Gritstone bio Presents Improvements to EDGE™ Platform at AACR 2024

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-- State-of-the-art neoantigen prediction platform (EDGE ™) now predicts HLA Class I presentation of epitopes with >80% accuracy --

-- Newly developed EDGE-II model achieves superior predictive performance of HLA Class II presentation and CD4+ immunogenicity over publicly available models --

-- Combined with Gritstone's vaccine vectors, EDGE has demonstrated best-in-class potential in identifying neoantigens capable of eliciting T cell immune responses for robust and durable immunity --

EMERYVILLE, Calif., April 08, 2024 (GLOBE NEWSWIRE) -- Gritstone bio, Inc. (Nasdaq: GRTS), a clinical-stage biotechnology company working to develop the world's most potent vaccines, today presented an update on its T cell epitope discovery platform, EDGE, at the 2024 American Association for Cancer Research (AACR) Annual Meeting in San Diego, CA. The presentation details improvements Gritstone has made in prediction of peptide presentation by HLA Class I, associated with CD8+ T cells, since the publication of the initial results in 2018 (Nature Biotechnology). It also reviews how Gritstone has expanded EDGE's application to predict peptide presentation by HLA Class II.

"Identifying which of the hundreds of tumor mutations are most likely to serve as neoantigens, key targets of tumor-specific T cells, is critical to the development of effective neoantigen-directed vaccines," said Andrew Allen, M.D., Ph.D., Co-founder, President, and Chief Executive Officer of Gritstone bio. "Since our Nature Biotechnology publication in 2018, we have further enhanced and expanded the application of EDGE in support of our cancer and infectious disease vaccines by improving our already-robust prediction of HLA Class I epitopes, associated with CD8+ T cell induction, and incorporating HLA Class II epitope prediction to enable CD4+ T cells to join the fight. Gritstone remains at the forefront of driving robust and broad T cell induction post-vaccination, and EDGE is an important asset and differentiator in that effort."

"Today, EDGE is able to predict HLA Class I presentation of epitopes with >80% accuracy, a significant increase since 2018 when we initially published the model," said Karin Jooss, Ph.D., Executive Vice President, and Head of R&D of Gritstone bio. "EDGE also now includes a comprehensive state-of-the-art model for predicting peptide presentation by HLA Class II in the context of active vaccination, which could serve to effectively broaden T cell response to our novel vaccines. The improvements we are making to EDGE, leveraging advances in protein large language models and in-house immunopeptidomics, have positioned EDGE as a leading HLA/peptide predictive platform in the neoantigen cancer vaccine field. The superior performance and association with cellular immunity seen across all our models compared to currently publicly available models support Gritstone's potential to develop highly potent vaccines for both oncology and infectious disease."

Abstract 904*:* EDGE™ enables state-of-the-art identification of peptide-HLAs for the development of T cell inducing vaccines in oncology and infectious diseases

EDGE for Oncology:

- Class I antigens – predicted using allele-specific and pan-specific models
  - Allele-specific model is an improved version of published 2018 EDGE model that predicts for 116 HLA alleles and achieves an Average Precision (AP) of 0.63 and Positive Predictive Value at 40% Recall (PPV40) of 0.79
  - Pan-specific model trains using the HLA allele sequence and is applicable to any Class I allele with known sequence, achieving an AP of 0.65 and PPV40 of 0.81
  - 2-fold better performance vs MHCFlurry 2.0 when ranking mutations from 80 cancer patients based on immunogenicity
  - Detectable CD8 responses to over half of the 20 administered candidate neoantigens per patient (n = 5) after treatment with Gritstone's personalized cancer vaccines
- Class II antigens – predicted using EDGE-II model
  - Uses a pretrained protein language model, a novel learned HLA allele-deconvolution strategy, and in-house immunopeptidomics training data
  - Achieves a test set AP of 0.92 and outperforms NetMHCIIpan and BERTMHC on an externally curated validation set with an AP = 0.71
  - CD4 immunogenicity in a personalized cancer vaccine context is better predicted by EDGE-II than NetMHCIIpan and MARIA

EDGE for Infectious Disease:

- Class I antigens – predicted using EDGE-ID model

- Optimizing EDGE for use on infectious diseases results in improved performance
- Trained using both human immunopeptidomics and infectious disease binding affinity datasets and tested on publicly available infectious disease datasets (HIV, Influenza A, and SARS-CoV-2)
- Better performance on HIV and Influenza A datasets vs. MHCFlurry 2.0; comparable SARS-CoV-2 performance

The poster has been added to the 'Scientific Publications' page of the Gritstone bio website.

About EDGE™ (Epitope Discovery for GEnomes)
Gritstone bio believes effective identification of the mutations that are most likely to serve as neoantigens is critical to developing effective neoantigen-directed vaccines. For this reason, we developed EDGE™, a proprietary platform technology that leverages artificial intelligence to identify which of the hundreds of mutations within a tumor are most likely to serve as targets for a patients' immune system. A key strategic asset, Gritstone leverages EDGE's capabilities to identify T cell targets for oncology and infectious disease.

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; the timing of commencement 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; 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'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 filed on March 5, 2024 and any subsequent current and periodic reports filed with the Securities and Exchange Commission.

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