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Synthetic Biologics Provides Update on Development of SYN-004 (ribaxamase), for the Prevention of C. difficile Infection

ROCKVILLE, Md., April 23, 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 preliminary agreement from the U.S. Food & Drug Administration (FDA), on a proposed clinical trial synopsis for its planned Phase 3 clinical trial for SYN-004 (ribaxamase). In accordance with recommendations and guidance received from the FDA, the Company expects the Phase 3 trial to include separate co-primary endpoints designed to evaluate the efficacy and safety of ribaxamase in a patient population being treated with a representative selection of intravenous (IV) beta-lactam antibiotics.

The proposed Phase 3 study discussed with the FDA comprises a global, event-driven clinical trial with a fixed maximum number of patients for total enrollment. The Phase 3 study proposes to evaluate the potential efficacy and safety of ribaxamase in a broader patient population by the inclusion of additional IV beta-lactam antibiotics with ceftriaxone and by enrolling patients with a variety of underlying infections. Based on a series of collaborative discussions with the FDA, the Company expects the primary efficacy endpoint of the proposed Phase 3 clinical trial will be the reduction of the incidence of *Clostridium difficile* infection (CDI) in the ribaxamase treatment group relative to placebo.

The Company also announced it has preliminary agreement from the FDA to evaluate mortality risk as the primary safety endpoint for the trial, which will be separate from the primary efficacy endpoint of reduction of the incidence of CDI. The designation of efficacy

and safety as separate and decoupled endpoints is critical for clinical studies of this nature, where the underlying population is projected to have a comparatively high incidence of safety events that may significantly dilute the smaller number of CDI events.

"Following recent collaborative discussions with the FDA, we have gained clarity on several significant elements of the proposed Phase 3 clinical program, which we believe provide a path forward to develop ribaxamase, a product which, if approved, may address the serious and unmet health impacts associated with antibiotic-mediated CDI," stated Steven A. Shallcross, Interim Chief Executive Officer and Chief Financial Officer. "We look forward to sharing the remaining elements of the proposed Phase 3 trial upon the completion of our End-of-Phase 2 meeting with the FDA during the second half of 2018, and anticipate initiating this trial during the second half of 2019."

Synthetic Biologics further announced that during the development of the proposed Phase 3 clinical trial, the FDA undertook an additional review of data and analysis submitted by the Company from the previously completed ribaxamase Phase 2b clinical trial. Following FDA's review of the additional data, it was determined that the requirements for Breakthrough Therapy Designation were no longer met due to the numerical imbalance in fatal adverse events observed in the study which could not be fully evaluated due to the limited safety database, and the study's method of statistical treatment of patients who did not complete the study for any reason. The Company has reached agreement with the FDA on how each of these factors will be addressed in the Phase 3 trial by evaluating safety and efficacy endpoints separately as described above. As a result, and with the consent of the FDA, the Company has voluntarily withdrawn the Breakthrough Therapy Designation for the ribaxamase program. The FDA stated in their official response to the Company that they remain committed to working with Synthetic Biologics on the development of the ribaxamase program, and the withdrawal of Breakthrough Therapy Designation will not affect interactions between the two parties.

"We are grateful to have received guidance and continued support from the FDA as part of ribaxamase's development and remain encouraged that a robust, controlled, and well-designed clinical trial may provide sufficient efficacy and safety data to support a pathway towards marketing approval for ribaxamase," concluded Shallcross.

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 poised for Phase 3 development 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 for the prevention of *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.

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].

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 expectations that the Phase 3 clinical trial for SYN-004 will include separate co-primary endpoints, comprise a global, event-driven clinical trial with a fixed maximum number of patients for total enrollment, evaluate the potential efficacy and safety of ribaxamase in a broader patient population by the inclusion of additional IV beta-lactam antibiotics with ceftriaxone and by enrolling patients with a variety of underlying infections, have as the primary efficacy endpoint the reduction of the incidence of Clostridium difficile infection (CDI) in the ribaxamase treatment group relative to placebo and evaluate mortality risk as the primary safety endpoint, which will be separate from the primary efficacy endpoint; the belief that the proposed Phase 3 clinical program will provide a path forward to develop ribaxamase which if approved, may address the serious and unmet health impacts associated with antibiotic-mediated CDI; the anticipated timing of the initiation of the Phase 3 clinical trial during the second half of 2019 following the end of Phase 2 meeting, which is anticipated to be during the second half of 2018, the belief that a robust, controlled, and well-designed clinical trial may provide sufficient efficacy and safety data to support a pathway towards marketing approval for ribaxamase, 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 implement the Phase 3 program as a global, event-driven clinical trial, Synthetic Biologics' ability to initiate the Phase 3 clinical program in the second half of 2019 following an end of Phase 2 meeting with the FDA during the second half of 2018, 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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