Gradalis Announces Peer-Reviewed Publication Demonstrating Potential of Novel 3D Scaffold Tissue Technology to Expand Vigil Platform

- *Technology leverages new coating process to create 3D scaffold matrix that is designed to mimic the tumor microenvironment and enable large scale tumor cell expansion*
- *Demonstrated successful increase in cell number by 38-fold with plans to use scaffold expanded tissue platform for future Vigil product construction*
- *Technology developed in collaboration with the Lahann lab at Biointerfaces Institute at the University of Michigan*

Dallas, Texas, June 6, 2023 – Gradalis Inc. announced the peer-reviewed publication in *Advanced NanoBioMed*, highlighting the therapeutic applications of a new extracellular matrix platform developed for tumor cell expansion in collaboration with the University of Michigan Biointerfaces Institute. The publication entitled, "A Scalable Engineered Extracellular Matrix Platform to Expand Tumor Cells," provides proof of principle for a large-scale three-dimensional (3D) platform that is designed for high throughput cell proliferation with clinical applications and potential use for Vigil product construction.

"We are encouraged by the transformational work that has advanced our 3D scaffold framework for the optimization of cellular growth, which has broad potential clinical applications," said Joerg Lahann, PhD Director, Biointerfaces Institute and Wolfgang Pauli Collegiate Professor of Chemical Engineering. "Compared to conventional tissue culturing systems, our system leverages a new coating process that successfully mimics the tumor microenvironment and enables large platform scalability. Further, results demonstrated that murine colorectal carcinoma cells grown on 3D scaffold rapidly reached a 38-fold increase and generally maintained their RNA expression profile."

The scaffold technology developed by the Lahann Lab, is a modular tissue engineering system with the ability to precisely control mechanical properties, protein composition and cellular constituents of cancer cellular growth and survival. Electrohydrodynamic (EHD) co-jetting is conducted to print hyper-porous polymer frameworks of stacked polymer fibers, creating3D compartments that can be optimized for growth advantage. The polymer scaffold is then coated with selected EHD proteins such as fibronectin to form a unique engineered extracellular matrix (ECM) for further growth optimization.

John Nemunaitis, MD., CSO of Gradalis, commented, "We look forward to utilizing this technology to further advance Vigil, a novel, personalized cellular immunotherapy platform that is designed to decloak the full repertoire of a patient's tumor antigens, reactivate the immune system, and summon key effector cells to deliver a durable anticancer clinical response. The magnitude of cell expansion would enable Vigil product to be constructed from much smaller tumor masses, potentially eliminating the need for surgical extraction and enabling a safer procedure for initial tumor harvest. This could expand the treatment opportunity of Vigil to a much larger population and across further indications."

Additional testing is ongoing in human tissue in preparation for IND development and Vigil clinical testing involving cancer patients with minimal resectable disease. The full text of the article can be found here. Highlights include:

- **Proof of Principle was demonstrated for a large-scale 3D scaffold platform:** Uniform fibrinogen deposition was achieved using a double coating process
- **Successful cell growth and re-expansion of a murine colorectal carcinoma cell line:** Following initial expansion on 3D scaffolds, cells were able to be isolated and re-expanded on a greater number of scaffolds to achieve increased cell harvest
- **Expansion of tumor tissue on 3D scaffolds for successful Vigil construction**

About Vigil
Vigil® is a novel, triple function immunotherapy platform that modifies a patient's tumor by using bi-shRNA to reduce furin, an enzyme which facilitates immunosuppressive TGF beta protein production, and to maximize DNA expression of GM-CSF, which stimulates the immune system and attracts key immune system effector cells, including T cells. By utilizing the patient's own tumor as the antigen source, Vigil is designed to elicit an immune response that is specifically targeted and broadly relevant to each patient's unique "clonal" tumor neoantigens. Vigil therapy has been well tolerated in Phase 1, 2a and 2b clinical studies.

In VITAL, a multicenter, randomized, double-blind, placebo-controlled Phase 2b trial in Stage III/IV newly diagnosed, frontline ovarian cancer patients, Vigil showed a positive trend in the primary endpoint of recurrence free survival (RFS) in the overall population and a statistically significant improvement in the secondary endpoint of recurrence free survival and overall survival (OS), with a median survival time of three years to date, in patients with the BRCAwt molecular profile. Importantly in patients with tumors of the HRP type, where there is a high unmet medical need, a statistically significant improvement was seen in RFS and OS.

Additionally, Phase 1 results in an "all-comer" clinical trial showed positive signals of activity in 19 tumor types and some patients treated with Vigil remained in the study 48 months later. The company is preparing to initiate a Phase 2 clinical study in platinum sensitive recurrent ovarian cancer patients with the HRP molecular profile.

About Gradalis, Inc.
Founded in 2003, Gradalis is a privately held, late-stage clinical biotechnology company developing a personalized immunotherapy called Vigil, that has been tested in multiple studies in ovarian and other cancer tumor types. Vigil is the first cellular immunotherapy to demonstrate survival benefits in a randomized controlled trial of patients with solid tumors. The results of the company's Phase 2b study have been published in *Lancet Oncology* and presented at the American Society of Clinical Oncology. Vigil is being studied in other women's cancer types and has shown positive results in combination with checkpoint inhibitors.

Gradalis' Vigil platform uses the patient's immune system to target the entire tumor. Based on multiple clinical studies, Gradalis has developed an oncology platform that is designed to decloak the full repertoire of a patient's tumor antigens, reactivate the immune system, and summon key effector cells to deliver a durable clinical response. When combined, these are a powerful Trifecta of anti-cancer activities, potentially eliminating even the elusive metastatic cells, and as shown in Phase 2 clinical studies in ovarian cancer, a potential gamechanger in oncology. Our clinical trials have also demonstrated that Gradalis' platform is better tolerated compared to standard cancer treatments since Vigil uses the patient's immune system operating within its natural state of balance rather than in an artificial overdrive as with some

technologies. Vigil utilizes proprietary bi-shRNA technology that has been proven to silence multiple genes in a variety of cancers and has the potential to be used in other diseases.

Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements regarding the success, cost, and timing of our product development activities and clinical trials, our plans to research, develop, and commercialize our product candidates, and our plans to submit regulatory filings and obtain regulatory approval of our product candidates. These forward-looking statements are based on Gradalis' current expectations and assumptions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks, and changes in circumstances that may differ materially from those contemplated by the forward-looking statements, which are neither statements of historical fact nor guarantees or assurances of future performance. Important factors that could cause actual results to differ materially from those in the forward-looking statements include but are not limited to: (a) the timing, costs, and outcomes of our clinical trials and preclinical studies, (b) the timing and likelihood of regulatory filings and approvals for our product candidates, and (c) the potential market size for our product candidates. These forward-looking statements speak only as of the date made and, other than as required by law, we undertake no obligation to publicly update or revise any forward-looking statements. This press release does not constitute an offer to sell, or a solicitation of an offer to buy, any securities.

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