Gritstone bio Announces Positive Preliminary Progression-free Survival and Long-term Circulating Tumor DNA (ctDNA) Data from Phase 2 Portion of Ongoing Phase 2/3 Study of its Personalized Cancer Vaccine, GRANITE, in Front-line Metastatic Microsatellite Stable Colorectal Cancer (MSS-CRC)

April 1, 2024

-- Early progression-free survival (PFS) trends favor GRANITE recipients with hazard ratios of 0.82 in the overall population ([95% CI, 0.34-1.67]; 62% censored) and 0.52 (48% relative risk reduction of progression or death with GRANITE vs. control) in a high-risk group, where clinical data are more mature ([95% CI, 0.15-1.38]; 44% censored); >90% of high-risk patients have liver metastases --

-- Short-term molecular response (as defined by protocol) is uninformative due to an unexpectedly persistent ctDNA drop beyond induction chemotherapy; long-term circulating tumor DNA (ctDNA) responses align with PFS trends and favor GRANITE vs. control patients --

-- GRANITE was generally well-tolerated with manageable adverse events; no patients have discontinued GRANITE due to adverse events --

-- Mature PFS data expected in the third quarter of 2024; overall survival data expected in 1H 2025 --

EMERYVILLE, Calif., April 01, 2024 (GLOBE NEWSWIRE) -- Gritstone bio, Inc. (Nasdaq: GRTS), a clinical-stage biotechnology company working to develop the world's most potent vaccines, today announced positive preliminary data from the ongoing, signal seeking Phase 2 portion of the Phase 2/3 study evaluating GRANITE, its personalized neoantigen cancer vaccine, in front-line metastatic microsatellite stable colorectal cancer (MSS-CRC). The randomized, controlled, open-label study is designed to quantify the clinical benefit of maintenance therapy with GRANITE (GRT-C901/GRT-R902) in combination with immune checkpoint blockade in addition to fluoropyrimidine/bevacizumab versus fluoropyrimidine/bevacizumab alone. Overall progression free survival (PFS) data show an early trend in benefit for GRANITE patients (HR=0.82, [95% CI, 0.34-1.67]; 62% censored) and extended PFS benefit in high-risk patients (HR=0.52 [95% CI, 0.15-1.38]; 44% censored), in whom progression occurs faster. Circulating tumor DNA (ctDNA) analysis over several months of treatment shows the expected relationship with disease progression and favors GRANITE, while short-term ctDNA response analysis (molecular response as defined per protocol) did not demonstrate a difference between study arms. Gritstone bio successfully manufactured GRANITE product candidate for every eligible patient (i.e., 100% vaccine manufacturing success rate).

"Today's preliminary Phase 2 results are highly encouraging and represent the first randomized trial evidence, albeit early, that a personalized neoantigen-directed vaccine can potentially drive efficacy in a metastatic 'cold' tumor. The overall trend of PFS improvement in GRANITE recipients is great to see, and the exploratory PFS hazard ratio of 0.52 in the high-risk group, a more mature dataset, is a striking signal," said Andrew Allen, MD, PhD, Co-founder, President & CEO of Gritstone bio. "Pioneering new spaces carries inherent risks, and with regard to defining molecular response, we simply got it wrong. ctDNA levels in both arms decreased on chemotherapy for longer than we anticipated, generating similar short-term molecular response rates across arms and rendering our protocol measure of ctDNA change uninformative. Fortunately, long-term analysis demonstrates the expected correlation of ctDNA with clinical benefit and favors GRANITE patients. We believe these preliminary findings put us in a strong position to share mature PFS data in the third quarter and then enter regulatory discussions regarding Phase 3. The growing body of evidence favoring GRANITE in this trial, including positive PFS and long-term ctDNA trends in both high and low-risk populations, is exciting and suggests GRANITE is working in this notoriously underserved patient population."

"Up to 97% of patients with metastatic colorectal cancer, the second most common cause of cancer death, are MSS. Unlike patients with melanoma and lung cancer, they have not benefited from standard immunotherapies such as checkpoint inhibitors. These preliminary results indicate that GRANITE is inducing a potentially significant immune response in a disease that has been felt to be immunologically cold," said J. Randolph Hecht, MD, Professor of Clinical Medicine and Director of the UCLA GI Oncology Program and an investigator in the GRANITE Phase 2/3 study. "The PFS difference, particularly in a poor prognosis group of patients, indicates the potential for clinical benefit and provides the rationale for a confirmatory Phase 3 trial, about which I am very excited. Furthermore, we are learning how to better analyze ctDNA continuously to study the efficacy of this novel immunotherapy. Expanding the scope of immunotherapy to a broader spectrum of cancer patients is the 'holy grail' of oncology, especially for MSS colorectal cancer. While early, these promising results suggest GRANITE has potential to deliver clinically meaningful benefit in MSS-CRC and other cold tumors."

