Synthetic Biologics Announces *Journal for ImmunoTherapy of Cancer* Publication of Phase 1 Trial of Intravenous VCN-01 Oncolytic Adenovirus in Patients With Advanced Solid Tumors

-Data support VCN-01 acceptable safety profile with encouraging biological and clinical activity, and identify recommended Phase 2 dose (RP2D)-

-Publication further supports the development of Synthetic Biologics' novel oncolytic adenovirus (OV) platform-

Rockville, MD, March 28, 2022 – Synthetic Biologics, Inc. (NYSE American: SYN), a diversified clinical-stage company developing therapeutics designed to treat diseases in areas of high unmet need, today announced the peer-reviewed publication of a Phase 1, multicenter, open-label, dose-escalation study investigating the therapeutic potential of intravenous VCN-01 oncolytic adenovirus with or without standard-of-care (SoC) chemotherapy (gemcitabine/nab-paclitaxel) in patients with advanced solid tumors. The data, published in the *Journal for ImmunoTherapy of Cancer,* suggests that treatment with VCN-01 is feasible and has an acceptable safety profile, with encouraging biological and clinical activity. These findings provide valuable dose-finding context and inform the clinical development strategy for VCN-01.

"The results in this publication support VCN-01 administration intravenously at doses ≥$3.3x10^{12}$ vp/patient, resulting in viral exposure in the primary tumor and liver metastases, replication within the tumor, and the potential to remodel the tumor matrix to further promote tumor inflammation," said Manel Cascalló, Ph.D., General Director of Synthetic Biologics' European Subsidiary. "These clinical data underscore VCN-01's differentiated mechanism of action and were used to inform our Phase 2 study in patients with metastatic pancreatic adenocarcinoma, which is expected to initiate in the second half of 2022. More broadly, these results will help guide our rapidly advancing clinical program for VCN-01 and further support the development of our novel OV platform."

In the Phase 1, multicenter, open-label, dose-escalation study (NCT02045602), researchers evaluated the administration of a single dose of VCN-01 alone, in patients with solid tumors (Part I), or in combination with SoC chemotherapy (gemcitabine/nab-paclitaxel) in patients with locally advanced or metastatic, unresectable, pancreatic adenocarcinoma (Parts II and III). In Part II, the VCN-01 was administered on the same day as the first dose of chemotherapy (Concomitant Regimen) and in Part III the VCN-01 was administered 7-days prior to the first dose of chemotherapy (Sequential Regimen). The objective was to determine the maximum tolerated dose (MTD)/recommended Phase 2 dose (RP2D) and dose-limiting toxicity (DLT) of the intravenous delivery of the replication-competent VCN-01 adenovirus.

Overall, systemic VCN-01 was well tolerated in the patient population. The most common treatment-related adverse events (AEs) were pyrexia, flu-like symptoms and increases in liver transaminases. These AEs were dose-dependent, reversible and consistent with AEs previously described for other adenovirus-based products. In Part II, transient increases in neutropenia and thrombocytopenia were observed when VCN-01 in combination with gemcitabine/nab-paclitaxel was administered using the Concomitant Regimen, and one patient suffered a fatal episode of enterocolitis and thrombocytopenia. The AE profile

was significantly reduced in Part III when VCN-01 and gemcitabine/nab-paclitaxel was administered using the Sequential Regimen, and was similar to the observed AE profile when VCN-01 was administered alone. There were no dose limiting toxicities observed in patients administered VCN-01 using the Sequential Regimen. The investigators determined the RP2D was $1x10^{13}$ viral particles (vp)/patient in Part I and Part III, and $3.3x10^{12}$ vp/patient in Part II.

The Phase 1 study provided encouraging clinical results and further confirmed the proposed VCN-01 mechanism of action. In patients with pancreatic adenocarcinoma, overall response rates were 50% (Part II) and 50% (Part III). VCN-01 viral genomes were detected in tumor tissue in five out of six biopsies (primary pancreatic tumor and liver metastases) on day eight. A second peak of virus concentrations in plasma and increased serum hyaluronidase levels suggest replication after IV injection in all patients. Higher peaks of hyaluronidase serum levels were associated with maximum tumor shrinkage and increased levels of immune biomarkers (IFNγ, sLAG3, IL-6, IL-10) were found in sera after VCN-01 administration. Several markers of tumor inflammation (including CD8 infiltration and indoleamine 2, 3-dioxygenase [IDO] upregulation) were described in tumor biopsies indicating that VCN-01 promotes a change in the tumor immune environment.

Synthetic Biologics anticipates the initiation of multiple international studies, including a Phase 2 clinical trial of intravenous VCN-01 in combination with SoC chemotherapy using the Sequential Regimen as a first-line therapy in newly diagnosed metastatic pancreatic adenocarcinoma patients in the fourth quarter of 2022, as well as a Phase 2/3 pivotal trial of intravitreal VCN-01 as either an adjunct to chemotherapy or a potential rescue therapy in pediatric patients with advanced retinoblastoma in early 2023.

About Synthetic Biologics, Inc.

Synthetic Biologics, Inc. (NYSE American: SYN) is a diversified clinical-stage company developing therapeutics designed to treat diseases in areas of high unmet need. The Company recently consummated the acquisition of VCN Biosciences, S.L. (VCN), which is developing a new oncolytic adenovirus (OV) platform designed for intravenous (IV), intravitreal and antitumoral delivery to trigger tumor cell death, improve access of co-administered cancer therapies to the tumor, and promote a robust and sustained anti-tumor response by the patient's immune system. In addition, the Company's lead candidates are: (1) SYN-004 (ribaxamase) which is designed to degrade certain commonly used 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.

Forward-Looking Statements

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 include statements regarding treatment with VCN-01 being feasible and having an acceptable safety profile, the administration of VCN-01 intravenously at doses ≥3.3x1012 vp/patient resulting in viral exposure in the primary tumor, liver metastases and replication within the tumor, as well as the potential to remodel the tumor matrix to further promote tumor inflammation, initiating a Phase 2 study of VCN-01 in patients with metastatic pancreatic adenocarcinoma in the second half of 2022 and plans to initiate multiple international studies, including a Phase 2 clinical trial of intravenous VCN-01 in combination with SoC chemotherapy using the Sequential Regimen as a first-line therapy in newly diagnosed metastatic pancreatic adenocarcinoma patients in the fourth quarter of 2022, as well as a Phase 2/3 pivotal trial of intravitreal VCN-01 as either an adjunct to chemotherapy or a potential rescue therapy in pediatric patients with advanced retinoblastoma in early 2023. 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; the ability to complete clinical trials on time and achieve the desired results and benefits; continuing clinical trial enrollment as expected; the ability to obtain regulatory approval for commercialization of product candidates or to comply with ongoing regulatory requirements, regulatory limitations relating to Synthetic Biologics' and VCN's ability to promote or commercialize their product candidates for the specific indications; acceptance of product candidates in the marketplace and the successful development, marketing or sale of Synthetic Biologics' and VCN's products; developments by competitors that render such products obsolete or non-competitive; Synthetic Biologics' and VCN's ability to maintain license agreements;, the continued maintenance and growth of Synthetic Biologics' and VCN's patent estate; the ability to continue to remain well financed;, and other factors described in Synthetic Biologics' Annual Report on Form 10-K for the year ended December 31, 2021 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.

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