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Synthetic Biologics Announces First Patient Dosed in Phase 1b/2a Clinical Trial of SYN-004 (ribaxamase) in Allogeneic Hematopoietic Cell Transplant Recipients

ROCKVILLE, Md., April 14, 2021 /PRNewswire/ --Synthetic Biologics, Inc. (NYSE American: SYN), a diversified clinical-stage company leveraging the microbiome to develop therapeutics designed to prevent and treat gastrointestinal (GI) diseases in areas of high unmet need, today announced enrollment has commenced and the first patient has been dosed in its Phase 1b/2a clinical trial of SYN-004 (ribaxamase) in allogeneic hematopoietic cell transplant (HCT) recipients for the prevention of acute graft-versus-host-disease (aGVHD). Broad spectrum intravenous (IV) beta-lactam antibiotics used to treat infection following conditioning chemotherapy for allogeneic HCT patients is a necessary and oftentimes lifesaving intervention. However, antibiotic-mediated damage of the gut microbiome in this patient population has been strongly associated with adverse outcomes including *C. difficile* infection (CDI), vancomycin-resistant enterococci (VRE) colonization, potentially fatal bacteremia, and aGVHD.

"Allogenic HCT recipients are at very high risk for infection and frequently receive antibiotics," said Erik Dubberke, MD, Professor of Medicine and Clinical Director of Transplant Infectious Diseases at Washington University School of Medicine in St. Louis. "There is increasing evidence that disruption of the microbiome caused by antibiotics results in additional complications, including further infections. If this trial shows that SYN-004 has a favorable safety profile and is able to protect the microbiome, it would warrant study in larger trials to determine if this treatment can improve outcomes in these highly susceptible

patients**."**

"We are very excited to begin enrollment of our SYN-004 Phase 1b/2a clinical trial in allogeneic HCT recipients," said Steve A. Shallcross, Chief Executive Officer of Synthetic Biologics. "We are very grateful for the tremendous support from Dr. Dubberke and his team at Washington University. This clinical program is a critical component of our efforts to expand and fortify the already well-established dataset for SYN-004 and our pursuit of a cost-effective development strategy in a highly specialized patient population. We look forward to reporting key clinical milestones as we advance the trial."

The single-center, randomized, double-blinded, placebo-controlled clinical trial will evaluate the safety, tolerability and potential absorption into the systemic circulation (if any) of 150 mg oral SYN-004 administered four times per day to allogeneic HCT recipients who receive an intravenous (IV) beta-lactam antibiotic to treat fever. Study participants will be enrolled into three sequential cohorts, with each receiving a different study-assigned IV beta-lactam antibiotic. Eight participants in each cohort will receive SYN-004 and four will receive placebo. A data readout for the first cohort is anticipated towards the end of 2021.

The study will also evaluate potential protective effects of SYN-004 on the gut microbiome as well as generate preliminary information on potential therapeutic benefits and patient outcomes of SYN-004 in allogeneic HCT recipients. Safety and pharmacokinetic data for each cohort will be reviewed by an independent Data and Safety Monitoring Committee, which will make a recommendation on whether to proceed to the next IV beta-lactam antibiotic.

Synthetic Biologics will serve as the sponsor of the clinical trial and supply SYN-004 to Washington University. Dr. Dubberke will serve as the principal investigator along with his Washington University colleague, Dr. Mark A. Schroeder, Associate Professor of Medicine, Division of Oncology, Bone Marrow Transplantation and Leukemia.

About the SYN-004 (ribaxamase) Phase 1b/2a Clinical Trial

SYN-004 (ribaxamase) is an oral 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 *Clostridioides difficile* infection (CDI), overgrowth of pathogenic organisms, the emergence of antimicrobial resistance (AMR) and acute graft-versus-host-disease (aGVHD) in allogeneic hematopoietic cell transplant (HCT) recipients. Allogeneic HCT recipients routinely receive long courses of IV beta-lactam antibiotics to treat infection following conditioning therapy. Antibiotic-mediated damage of the gut microbiome in allogeneic HCT recipients may lead to adverse outcomes including CDI, VRE colonization and potentially fatal bacteremia and aGVHD. A previously completed placebo-controlled Phase 2b clinical trial of 412 patients demonstrated SYN-004 protected the gut microbiome from antibiotic-mediated dysbiosis. Patients who received SYN-004 also demonstrated significantly better maintenance and recovery of the gut microbiome as well as lower incidences of new colonization by opportunistic and potentially pathogenic microorganisms such as VRE.

About Synthetic Biologics, Inc.

Synthetic Biologics, Inc. (NYSE American: SYN) is a diversified clinical-stage company

leveraging the microbiome to develop therapeutics designed to prevent and treat gastrointestinal (GI) diseases in areas of high unmet need. The Company's lead candidates are: (1) SYN-004 (ribaxamase) which is designed to degrade certain commonly used intravenous (IV) beta-lactam antibiotics within the gastrointestinal (GI) tract to prevent (a) microbiome damage, (b) *Clostridioides difficile* infection (CDI), (c) overgrowth of pathogenic organisms, (d) the emergence of antimicrobial resistance (AMR), and (e) acute graft-versus-host-disease (aGVHD) in allogeneic hematopoietic cell transplant (HCT) recipients, and (2) SYN-020, a recombinant oral formulation of the enzyme intestinal alkaline phosphatase (IAP) produced under cGMP conditions and intended to treat both local GI and systemic diseases. 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 data readout from the first cohort towards the end of 2021, the potential of SYN-004 to significantly improve outcomes for allogenic HCT recipient and the intended benefits to be derived from SYN-004 and SYN-020. 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 provide data towards the end of 2021, the ability to continue to comply with 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 and/or beginning enrollment as expected, a failure to receive the necessary regulatory approvals for commencement of clinical trials and 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-020 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' Form 10-K for the year ended December 31, 2020 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

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