Gritstone Presents Positive Initial Phase 2 Data in Late-Line Solid Tumor Patients Treated With KRAS-Directed Immunotherapy (SLATE) at ESMO 2022

September 12, 2022

-- SLATE vaccines (version 1 and SLATE-KRAS) demonstrate early evidence of efficacy with a 39% molecular response rate in evaluable patients with late-line microsatellite-stable colorectal cancer (MSS-CRC) and non-small cell lung cancer (NSCLC) --

-- Molecular response, as measured by reduction in circulating tumor DNA (ctDNA) from baseline, demonstrates a correlation with overall survival (OS) in NSCLC, consistent with industry literature --

-- SLATE-KRAS vaccine candidate elicits robust KRAS neoantigen-specific CD8+ T cell responses --

-- Data support moving SLATE-KRAS into earlier lines of treatment --

EMERYVILLE, Calif., Sept. 12, 2022 (GLOBE NEWSWIRE) -- Gritstone bio, Inc. (Nasdaq: GRTS), a clinical-stage biotechnology company that aims to develop the world's most potent vaccines, presented positive safety, immunogenicity, and early efficacy data from its SLATE program, an "off-the-shelf" vaccine program targeting shared neoantigens, in combination with immune checkpoint blockade, for patients with advanced solid tumors at the 2022 European Society for Medical Oncology (ESMO) Congress. The presentation included initial data with SLATE-KRAS, a shared mutant KRAS-specific neoantigen vaccine candidate, in addition to updated data using the first version of the vaccine candidate (SLATE v1), which contains both KRAS and non-KRAS neoantigens. The data were presented by Chrisann Kyi, MD of Memorial Sloan Kettering Cancer Center during a mini-oral presentation on Saturday, September 10th.

This Phase 1/2 study (NCT03953235) is evaluating the safety, immunogenicity, and early clinical activity of both SLATE v1 and SLATE-KRAS in combination with PD-1 checkpoint inhibitor Opdivo® (nivolumab) and subcutaneous anti-CTLA-4 antibody Yervoy® (ipilimumab) in patients with metastatic solid tumors harboring select KRAS mutations. SLATE v1 targets 20 shared neoantigens from KRAS, TP53, β-catenin, and BRAF genes, while SLATE-KRAS is optimized to exclusively target KRAS neoantigens including the highly prevalent G12C, G12D, G12V and Q61H driver mutations. Gritstone developed the KRAS-optimized candidate (SLATE-KRAS) after initial testing of SLATE v1 suggested non-KRAS neoantigens (including TP53) might exhibit immunodominance over $KRAS^{mut}$, thus attenuating efficacy.

A total of 38 patients with advanced solid tumors have been enrolled in the study across cohorts using SLATE v1 (n=26) or SLATE-KRAS (n=12). The majority of patients enrolled (31/38) had either advanced non-small cell lung cancer (NSCLC; n=18) or microsatellite stable colorectal cancer (MSS-CRC; n=13).

In the Phase 1/2 study, both SLATE-KRAS and SLATE v1 vaccine-based immunotherapies demonstrated:

- A favorable safety and tolerability profile
  - Majority of treatment-related adverse events were Grade 1/2, with three ≥ Grade 3 events reported with SLATE v1 and no ≥ Grade 3 events reported with SLATE-KRAS
- Consistent and potent immunogenicity
  - Induction of KRAS-specific CD8+ T cells: 55% of patients treated with SLATE-KRAS versus 31% of patients treated with v1 (by ex vivo ELISpot assay)
- Early objective evidence of efficacy as measured by reduction in ctDNA (molecular response)
  - 39% (7/18) molecular response rate in evaluable patients with MSS-CRC and NSCLC. Evaluable subjects had detectable $KRAS^{mut}$ ctDNA at baseline and a post-baseline sample. All patients with NSCLC had progressed on prior (chemo)immunotherapy.
  - In 18 patients with NSCLC, a molecular response was correlated with extended OS. NSCLC patients with a molecular response demonstrated a median OS (9.6 months) more than double those without (4.5 months). The OS analysis included patients with no detectable ctDNA or no data at baseline (n=7) in the "no molecular response group." At the time of data cut-off, there were insufficient evaluable patients in the CRC patient set to support a similar analysis.

