



Gritstone Announces Positive Clinical Results from First Cohort of a Phase 1 Study (CORAL-BOOST) Evaluating a T Cell-Enhanced Self-Amplifying mRNA (samRNA) Vaccine Against COVID-19

January 4, 2022

-- Single 10 µg dose of samRNA vaccine containing Spike plus additional T cell epitopes (TCE) induced robust neutralizing antibody titers in ten healthy adults ≥60yrs who had received two prior doses of AstraZeneca's COVID-19 vaccine --

-- samRNA vaccine elicited broad CD8+ T cell responses against conserved non-Spike SARS-CoV-2 epitopes and boosted pre-existing Spike-specific T cells --

-- samRNA vaccine was well-tolerated in these subjects, with no grade 3 or 4 adverse events observed --

-- Gritstone is expanding CORAL-BOOST to 120 subjects, potentially enabling more rapid advancement into a pivotal study --

-- Webcast to be held today, January 4 at 8:30 a.m. ET --

EMERYVILLE, Calif., Jan. 04, 2022 (GLOBE NEWSWIRE) -- Gritstone bio, Inc. (Nasdaq: GRTS), a clinical-stage biotechnology company developing the next generation of cancer and infectious disease immunotherapies, today shared positive Phase 1 clinical data from the first cohort (10 µg dose of CORAL self-amplifying mRNA (samRNA) vaccine) of its CORAL-BOOST study, demonstrating both strong neutralizing antibody responses to Spike and robust CD8+ T cell responses. Recognizing the increased focus on T cell immunity as a key source of protection against current and future Spike variants, Gritstone's CORAL program is developing a second-generation COVID-19 vaccine designed to drive both robust neutralizing antibodies and induce broad CD8+ T cell immunity. CORAL-BOOST, one of four trials in the company's CORAL program, is evaluating the safety, reactogenicity, and immunogenicity of a samRNA vaccine directed against Spike and highly conserved non-Spike T cell epitopes (TCE) as a booster against SARS-CoV-2 in healthy adults ≥60 years (n=20 at two dose levels) who previously received two doses of AstraZeneca's first-generation COVID-19 vaccine AZD1222 (Vaxzevria).

"We are thrilled to share that our T cell-enhanced samRNA vaccine from the CORAL program is driving both robust CD8+ T cell responses to a broad array of viral epitopes and strong neutralizing antibody responses to Spike, which we believe validates the potential of our infectious disease platform," said Andrew Allen, M.D., Ph.D., Co-Founder, President and Chief Executive Officer of Gritstone. "As we have seen with the Omicron variant, viral surface proteins such as Spike are mutating at a high rate, leaving the immunity provided by Spike-dedicated vaccines vulnerable to variants containing numerous Spike mutations. We designed our COVID-19 vaccines to drive broad CD8+ T cell immunity, an additional key layer of protection against viruses. This innovation enables inclusion of a wide array of highly conserved viral epitopes, potentially creating an immune state that may offer more robust clinical protection against current and future SARS-CoV-2 variants and be a first step toward developing a pan-coronavirus vaccine."

Results from First Cohort

A single 10 µg dose of the CORAL program's samRNA vaccine administered to healthy adults ≥60 years (n=10) at least 22 weeks after two-dose series of Vaxzevria induced:

- New CD8+ T cell responses across a wide set of non-spike epitopes, including many validated T cell targets in convalescent individuals, demonstrating the potential for variant-proof immunity
 - Proportion of responses to TCE targets assessed by ELISpot:
 - 36% Nucleoprotein (N)
 - 22% Membrane (M)
 - 42% ORF3a
- A boost to pre-existing T cell responses to Spike epitopes believed to be additive to antibody-based clinical protection conferred by Spike-dedicated vaccines:
 - 120 at peak treatment day vs. 55 at pre-boost (Spot-forming units per 10⁶ cells; assessed by IFNγ ELISpot)
- Broad and potent neutralizing antibodies against SARS-CoV-2 Spike protein, at levels consistent with published data from higher doses of first-generation mRNA vaccines in a similar clinical context (COV-BOOST study; Munro et al., Lancet 2021)
 - 2,370 Geomean ID₅₀ titer values observed at day 29 against Wild Type variant vs. 108 at treatment day 1 (~20-fold increase)
 - 503 Geomean ID₅₀ titer values observed at day 29 against Beta variant vs. 50 at treatment day 1 (~10-fold increase)
 - 525 Geomean ID₅₀ titer values observed at day 29 against Delta variant vs. 69 at treatment day 1 (~8-fold increase)

CORAL's samRNA vaccine was well-tolerated and demonstrated a favorable safety profile with no grade 3/4 adverse events or unexpected reactogenicity or safety events in ten healthy adults ≥60 years.

Professor Andrew Ustianowski, who is lead investigator for the study at the University of Manchester and Clinical Lead for the NIHR (National Institute for Health Research) COVID Vaccine Research Programme, added, "These initial data with Gritstone's innovative samRNA COVID program strongly support its unique approach of CD8+ T cell priming and potent neutralizing antibody generation with a dose of samRNA potentially up to 10-fold lower than that required for first generation mRNA vaccines. We are increasingly realizing the importance of both the T cell response and non-spike protein targets for protection against severe disease, hospitalization, and death, and to allow protection against current and future variants of the virus. We are excited to expand the footprint of this trial and continue working with Gritstone in the clinical development of this promising, next generation, T cell-enhanced COVID-19 vaccine."

The CORAL-BOOST Phase 1 study is ongoing in the United Kingdom and has now dose escalated as planned to a 30 mg dose. Based on these positive Phase 1 data, Gritstone is amending this trial to increase enrollment to 120 subjects and evaluate the addition of a second samRNA-Spike-TCE dose, potentially enabling more rapid advancement into a pivotal study. Immunogenicity and reactogenicity data for additional cohorts is anticipated in coming months.

Webcast

Gritstone will host a live webcast to discuss the results of this study today at 8:30 a.m. ET. To register for the webcast, please click [here](#). To access the webcast via phone, please dial 1-877-407-4018 (domestic) or 1-201-689-8471 (international). Please use the confirmation number 13725825.

A replay of the webcast will be available on the Gritstone website approximately two hours after its completion.

Gritstone's CORAL Program

Gritstone's CORAL program is a second-generation SARS-CoV-2 vaccine platform delivering Spike and additional SARS-CoV-2 T cell epitopes, offering the potential for more durable protection and broader immunity against SARS-CoV-2 variants. Delivery vectors can comprise self-amplifying mRNA (samRNA), chimpanzee adenovirus (ChAd), or both (mix and match). In a non-human primate viral challenge study published online in November 2021, a CORAL Spike vaccine demonstrated enhanced viral clearance alongside strong anti-Spike neutralizing antibody titers. The program is supported by several key relationships: Bill & Melinda Gates Foundation, National Institute of Allergy and Infectious Disease (NIAID), and the Coalition for Epidemic Preparedness Innovations (CEPI). CORAL is being evaluated across different populations including elderly adults, immunocompromised individuals, those naïve to the virus, and previously vaccinated individuals using different vaccine regimens.

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 machine learning-based platform, Gritstone EDGE™, 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 and manufacture potent immunotherapies utilizing these antigens to potentially drive the patient's immune system to specifically attack and destroy disease-causing 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 (LJI). Additionally, the company has a global collaboration for the development of a therapeutic HIV vaccine with Gilead Sciences. For more information, please visit 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 the company's ongoing clinical trials; the timing of data announcements related to ongoing clinical trials, the expansion of 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' 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 November 3, 2021 and any current and periodic reports filed with the Securities and Exchange Commission.

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