Gritstone Oncology Announces First Patient Dosed with SLATE, its "Off-The-Shelf" Neoantigen Immunotherapy

August 14, 2019

First patient dosed is a metastatic non-small cell lung cancer patient with a KRAS G12C mutation

EMERYVILLE, Calif., Aug. 14, 2019 (GLOBE NEWSWIRE) -- Gritstone Oncology, Inc. (Nasdaq: GRTS), a clinical-stage biotechnology company developing the next generation of immunotherapies to fight multiple cancer types, today announced that the first SLATE patient has been dosed. SLATE is an investigational immunotherapy directed at shared tumor-specific neoantigens (TSNA) which are derived from driver mutations, functionally important gene alterations recurrently observed in cancer patients (such as *KRAS*). Gritstone has used its proprietary EDGE™ artificial intelligence platform to identify the top twenty immunogenic shared TSNA to engineer into the cassette of its first SLATE immunotherapy. SLATE is designed to induce robust anti-tumor T-cell responses that result in selective tumor cell destruction through the recognition of TSNA on tumor cells. The ongoing Phase 1 study is evaluating SLATE in combination with the anti-PD-1 antibody nivolumab and the anti-CTLA-4 antibody ipilimumab for the treatment of patients with advanced solid tumors, including metastatic lung adenocarcinoma, pancreatic ductal carcinoma and microsatellite-stable colorectal cancer, as well as in patients with other solid tumor types who have relevant mutation/HLA (human leukocyte antigen) combinations. This study is being conducted by Gritstone, under a clinical collaboration agreement with Bristol-Myers Squibb.

"Our ability to predict common shared neoantigens using EDGE is one of the unique differentiators for SLATE," said Andrew Allen, M.D., Ph.D., co-founder, president and chief executive officer of Gritstone Oncology. "The robustness of the prediction model is important as not all driver mutations create neoantigens in tumors. To act as a neoantigen, a mutated protein must be processed by the tumor cell into a short mutant peptide which is stably presented on the cell surface by an HLA molecule. It is this HLA-peptide complex that is recognized by cytotoxic T cells. Using EDGE, we predicted common shared neoantigens, and directly observed many of them on the surface of human tumor samples with immunopeptidomics. The existence of T-cell precursors against the neoantigens was demonstrated for the majority of cases examined. We have identified shared neoantigens in well-known driver mutations, such as *KRAS* (G12C, G12D, G12V, etc.) and *TP53*, that are often found in common tumor types."

Dr. Allen continued, "This has enabled us to develop an 'off-the-shelf' immunotherapy for patients who, following routine tumor mutation and blood HLA analysis, are expected to possess at least one shared neoantigen contained in the SLATE immunotherapy on their tumor. The appeal of SLATE lies in the potential for one pre-made therapy to target tumor-specific mutations across a number of patients and cancer types. We are pleased to have been able to advance this study well ahead of schedule and look forward to presenting preliminary data at year-end."

SLATE immunotherapy consists of two components: first, a priming adenoviral vector, that has been shown to be highly immunogenic in humans in other disease settings, is used to deliver the cassette of 20 shared TSNA; and second, the same shared TSNA cassette is delivered using a self-amplifying RNA vector in a repeated boost sequence to drive and sustain high numbers of tumor-targeted T cells. To develop SLATE, Gritstone is utilizing its genomics, proteomics, and informatics labs in Cambridge, MA and its 43,000 square foot biomanufacturing facility in Pleasanton, CA. Additionally, the company partners with third-party contract manufacturing organizations such as AmpTec GmbH, a leading provider of RNA technology products and GMP manufacturing, to support the production of SLATE for clinical trial use.

About EDGE™ (Epitope Discovery in cancer Genomes) Platform

The EDGE artificial intelligence platform is designed to be a best-in-class tool for the identification of tumor neoantigens presented on the surface of tumor cells. Neoantigens identified by EDGE are being utilized in our lead immunotherapy programs, GRANITE and SLATE, to educate the immune system to attack these key tumor targets. EDGE's prediction model was initially trained using a large dataset of human tumor and normal tissue samples with paired class I HLA-presented peptide sequences, HLA types and transcriptome RNA sequencing. The training dataset for EDGE includes hundreds of tumor and normal tissue samples, yielding over one million peptides, from patients of various ancestries with diverse HLA types. EDGE leverages a novel integrated neural network model architecture to model key features that are essential for accurate prediction of true tumor-specific neoantigens. Data demonstrating the neoantigen identification capabilities of EDGE were published in Nature Biotechnology in December 2018. EDGE is also increasingly capable of predicting class II HLA-presented peptides, as presented at the American Association for Cancer Research meeting in 2019, which we expect to leverage in the antigen selection process for the design of future product cassettes. Gritstone has issued patent coverage on EDGE.

About Gritstone Oncology

Gritstone Oncology (Nasdaq: GRTS), a clinical-stage biotechnology company, is developing the next generation of cancer immunotherapies to fight multiple cancer types. Gritstone develops its products by leveraging two key pillars—first, a proprietary machine learning-based platform, Gritstone EDGE™, which is designed to predict, from a routine tumor biopsy, the tumor-specific neoantigens (TSNA) that are presented on a patient's tumor cells; and second, the ability to develop and manufacture potent immunotherapies utilizing patients' TSNA to potentially drive the patient's immune system to specifically attack and destroy tumors. The company's lead product candidate, GRANITE, is a personalized neoantigen-based immunotherapy in Phase 1 clinical testing. Gritstone's second product candidate, SLATE, is a shared neoantigen, "off-the-shelf" immunotherapy which is also being evaluated in a Phase 1 clinical study. Novel tumor-specific antigens can also provide targets for bispecific antibody (BiSAb) therapeutics

for solid tumors, and Gritstone's BiSAb program is currently in lead optimization. For more information, please visit gritstoneoncology.com.

Gritstone Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to the expected timing for preliminary efficacy data from the Phase 1 SLATE study and its investigational immunotherapies. Such forward-looking statements involve substantial risks and uncertainties that could cause Gritstone's research and clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainties inherent in the drug development process, including Gritstone's programs' early stage of development, the process of designing and conducting preclinical and clinical trials, the regulatory approval processes, the timing of regulatory filings, the challenges associated with manufacturing drug products, Gritstone's ability to successfully establish, protect and defend its intellectual property and other matters that could affect the sufficiency of existing cash to fund operations. Gritstone undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the company in general, see Gritstone's most recent Quarterly Report on Form 10-Q filed on August 12, 2019 and any current and periodic reports filed with the Securities and Exchange Commission.

Contacts
Media:
Dan Budwick
1AB
(973) 271-6085
dan@1abmedia.com

Investors:
Alexandra Santos
Wheelhouse Life Science Advisors
(510) 871-6161
asantos@wheelhouselsa.com

Source: Gritstone Oncology, Inc