Key Findings from Preliminary Phase 2 Data in Front-Line Metastatic MSS-CRC
Clinical data cut as of March 8, 2024; ctDNA data cut as of March 12, 2024

One hundred and four (104) patients were randomized (1:1) in the study: Sixty-seven (67) patients (39 GRANITE arm, 28 control arm) are included in the treated analysis below. Thirty-six patients have left the study prior to randomized treatment primarily due to early progressive disease or withdrawal of consent, and one patient has yet to begin study treatment start. Demographics and clinical characteristics were balanced between arms (stage, sidedness, presence of liver metastases), with approximately 75% of patients having liver metastases.

Progression Free Survival (PFS)

- Early trend in PFS benefit was observed for GRANITE recipients
  - Hazard ratio of 0.82 ([95% CI, 0.34-1.67]; 62% censored) in all patients
  - Hazard ratio of 0.52 ([95% CI, 0.15-1.38]; 44% censored) in high-risk patients[1] (>90% have liver metastases). Median PFS of 12 months (GRANITE) vs. 7 months (control).

        - [1]High-risk subgroup defined as baseline ctDNA above the median value (2%) for the control group (ctDNA quantified as mean variant allele frequency [VAF] at time of study randomization). This analysis was performed on 44 patients who received study treatment (control and GRANITE arms) and have available baseline ctDNA data.
    - GRANITE and control arms begin separating 1-2 months after initiation of GRANITE treatment, consistent with expected kinetics of GRANITE-induced immune response

Biomarker Results – Circulating Tumor DNA (ctDNA)

- Short-term molecular response (>30% reduction in ctDNA using single time-point analysis, defined per protocol) is uninformative due to unanticipated continuation of ctDNA drop beyond induction chemotherapy.
    - Molecular response, similar in both arms (30% [6/20] in vaccine arm; 42% [5/12] in control arm)
- Long-term ctDNA responses align with PFS trends and favor GRANITE vs. control patients
    - Analysis in the high-risk group[1] shows that between first blood draw (time of randomization) and last blood draw (most recent study visit), ctDNA shifted from high (>2% VAF) to low (≤2% VAF) in 56% (9/16) of GRANITE patients vs 22% (2/9) of control patients. Progressive disease was observed in 44% (7/16) vs 78% (7/9), respectively, within this group.
    - Analysis in patients whose ctDNA was negative after induction chemotherapy, a low-risk group, favors GRANITE. Sustained ctDNA negativity was observed in 67% (6/9) of GRANITE recipients vs 38% (3/8) control patients. Progressive disease was observed in 11% (1/9) and 38% (3/8) of these patients, respectively.

Safety and Tolerability

- GRANITE demonstrated a favorable safety and tolerability profile
    - Vast majority of adverse events (AEs) were Grade 1/2
    - Common AEs were mild systemic and local effects typically associated with any potent vaccine (i.e., transient flu-like illness)
    - No patients discontinued study treatment due to an AE

A presentation reviewing these results has been added to the Presentations page of Gritstone's website, https://ir.gritstonebio.com/investors/presentations.

About Gritstone bio
Gritstone bio, Inc. (Nasdaq: GRTS) is a clinical-stage biotechnology company that aims to develop 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 our clinical and regulatory development plans for our product candidates; our expectations regarding the data to be derived in our ongoing and planned clinical trials, including, the preliminary nature of the data disclosed in this press release and potential for such data to change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data; the timing of commencement and results of our future nonclinical studies, clinical trials and research and development programs; our ability to discover, develop and advance product candidates into, and successfully complete, clinical trials (including the timing of our expected PFS and OS data readout); and our plans and strategy regarding maintaining existing and entering into new collaborations and/or partnerships. Such forward-looking statements involve substantial risks and uncertainties that could cause Gritstone bio'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 bio'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 product candidates, Gritstone bio'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 bio 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 bio's most recent Annual Report on Form 10-K filed on March 5, 2024 and any subsequent current and periodic reports filed with the Securities and Exchange Commission.

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