic effects of SYNB1010 were also studied in a UCD mouse model. The data demonstrated that orally administered SYNB1010 functioned in the GI tract and prevented systemic hyperammonemia caused by a high-protein diet, significantly increasing survival of these animals.

About SYNB1020 and SYNB1618
Earlier this year, Synlogic initiated a Phase 1 clinical trial in healthy volunteers designed to evaluate the safety and tolerability of its lead compound, SYNB1020, as a potential treatment for UCD. Pending the success of this first study, Synlogic plans to initiate two additional clinical trials with the investigational candidate in symptomatic patients with urea cycle disorders (UCD) or hepatic encephalopathy (HE), both conditions in which patients experience elevated and toxic blood 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 Synthetic Biotic™ Medicines

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.

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 including UCD, PKU and MSUD, the future clinical development of SYNB1020 and its prospects as a potential treatment for hyperammonemia, the future development of other product candidates, such as SYN-PKU and SYN-MSUD and the approach Synlogic is taking to discover and develop novel therapeutics using synthetic biology. 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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