Gritstone Announces Positive Clinical Data with GRANITE (Individualized Neoantigen Immunotherapy Program) during ESMO 2021 and Launch of Randomized Clinical Trial Program in Colorectal Cancer with Registrational Intent

September 17, 2021

- *GRANITE individualized immunotherapy demonstrates objective evidence of efficacy in end-stage colorectal cancer (CRC) patients (3rd line or greater) who have "cold" tumors at baseline*
  - *44% molecular response rate (4/9) by ctDNA (circulating tumor DNA) analysis*
  - *Molecular response associated with extended median overall survival >17 months*

- *Phase 2/3 randomized, controlled trial of maintenance GRANITE immunotherapy in newly diagnosed, metastatic, microsatellite-stable (MSS)-CRC patients expected to start in 1H 2022, has registrational intent and has been discussed with the FDA*

- *Randomized, controlled phase 2 trial of adjuvant GRANITE immunotherapy in MSS-CRC patients with stage II/III disease who are ctDNA+ after definitive surgery is expected to start in 1H22*

Webcast today, September 17 at 1:30pm ET

EMERYVILLE, Calif., Sept. 17, 2021 (GLOBE NEWSWIRE) -- Gritstone bio, Inc. (Nasdaq: GRTS), a clinical-stage biotechnology company developing next generation cancer and infectious disease immunotherapies, today announced updated results from the Phase 1/2 study evaluating the safety, immunogenicity, and clinical activity of GRANITE individualized neoantigen immunotherapy (heterologous prime-boost in combination with PD-1 checkpoint inhibitor Opdivo® [nivolumab] and subcutaneous anti-CTLA-4 antibody Yervoy® [ipilimumab]) in advanced solid tumors. The data were presented during a mini-oral presentation by investigator and Associate Professor of Medicine at the University of Chicago, Dan Catenacci, MD, as part of the European Society of Medical Oncology (ESMO) Annual Meeting.

In the 26 patients treated in the study with metastatic solid tumors largely focused on MSS-CRC and gastro-esophageal adenocarcinoma (GEA), GRANITE immunotherapy demonstrated good tolerability, consistent and potent immunogenicity (CD8+ neoantigen-specific T cell induction in all subjects), and objective evidence of efficacy as measured by reduction in ctDNA (molecular response). In particular, MSS-CRC patients exhibited "cold" tumors at baseline, with low PD-L1 and IFN-g expression and low tumor mutational burden.

Based on these data, Gritstone has discussed the registrational path with the U.S. Food & Drug Administration (FDA), and is advancing GRANITE into a randomized, controlled, phase 2/3 clinical trial (single protocol) for the maintenance treatment of newly diagnosed metastatic MSS-CRC patients who have completed FOLFOX-bevacizumab induction therapy. Additionally, the company will conduct a separate randomized, controlled phase 2 trial evaluating GRANITE in the adjuvant setting for stage II/III MSS-CRC patients who are ctDNA+ after definitive surgery. The trials are expected to begin in the first half of 2022. The checkpoint inhibitors being used for these studies have not yet been disclosed.

"GRANITE is demonstrating a favorable safety and tolerability profile and is consistently inducing high numbers of neoantigen-specific CD8+ T cells" said Andrew Allen, MD, PhD, Gritstone's Co-Founder and CEO. "Most strikingly, even in these advanced patients, there is clear evidence of tumor destruction as measured by reduction in ctDNA, a sensitive biomarker of disease burden. Furthermore, in a disease setting such as MSS-CRC that does not respond to checkpoint blockade therapy, our patients with GRANITE-induced molecular responses appear to be living longer, providing hope where historically there has been very little."

As of the August 5, 2021 data cutoff, the GRANITE Phase 1/2 study treated 26 patients; 14 in the Phase 1 dose escalation portion, and 12 in the Phase 2 portion across three tumor-specific expansion cohorts – MSS-CRC, gastroesophageal adenocarcinoma (GEA), and non-small cell lung cancer (NSCLC). All patients receive Gritstone's proprietary heterologous prime-boost consisting of Chimpanzee Adenovirus Vector (ChAdV) and Self-Amplifying mRNA (SAM) in combination with intravenous nivolumab and subcutaneous ipilimumab.

In MSS-CRC patients, where checkpoint inhibitors have shown minimal activity, GRANITE elicited a 44% molecular response rate in 9 evaluable patients (defined as a 50% or greater reduction in ctDNA from baseline) which is an increasingly well recognized objective efficacy biomarker for novel immunotherapy. Patients who demonstrated molecular response had median overall survival of >17 months (median not reached) whereas those without molecular response exhibited a median overall survival of 7.8 months, consistent with expected outcomes in 3rd line treatment of MSS-CRC.