Additionally, treatment with SLATE-KRAS induced a molecular response (normalization of tumor markers and reduction in ctDNA) and clinical benefit were observed in a patient with Stage IV KRAS G12V mutant MSS-CRC and multiple liver metastases who had progressed on two prior therapies.

"We are highly encouraged by the early signs of efficacy from the SLATE immunotherapy program, in particular, from our product candidate targeting multiple KRAS oncogenic mutations in patients with advanced, treatment-refractory disease (SLATE-KRAS)," said Andrew Allen, M.D., Ph.D., Co-founder, President, and Chief Executive Officer of Gritstone. "We observe molecular responses in approximately 40% of all evaluable subjects receiving SLATE, and those seen in our NSCLC patients are correlating nicely with extended overall survival, which has been described in recent publications with checkpoint inhibitors. This relationship between OS and ctDNA response was also observed in our GRANITE individualized immunotherapy study in patients with advanced CRC, as published recently in Nature Medicine. Patients with NSCLC without a molecular response

had a median overall survival of just 4.5 months, underscoring the encouraging efficacy signal with SLATE in this challenging context with high unmet need for alternative treatment options. The clinical and mechanistic observations across our shared and individualized neoantigen vaccine programs is strikingly consistent, as is the favorable safety and tolerability profile, reinforcing the therapeutic potential of our oncology vaccine programs."

Karin Jooss, Ph.D., Head of R&D, added, "SLATE-KRAS was optimized to simultaneously target multiple KRAS mutations with the aim of driving robust immunity across a broad array of KRAS positive tumor types. Vaccines targeting neoantigens identified from common oncogenic driver mutations are of increasing interest. The results shared at ESMO highlight our ability to develop and deliver differentiated, targeted vaccine candidates that can generate robust and durable immune responses in patients with late-line cancer. These data also support moving SLATE-KRAS into earlier lines of therapy to allow the immune system more opportunity to mount a robust immune response to neoantigens after multiple vaccination boosts before progression. We look forward to providing additional data and longer follow-up from the SLATE program in 2023."

Opdivo® and Yervoy® are trademarks of Bristol-Myers Squibb Company.

About SLATE
Gritstone's neoantigen-based immunotherapy candidates are engineered to elicit a significant T cell response (particularly CD8+ cytotoxic T cells) against mutation-derived tumor-specific neoantigens, or TSNA, that are identified by Gritstone using its proprietary EDGE™ artificial intelligence platform and tumor HLA peptide sequencing. Gritstone's SLATE "off-the-shelf" immunotherapy program uses a priming adenoviral vector and a self-amplifying mRNA (samRNA) vector to deliver a cassette of shared TSNA, representing mutated gene sequences that are found in multiple patients (such as KRAS mutations). A KRAS-specific product candidate, SLATE-KRAS, is being evaluated in combination with immune checkpoint blockade in the Phase 2 portion of its clinical study (NCT03953235). The SLATE program represents the potential to develop a suite of "off-the-shelf" product candidates that target tumor-specific mutations across a number of patient populations and cancer types.

About Gritstone
Gritstone bio, Inc. (Nasdaq: GRTS) is a clinical-stage biotechnology company that aims to create the world's most potent vaccines. We leverage our innovative vectors and payloads to train multiple arms of the immune system to attack critical disease targets. Independently and with our collaborators, we are advancing a portfolio of product candidates to treat and prevent viral diseases and solid tumors in pursuit of improving patient outcomes and eliminating disease. www.gritstonebio.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; the advancements in Gritstone's ongoing clinical trials; the timing of data announcements related to ongoing clinical trials and the initiation of future clinical trials. 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' clinical 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 Annual Report on Form 10-K files on March 10, 2022, as well as Gritstone's Quarterly Reports on Form 10-Q filed on May 5, 2022 and August 4, 2022 and any current and periodic reports filed with the Securities and Exchange Commission.

Gritstone Contacts
Investors:
George E. MacDougall
Director, Investor Relations & Corporate Communications
Gritstone bio
lr@gritstone.com

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