November 21, 2018

Synthetic Biologics Announces Positive Outcome of End-of-Phase 2 Meeting with FDA on SYN-004 (ribaxamase) Development

-- Single Phase 3 Clinical Trial May be Sufficient for Approval for Prevention of Antibiotic-Mediated Clostridium difficile Infection (CDI) --

-- SYN-004 (ribaxamase) is in Development as Potentially the First Intervention Designed to Specifically Prevent Antibiotic Damage to the Microbiome --

ROCKVILLE, Md., Nov. 21, 2018 /PRNewswire/ --Synthetic Biologics, Inc. (NYSE American: SYN), a late-stage clinical company developing therapeutics designed to preserve the microbiome to protect and restore the health of patients, today announced that it has successfully completed an End-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA) to discuss development of SYN-004 (ribaxamase) for the prevention of antibiotic-mediated *Clostridium difficile* infection (CDI). Pursuant to the meeting, the FDA has proposed criteria for Phase 3 clinical efficacy and safety which, if achieved, may support submission for marketing approval of ribaxamase on the basis of a single Phase 3 clinical trial. Final agreement on these criteria is contingent on FDA evaluation of a detailed Phase 3 clinical trial protocol.

"We are very pleased with the productive advice we have received from the FDA during our

recent End-of-Phase 2 meeting," said Steven A. Shallcross, Interim Chief Executive Officer and Chief Financial Officer. "Having a clear path forward in the form of a Phase 3 clinical program for ribaxamase is an exciting and important milestone for our company and should be highly beneficial in our ongoing strategic partnering discussions."

Synthetic Biologics, in consultation with the FDA, has confirmed the key elements of the Phase 3 clinical program to support a marketing application for ribaxamase, the Company's first-in-class oral enzyme designed to degrade certain intravenous (IV) beta-lactam antibiotics within the gastrointestinal (GI) tract to prevent microbiome damage, *Clostridium difficile* infection (CDI), overgrowth of pathogenic organisms and the emergence of antimicrobial resistance (AMR). The proposed ribaxamase Phase 3 clinical program will entail a single, global, event-driven clinical trial with a fixed maximum number of patients for total enrollment and will evaluate the potential efficacy and safety of ribaxamase in a broad patient population by enrolling patients with a variety of underlying infections treated with a range of IV beta-lactam antibiotics.

The primary efficacy endpoint of the Phase 3 clinical trial will be the reduction in the incidence of CDI at one month after the last drug dose in the ribaxamase treatment group versus placebo. The Company also confirmed that the FDA agreed to a primary safety endpoint of noninferiority in mortality between the ribaxamase treatment group versus placebo at 3 months post-randomization. The designation of efficacy and safety as separate and decoupled endpoints is critical for clinical studies of this nature, where the underlying population, regardless of treatment group, is projected to have a comparatively high incidence of safety events that may significantly dilute the smaller number of CDI events.

Synthetic Biologics anticipates initiating the Phase 3 clinical program after securing additional potential financing via a strategic partnership. In parallel, the Company is evaluating opportunities to advance ribaxamase through the pursuit of a more focused clinical indication in a specialty patient population with multiple potential disease endpoints associated with IV beta-lactam-induced gut microbiome damage. Such a dual approach is designed to advance ribaxamase in areas of clear unmet medical need while also expanding upon ribaxamase's current data set and providing further validation for use in the broader indication for the prevention of CDI.

About *Clostridium difficile* infection

Clostridium difficile infection (CDI) is a leading hospital acquired infection in the U.S., with more than 453,000[1] patients diagnosed annually. CDI results in approximately 29,000 deaths[1], $5.4[2] billion in additional healthcare costs, as well as significant and sometimes prolonged illness. Approximately 1 in 5 CDI patients experience at least one CDI recurrence[3].

About SYN-004 (ribaxamase) and the Phase 2b proof-of-concept clinical trial

SYN-004 (ribaxamase) is a first-in-class oral enzyme prophylactic therapy designed to degrade certain IV beta-lactam antibiotics within the GI tract and maintain the natural balance of the gut microbiome for the prevention of *Clostridium difficile* infection (CDI), overgrowth of pathogenic organisms and the emergence of antimicrobial resistance (AMR). A previously completed randomized, double-blind, placebo-controlled Phase 2b proof-of-

concept clinical trial of 412 patients met its primary endpoint of significantly reducing *C. difficile* infection (CDI). Preliminary analysis of the data indicated seven confirmed cases of CDI in the placebo group compared to two cases in the ribaxamase treatment group. Patients receiving ribaxamase achieved a 71.4% relative risk reduction (p-value=0.045) in CDI rates compared to patients receiving placebo.

About Synthetic Biologics, Inc.

