September 5, 2022

Synthetic Biologics Announces Presentation at ESMO Congress 2022 Describing Phase 1 Investigator-sponsored Study Evaluating VCN-01 in Combination with Durvalumab in Patients with Recurrent/ Metastatic Squamous Cell Carcinoma of the Head and Neck

-Treatment with VCN-01 in combination with durvalumab demonstrated an acceptable safety profile and encouraging biological activity-

ROCKVILLE, Md., Sept. 05, 2022 (GLOBE NEWSWIRE) -- 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 a presentation of initial data from a Phase 1 investigator-sponsored study evaluating VCN-01 in combination with durvalumab for patients with recurrent/metastatic squamous cell carcinoma of the head and neck (R/M HNSCC). Data will be featured in a poster presentation at the European Society for Medical Oncology (ESMO) Congress, being held both virtually and in Paris from September 9-13, 2022.

“We are encouraged by the acceptable safety profile seen in the sequential arm of this study as well as the biological activity observed in R/M HNSCC patients previously treated with anti-PD(L)-1 agents, which speak to the promise of VCN-01-based combination approaches for devastating cancers with high unmet need,” said Manel Cascalló, Ph.D., General Director of Synthetic Biologics’ European Subsidiary. “Further, these results provide valuable dose-finding context and build upon our compelling foundation of data that highlight VCN-01’s differentiated mechanism of action that may transform cancer therapy. We look forward to leveraging our findings as we advance VCN-01 through clinical development and we remain on track to deliver on several value-driving milestones, including the initiation of our Phase 2 study in patients with metastatic pancreatic adenocarcinoma in the fourth quarter of 2022 and our Phase 2/3 study in retinoblastoma in the second half of 2023.”

Key data and conclusions featured in the ESMO presentation include:

- **Safety**: Treatment with VCN-01 had an acceptable safety profile when administered with durvalumab in the sequential regimen (single dose of VCN-01 administered 14 days prior to the first dose of durvalumab; n=14).
    - The most common treatment-related adverse events (TRAEs) were pyrexia, flu-

like symptoms and increases in liver transaminases.
    - TRAEs were dose-dependent, reversible and consistent with TRAEs previously described for other adenovirus-based products.
- **Pharmacokinetics (PK) and pharmacodynamics (PD)**: Based on toxicology and PK/PD analysis the recommended Phase 2 dose is $1x10^{13}$ viral particles (vp)/patient.
- **Biological activity**: Sustained blood levels of VCN-01 viral genomes and increased serum hyaluronidase levels were maintained for over six weeks.
    - Observed an increase in CD8 T cells, a marker of tumor inflammation and an upregulation of PD-L1 in tumors.
    - Analysis of serial tumor biopsies revealed differential gene expression profiles and downregulation of matrix-related pathways after VCN-01 administration.

The full abstract (#1231P) is accessible on the ESMO Congress portal and the e-Poster will be available on-demand starting Saturday, September 10 at 9:00 a.m. CEST. Additional details of the poster are provided below.

- Title: Phase I Study to Evaluate the Safety, Tolerability, and Efficacy of VCN-01 in Combination With Durvalumab (MEDI4736) in Subjects With Recurrent/ Metastatic Squamous Cell Carcinoma of the Head and Neck (R/M HNSCC)
- Presenting Author: Dr. Ricard Mesia (Head of the Medical Oncology Department at Institut Català d'Oncologia- Barcelona, Spain)
- Poster Session Date and Time: Monday, September 12 at 12:00 p.m. CEST

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 advanced into oncology through the acquisition of VCN Biosciences, S.L. (VCN), who have developed a new oncolytic adenovirus 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. The Company's lead candidates are: (1) VCN-01, an oncolytic adenovirus designed to replicate selectively and aggressively within tumor cells, and to degrade the tumor stroma barrier that serves as a significant physical and immunosuppressive barrier to cancer treatment; (2) 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 (3) 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 Statement

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 the promise of VCN-01-based combination approaches for devastating cancers with high unmet need, VCN-01's differentiated mechanism of action transforming cancer therapy, leveraging findings as VCN-01 is advanced through clinical development, and remaining on track to deliver on several value-driving milestones, including the initiation of our Phase 2 study in patients with metastatic pancreatic adenocarcinoma in the fourth quarter of 2022 and our Phase 2/3 study in retinoblastoma in the second half of 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, VCN-01's differentiated mechanism of action transforming cancer therapy, Synthetic Biologics' and VCN's ability to reach clinical milestones when anticipated including initiation of a Phase 2 study in patients with metastatic pancreatic adenocarcinoma in the fourth quarter of 2022 and a Phase 2/3 study in retinoblastoma in the second half of 2023 , Synthetic Biologics' ability to successfully combine and operate the business of Synthetic Biologics and VCN, Synthetic Biologics' and VCN's product candidates demonstrating safety and effectiveness, as well as results that are consistent with prior results; 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 current reports on Form 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.

For further information, please contact:

Investor Relations:

Chris Calabrese

LifeSci Advisors, LLC

ccalabrese@lifesciadvisors.com

917-680-5608

Source: Synthetic Biologics, Inc.