



Synlogic Presents Preclinical Data from Synthetic Biotic Immuno-Oncology Program at the American Association for Cancer Research 2018 Annual Meeting

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– Data highlight the application of Synthetic Biotic medicines for the potential treatment of a variety of solid tumors –

– Company is advancing the first candidate from this program into IND-enabling studies in 2018–

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 16, 2018-- Synlogic, Inc. (Nasdaq: SYBX), a clinical-stage drug discovery and development company applying synthetic biology to probiotics to develop novel living medicines, today announced that preclinical data from its immuno-oncology (IO) program were featured in two presentations at the annual meeting of the American Association for Cancer Research (AACR). The data demonstrate that, in mouse models, Synlogic's Synthetic Biotic medicines were shown to stimulate an antitumor response and robustly reprogram the tumor microenvironment potentially enabling the treatment of a variety of cancers.

"Our IO program highlights the potential of our Synthetic Biotic platform for the design and engineering of novel living medicines with multiple mechanisms of action to treat a broad range of diseases, including cancer," said J.C. Gutiérrez-Ramos, Ph.D., Synlogic's president and chief executive officer. "Our approach enables us, in a single treatment, to locally deliver multiple, regulatable activities that stimulate an immune response and modulate the tumor environment in order to mobilize the immune system against the tumor and its metastases. We intend to advance our first IO program into IND enabling studies this year."

Synlogic is focused initially on developing Synthetic Biotic medicines to treat so-called "cold tumors," which lack infiltrating anti-tumor T-cells by first stimulating an innate anti-tumor response to make the tumor "hot" and then modifying the tumor microenvironment (TME) to enable T cell expansion and the development of memory, using a single agent to both prime T-cells to mount an immune response and sustain the response. Recent studies have demonstrated that activation of the stimulator of interferon genes (STING) pathway can play a critical role in the initiation of an anti-tumor immune response via activation of antigen presenting cells (APCs) and presentation of tumor antigens. The TME has long been understood to have a role in preventing or interrupting this process. Certain metabolites produced within the tumor such as kynurenine or adenosine can lead to T cell dysfunction and exhaustion, significantly blunting anti-tumor immune responses. Data presented at AACR demonstrate the potential of Synlogic's Synthetic Biotic medicines to manipulate both pathways to enable efficient anti-tumor activity in mouse models.

In a presentation in the late-breaking research immunology session, *Activation of Innate and Adaptive Immunity via Combinatorial Immunotherapy using Synthetic Biotic Medicines*, Synlogic described two new genetic circuits engineered into *E. coli* Nissle, an immune "initiator" STING activating circuit (SYN-STING) and an immune "sustainer" kynurenine consuming circuit (SYN-Kyn). SYN-STING can be delivered directly into the tumor enabling its localized site of action. The approach of using intra-tumoral injection elicits innate responses in the tumor but not in the circulation, potentially decreasing the risk of adverse events that may arise from the production of systemic type I interferon. In contrast to other therapeutic approaches in development, SYN-Kyn lowers levels of the kynurenine metabolite by degrading it, a mechanism that is independent of the enzyme(s) used by both immune and tumor cells to produce kynurenine (IDO1/2 and/or TDO).

In preclinical studies, Synlogic has demonstrated that:

- *In vitro*, SYN-STING produces biologically-relevant levels of ci-di-AMP, activating APCs, while SYN-Kyn consumes kynurenine at concentrations comparable to those found in patients' tumors;
- SYN-STING treatment of either B16.F10 or A20 tumors results in robust tumor rejection or control, which correlates with an early rise in innate-immune cytokines and later results in T cell activation in tumors and tumor-draining lymph nodes;
- Combining SYN-Kyn with a checkpoint inhibitor led to profound anti-tumor activity in the CT26 immunocompetent tumor model; and
- A strain engineered to combine both genetic circuits (SYN-STING:Kyn) demonstrates equivalent production of ci-di-AMP and consumption of kynurenine *in vitro* compared to the individual strains SYN-STING and SYN-Kyn, respectively.

A second presentation entitled *Metabolic Modulation of the Tumor Microenvironment using Synthetic Biotic Medicines* demonstrated that engineered bacterial strains designed to consume either kynurenine (SYN-Kyn) or adenosine (SYN-Ade) effectively relieved TME immunosuppression and promoted anti-tumor activity.

In summary:

- *In vitro* SYN-Kyn and SYN-Ade can deplete kynurenine and adenosine, respectively, at concentrations that are clinically relevant;
- SYN-Kyn demonstrated rapid and near-complete reductions in tumor kynurenine levels *in vivo*;
- A combination of either SYN-Kyn or SYN-Ade with checkpoint inhibition led to superior anti-tumor activity in the MC38 immunocompetent tumor model compared with checkpoint inhibitors alone.

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, SYN1020 and SYN1618, target hyperammonemia as a result of liver damage or genetic disease, and phenylketonuria, respectively. Patients with these diseases are unable 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, with the potential to significantly improve symptoms of disease for affected patient. Synlogic has earlier-stage programs that apply the broad potential of its Synthetic Biotic platform in other disease areas, from inflammatory and immune

disorders to cancer.

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'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).

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: 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; the potential of Synlogic's technology to treat cancer, hyperammonemia, and phenylketonuria. 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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