Synthetic Biologics, Inc. (NYSE American: SYN) is a late-stage clinical company developing therapeutics that preserve the microbiome to protect and restore the health of patients. The Company's lead candidates are: (1) SYN-004 (ribaxamase) which is designed to protect the gut microbiome from the effects of certain commonly used intravenous (IV) beta-lactam antibiotics to prevent microbiome damage, *C. difficile* infection (CDI), overgrowth of pathogenic organisms and the emergence of antimicrobial resistance (AMR), and (2) SYN-010 which is intended to reduce the impact of methane producing organisms in the gut microbiome to treat an underlying cause of irritable bowel syndrome with constipation (IBS-C). The Company's preclinical pursuits include an oral formulation of the enzyme intestinal alkaline phosphatase (IAP) to treat both local GI and systemic diseases as well as monoclonal antibody therapies for the prevention and treatment of pertussis, and novel discovery stage biotherapeutics for the treatment of phenylketonuria (PKU). For more information, please visit Synthetic Biologics' website at www.syntheticbiologics.com.

This release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases forward-looking statements can be identified by terminology such as "may," "should," "potential," "continue," "expects," "anticipates," "intends," "plans," "believes," "estimates," and similar expressions, and includes statements regarding a single Phase 3 clinical trial being sufficient for approval for prevention of antibiotic-mediated clostridium difficile infection, the achievement of the FDA proposed criteria for Phase 3 clinical efficacy and safety supporting submission for marketing approval of SYN-004 (ribaxamase) on the basis of a single Phase 3 clinical trial, having a clear path forward in the form of a Phase 3 clinical program for SYN-004 being highly beneficial in our ongoing strategic partnering discussions, the anticipated initiation of the Phase 3 clinical program after securing additional potential financing via a strategic partnership, development of SYN-004 (ribaxamase) as potentially the first intervention designed to specifically to prevent antibiotic damage to the microbiome, opportunities that would enable the advancement of SYN-004 through the pursuit of a more focused clinical indication in a specialty patient population with multiple potential disease endpoints associated with IV beta-lactam-induced gut microbiome damage and the potential benefits of SYN-004 and SYN-010. These forward-looking statements are based on management's expectations and assumptions as of the date of this press release and are subject to a number of risks and uncertainties, many of which are difficult to predict that could cause actual results to differ materially from current expectations and assumptions from those set forth or implied by any forward-looking statements. Important factors that could cause actual results to differ materially from current expectations include, among others, Synthetic Biologics' ability to design a Phase 3 trial with the co-primary endpoints and receive FDA approval for such design, Synthetic Biologics' ability to initiate the Phase 3 clinical program after securing additional financing via a strategic partnership, Synthetic Biologics' ability to establish a path forward to develop ribaxamase and conduct a robust, controlled and well-designed clinical trial that may provide sufficient efficacy and safety data to support a

pathway towards marketing approval for ribaxamase, Synthetic Biologics' ability to regain compliance with the continued listing standards of the NYSE American by September 2, 2019, Synthetic Biologics' ability to comply with other continued listing requirements of the NYSE American, the ability of its product candidates to demonstrate safety and effectiveness, as well as results that are consistent with prior results, Synthetic Biologics' clinical trials continuing enrollment as expected, a failure to receive the necessary regulatory approvals for commercialization of Synthetic Biologics' therapeutics, including approval of proposed trial designs, a failure of Synthetic Biologics' clinical trials, and those conducted by investigators, for SYN-004 and SYN-010 to be commenced or completed on time or to achieve desired results and benefits, a failure of Synthetic Biologics' clinical trials to continue enrollment as expected or receive anticipated funding, a failure of Synthetic Biologics to successfully develop, market or sell its products, Synthetic Biologics' inability to maintain its material licensing agreements, or a failure by Synthetic Biologics or its strategic partners to successfully commercialize products, Synthetic Biologics' ability to achieve acceptance of its product candidates in the marketplace and the successful development, marketing or sale of Synthetic Biologics' products by competitors that render Synthetic Biologics' products obsolete or non-competitive, the continued maintenance and growth of Synthetic Biologics' patent estate, Synthetic Biologics becoming and remaining profitable, Synthetic Biologics' ability to obtain or maintain the capital or grants necessary to fund its research and development activities, a loss of any of Synthetic Biologics' key scientists or management personnel and other factors described in Synthetic Biologics' most recent Form 10-K and its other filings with the SEC, including subsequent periodic reports on Forms 10-Q and 8-K. The information in this release is provided only as of the date of this release, and Synthetic Biologics undertakes no obligation to update any forward-looking statements contained in this release on account of new information, future events, or otherwise, except as required by law.

References:

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