Gritstone Oncology Announces Data on Novel Shared Tumor-Specific Neoantigens Identified by its EDGE Platform and Contained Within its SLATE Immunotherapy

November 5, 2019

-Poster Presentation at SITC 2019 Annual Meeting-

EMERYVILLE, Calif., Nov. 05, 2019 (GLOBE NEWSWIRE) -- Gritstone Oncology, Inc. (Nasdaq: GRTS), a clinical-stage biotechnology company developing the next generation of cancer immunotherapies to fight multiple cancer types, today announced data on novel shared tumor-specific neoantigens (TSNA) arising from recurrent cancer driver mutations that have been identified by its EDGE platform. These functionally important gene alterations recurrently observed in cancer patients have been engineered into its first SLATE immunotherapy, which is being evaluated in a Phase 1 clinical study and is designed to generate a potent T cell response that is specific to those encoded neoantigens, thereby driving selective tumor cell destruction. These data will be included in a poster presentation on November 8, 2019 from 7:00 a.m. to 8:00 p.m. ET at the Society for Immunotherapy of Cancer's 34th annual meeting (SITC 2019) in National Harbor, MD.

“Real tumor-specific neoantigens are rare, representing just one to two percent of all tumor mutations,” said Roman Yelensky, Ph.D., executive vice president and chief technology officer of Gritstone Oncology. “The challenge in identifying TSNA lies in the complication that in order to be a real neoantigen, a mutated gene must be made into a protein, processed into a short peptide and then presented on the tumor cell surface by a human leukocyte antigen (HLA) molecule. Through our extensive work on the development of EDGE, we have identified sequence patterns within mutation fragments (i.e. peptides) which are most likely to be presented. The fact that within a short period of time we have been able to identify several new shared TSNA on human tumors that have not been previously characterized– significantly increasing the number of shared neoantigens known -- speaks to the power of our EDGE platform.”

Andrew Allen, M.D., Ph.D., co-founder, president and chief executive officer of Gritstone Oncology added, “We believe that a significant minority of patients with certain common cancers may have class I shared neoantigens, including up to approximately 10-15% in lung and colon cancer. Shared neoantigens are most prevalent in cancers driven by KRAS mutations, and many shared neoantigens are shared across indications. This has enabled us to design an off-the-shelf neoantigen-directed immunotherapy, SLATE, which is now in a Phase 1 clinical trial. These shared TSNA may also be used as targets for other immunotherapy approaches, such as bispecific antibodies or adoptive cell therapy. Importantly, through this work, we are developing a valuable intellectual property portfolio covering the use of these newly identified TSNA as part of neoantigen-targeted immunotherapy.”

In order to identify shared TSNA, the neoantigen landscape across human cancer was comprehensively characterized using accurate prediction of HLA class I peptide presentation by EDGE. From over 24,000 patients with clinical cancer gene sequencing data, EDGE ranked a large number of candidate mutation/HLA pairs based on the probability of HLA-peptide presentation. EDGE predicted nearly 200 mutations to be possible shared neoantigens across indications. Through targeted HLA class I peptide mass spectrometry sequencing of human tumors and a novel *in vitro* system, Gritstone was able to demonstrate HLA presentation of more than 10 new HLA class I shared neoantigens, many of which were directly observed on real human tumors. This work is ongoing to evaluate the full set of TSNA predictions. Importantly, the immunogenicity of several of these shared neoantigens was confirmed by demonstrating the presence of cognate T-cell precursors in healthy donors. The poster can be accessed on the Investors & Media section of the Gritstone Oncology website at https://ir.gritstoneoncology.com/investors/presentations.

Poster Presentation Details

Title:	Identification and Validation of Shared Neoantigens for Cancer Immunotherapy
Abstract ID:	P731
Date:	Friday, November 8, 2019
Time:	7:00 a.m. – 8:00 p.m. ET
Location:	Poster Hall (Prince George AB)

Ongoing Phase 1/2 Clinical Study

SLATE in combination with immune checkpoint blockade is being evaluated in a Phase 1/2 clinical study called GO-005 for the treatment of patients with advanced solid tumors, including metastatic non-small cell lung cancer, pancreatic ductal adenocarcinoma and microsatellite-stable colorectal cancer, as well as in patients with other solid tumor types who have relevant mutation/HLA (human leukocyte antigen) combinations. In the dose-escalation Phase 1, all patients receive a fixed dose of intramuscular adenovirus-based prime with three escalating doses (30, 100 and 300 µg) of intramuscular RNA-based boost vaccinations in combination with intravenous anti-PD-1 therapy. Following dose escalation of the RNA-based boost vaccine to 30 µg, subcutaneous anti-CTLA-4 is added to the treatment regimen.

About SLATE

SLATE is Gritstone’s shared neoantigen (“off-the-shelf”) immunotherapy. It is engineered to elicit a significant T-cell response (particularly CD8+ cytotoxic T cells) against encoded TSNA. 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 designed to drive and sustain high numbers of tumor-targeted T cells. These TSNA were identified by Gritstone using the EDGE artificial intelligence platform and tumor HLA peptide sequencing, and represent mutated gene sequences that are shared across patients (such as KRAS mutations). Suitable patients must possess both the appropriate DNA mutation and, importantly, a relevant HLA type that can present the mutant sequence to the patient's T cells. Gritstone is continuing its research efforts to identify new TSNA which can enable the development of additional SLATE product candidates targeting different mutations and/or tumor types.

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 potential of Gritstone's therapeutic programs. 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.

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Source: Gritstone Oncology, Inc