



Synlogic Presents New Preclinical Data from Synthetic Biotic™ Immuno-Oncology Program at FOCIS 2018

June 25, 2018

- Data highlight broad capabilities of Synlogic's Synthetic Biotic platform to generate candidates for the potential treatment of cancer –

- First program advancing into IND-enabling studies in 2H2018 –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 25, 2018-- Synlogic, Inc. ([Nasdaq: SYBX](#)), a clinical-stage drug discovery and development company applying synthetic biology to probiotics to develop novel living medicines, announced the presentation of new preclinical data from its Synthetic Biotic medicine oncology program at the annual meeting of the Federation of Clinical Immunology Societies (FOCIS 2018) held June 20-23, in San Francisco, CA. The data demonstrate the breadth of the company's platform to generate Synthetic Biotic medicines that secrete or consume immunologically relevant compounds for the potential treatment of cancer and inflammation.

"These data highlight the plasticity of our Synthetic Biotic platform and its potential as a robust engine for the production and delivery of a variety of immunological payloads, which can have a profound effect on the tumor microenvironment and potential therapeutic use in immune-related conditions," said Jose Lora, Ph.D., Synlogic's vice president of research. "Our ability to control the expression of these payloads using the tools of synthetic biology, and to combine multiple effectors into a single Synthetic Biotic medicine has the potential to provide potent stimulation of the immune response locally while limiting systemic toxicity. We continue to explore the capability of this platform in immunomodulation and look forward to advancing our first immuno-oncology program into IND-enabling studies in the second half of 2018."

These preclinical data demonstrate that intra-tumorally injected *E. coli* Nissle has the ability to colonize and persist in the tumor. Synlogic uses a strain of probiotic bacteria, *E. coli* Nissle, as the parent strain or "chassis" for its Synthetic Biotic medicines as it is well-characterized, readily engineerable and non-pathogenic. In addition, multiple functions can be engineered into a single bacterial strain. These properties support the development of a Synthetic Biotic immuno-oncology approach for the potential treatment of solid tumors, particularly "cold" tumors that may be resistant to current immunotherapies due to their lack of infiltrating immune cells or a highly immunosuppressive tumor microenvironment.

In a presentation at FOCIS: *A Synthetic Biology Approach for the Treatment of Cancer and Inflammation*, Synlogic described the engineering of Synthetic Biotic strains to execute a range of functions that are potentially useful for the treatment of cancer, including:

- Consumption of immune-suppressive metabolites that accumulate in tumors, such as adenosine and kynurenine. Synthetic Biotic strains capable of consuming these metabolites have the potential to relieve immunosuppression in the tumor microenvironment, enabling immune cells to initiate an anti-tumor response;
- Secretion of proteins, including immunomodulatory cytokines such as IL-15, TNF-alpha and IFN-gamma, and production of small molecules, such as STING agonists, that are able to trigger robust anti-tumor immune responses as single agents; and
- *In situ* conversion of pro-drugs, such as 5FC, to enable local release of an active chemotherapy agent, 5FU, potentially reducing the systemic toxicity of such drugs.

The data also demonstrate the use of "switches" to control the engineered genetic circuits; Synthetic Biotic medicines can be engineered to perform functions in response to environmental cues or exogenously administered small molecules, such as tetracycline, salicylate and cumate.

In a second presentation, *Using Synthetic Biotic Medicines to Activate Innate and Adaptive Immunity and Drive Antitumor Immune Responses*, data were presented from mouse tumor model studies of two genetic circuits engineered into *E. coli* Nissle to generate two bacterial strains, an immune "initiator" STING activating circuit (SYN-STING) and an immune "sustainer" kynurenine consuming circuit (SYN-Kyn). In contrast to other therapeutic approaches in development, SYN-Kyn lowered levels of the kynurenine metabolite by degrading it, a mechanism that is independent of the enzymes used by both immune and tumor cells to produce kynurenine (IDO1/2 and/or TDO). The preclinical data demonstrate:

- SYN-STING treatment of either B16.F10 or A20 tumors resulted 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 checkpoint inhibitors led to significant anti-tumor activity in multiple immunocompetent tumor models; 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.

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. 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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