MSS-CRC	All (n=12[1])	No Molecular Response (n=5)	Molecular Response (n=4)
Median Overall Survival (months)	8.7	7.8	Not reached (>17)
Median iPFS per iRECIST (months)	3.9	2.0	11.8
Median PFS per RECIST (months)	2.0	2.0	4.9

i=immune-based; PFS = progression-free survival; RECIST=Response Evaluation Criteria in Solid Tumors

1. 12 MSS-CRC patients treated; 9 patients eligible for analysis of ctDNA changes relative to baseline

A confirmed complete RECIST response was observed in a GEA patient (ctDNA negative at baseline). Multiple patients remained on treatment for over 6 months with lack of confirmed disease progression including 2/9 MSS-CRC patients receiving treatment beyond 12 months and one patient currently at 11+ months, which contrasts sharply with the expected outcome for these patients. 50% of patients (3/6) had a slow decrease in volume of multiple pulmonary metastasis during the first year of therapy, even though these objective radiological responses did not meet RECIST criteria. These radiological observations were associated with prolonged time on study and decrease in biomarkers such as ctDNA.

"The unmet need in our many patients with metastatic colorectal cancer is profound –third-line therapy offers limited additional benefit and checkpoint inhibitors are ineffective in this setting" said Dr. Daniel Catenacci. "The early, but strikingly consistent, clinical and translational data from the Gritstone program are very encouraging, and the suggestion that immunologically cold tumors can become viable targets for the immune system could be a game-changer in treating MSS-CRC. I am excited to see how well GRANITE can perform in healthier, earlier-stage patients where we expect to see fewer patients progress rapidly before active immunotherapy."

Additional information about the trial can be found at www.clinicaltrials.gov, NCT03639714

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Webcast Information
To register for the webinar, please click here. The call and accompanying slides will be webcast live on the "Events" page under the "Investors & Media" section of the company's website at www.gritstone.com. A replay of the webcast will be accessible at the same link approximately one day after its completion.

About GRANITE
Gritstone's neoantigen-based immunotherapies 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 the company using its proprietary Gritstone EDGETM artificial intelligence platform and tumor HLA peptide sequencing. GRANITE is an individualized neoantigen-based immunotherapy and uses a priming adenoviral vector (GRT-C901) and self-amplifying mRNA vector (GRT-R902) to deliver personalized immunotherapy containing the relevant neoantigens. It is being evaluated in the Phase 2 portion of a Phase 1/2 clinical study in combination with checkpoint inhibitors for patients with microsatellite stable colorectal cancer (MSS CRC) who have progressed on FOLFOX/FOLFIRI therapy and a second cohort for patients with gastro-esophageal cancer who have progressed on chemotherapy (NCT03639714). GRANITE was granted Fast Track designation by the U.S. Food and Drug Administration for the treatment of MSS CRC.

About Gritstone
Gritstone bio, Inc. (Nasdaq: GRTS), a clinical-stage biotechnology company, is developing the next generation of immunotherapies against multiple cancer types and infectious diseases. Gritstone develops its products by leveraging two key pillars—first, a proprietary AI -based platform, Gritstone EDGE^{TM}, which is designed to predict antigens that are presented on the surface of cells, such as tumor or virally-infected cells, that can be seen by the immune system; and, second, the ability to develop, manufacture, and deliver selected antigens to the patient's immune system to drive the destruction of tumors or virally-infected cells. The company's lead oncology programs include an individualized neoantigen-based immunotherapy, GRANITE, and an "off-the-shelf" shared neoantigen-based immunotherapy, SLATE, which are being evaluated in clinical studies. Within its infectious disease pipeline, Gritstone is advancing CORAL, a COVID-19 program to develop a second-generation vaccine, with support from departments within the National Institutes of Health (NIH), the Bill & Melinda Gates Foundation, the Coalition for Epidemic Preparedness Innovations (CEPI) and through a license agreement with La Jolla Institute for Immunology. Additionally, the company has a global collaboration for the development of a therapeutic HIV vaccine with Gilead Sciences. For more information, please visit gritstone.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 the company'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, including interim results obtained may differ from those at completion of the studies and clinical trials. 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 5, 2021 and any current and periodic reports filed with the Securities and Exchange Commission.

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