Synlogic Announces Advancement of SYNB1891 to Combination Arm Dosing with PD-L1 Checkpoint Inhibitor in the on-going Phase 1 Study for the Treatment of Solid Tumors and Lymphoma

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- SYNB1891 demonstrates STING activation and target engagement in the tumor microenvironment in monotherapy cohorts -

CAMBRIDGE, Mass., Dec. 14, 2020 /PRNewswire/ -- Synlogic, Inc. (Nasdaq: SYBX), a clinical stage company bringing the transformative potential of synthetic biology to medicine, today announced SYNB1891 has advanced into the combination therapy stage of the ongoing Phase 1 trial. SYNB1891 is an investigational drug for the intra-tumoral treatment of solid tumors and lymphoma, composed of an engineered Synthetic Biotic designed to activate the STING pathway in the tumor microenvironment in order to upregulate the patient's immune response.

SYNB1891 is being advanced due to acceptable safety at doses evaluated to date, intratumoral injection feasibility, successful escalation to clinically relevant dose levels, and evidence of target engagement and immune system upregulation.

"Our goal is to bring the benefits of immunotherapy to patients fighting cancer who do not have the option of immunotherapies today," said Aoife Brennan, M.B. Ch.B., Synlogic's President and Chief Executive Officer. "Synlogic is designing Synthetic Biotic medicines that work uniquely inside the tumor microenvironment, boosting the patient's immune response and promoting the body's ability to detect and destroy cancer cells. The interim results of our monotherapy cohorts suggest SYNB1891 is working as designed, upregulating the immune system in the tumor microenvironment via the STING pathway. We are excited to move this study forward."

"The body of data validating our unique approach to immunomodulation with Synthetic Biotic medicines continues to grow," said Dr. Richard Riese, M.D., Synlogic's Chief Medical Officer. "The investigation of SYNB1891 combined with the PD-L1 checkpoint inhibitor atezolizumab (Tecentriq®) is warranted by the encouraging and consistent results we have seen thus far across preclinical models, tumor response, and biomarkers of target engagement. We would like to thank the investigators, patients, and their families who continue to work closely with us as we advance this novel therapy."

SYNB1891 Highlights

- SYNB1891 is being evaluated in a Phase 1, open-label, multicenter study administered by intratumoral injection to patients with advanced, metastatic solid tumors or lymphomas (NCT04167137).
- The monotherapy arm of the study has enrolled four dose cohorts to date. A maximum tolerated dose has not been reached. Enrollment of additional monotherapy dose escalation cohorts will continue.
- Study results to date across four dose cohorts of SYNB1891 monotherapy demonstrate:
    - SYNB1891 is safe and well-tolerated at currently evaluated dose levels, as an intratumoral injection in a heterogenous patient population with no dose limiting toxicities or infections to date.
    - Treatment with SYNB1891 demonstrates activation of the STING pathway and target engagement as assessed by:
        - Upregulation of IFN-stimulated genes, chemokines, cytokines, and T-cell response
        - Pharmacodynamic effects including increases in serum cytokines
    - Evidence of durable stable disease was observed in two patients being treated for metastatic melanoma and metastatic small cell lung cancer. Both patients experienced disease progression on immunotherapy with anti-PD-1/PDL-1 antibodies prior to enrollment in the study.
- The combination arm of the study will combine escalating dose levels of SYNB1891 with a fixed dose of the PD-L1 checkpoint inhibitor atezolizumab, to establish a recommended Phase 2 dose for the combination regimen.
- The study protocol has been amended to allow for the injection of visceral lesions in addition to cutaneous and subcutaneous lesions in both monotherapy and combination therapy cohorts.
- Results of the SYNB1891 Phase 1 study will be presented at a future medical meeting.

The clinical development plan for SYNB1891 is based on compelling research from preclinical studies that demonstrate anti-tumor activity and generation of immunological memory by SYNB1891 in mouse models of cancer, as well as its robust activation of human antigen presenting cells (APCs) that are key to the generation of an anti-tumoral immune response. The *Nature Communications* publication titled, "Immunotherapy with an engineered bacteria by targeting the STING pathway for anti-tumor immunity," details the engineering and characterization of SYNB1891 (Leventhal, D.S., Sokolovska, A., Li, N. et al. Nature Communications 11, 2739 (2020)).

Learn more about Synlogic's programs and pipeline by visiting https://www.synlogictx.com/.

About SYNB1891

SYNB1891 is an investigational drug for the intra-tumoral treatment of solid tumors and lymphoma, composed of an engineered Synthetic Biotic strain of E. coli Nissle that produces cyclic di-AMP (CDA), a stimulator of the STING (STimulator of INterferon Genes) pathway. This mechanism can play a critical role in the initiation of an anti-tumor immune response via activation of APCs and presentation of tumor antigens. The bacterial chassis of SYNB1891 also stimulates the innate immune system by several other mechanisms, including via Toll-like receptors (TLRs), potentially adding to the

magnitude of the overall immune response. While SYNB1891 has been engineered with safety features that are designed to prevent its replication unless supplemented with specific nutrients, the bacteria remain active for several days within the injected tumor to stimulate a local immune response. SYNB1891 is being evaluated in a Phase 1 clinical trial.

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 (HOX). 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; 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 including the Phase 1 study for SYNB1891, and availability of clinical trial data from that study and other studies.

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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