# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**Washington, D.C. 20549**

# FORM 8-K

**CURRENT REPORT**
**Pursuant to Section 13 or 15(d)**
**of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): January 4, 2022**

# Gritstone bio, Inc.
**(Exact name of registrant as specified in its charter)**

| **Delaware** | **001-38663** | **47-4859534** |
|---|---|---|
| **(State or other jurisdiction of incorporation)** | **(Commission File Number)** | **(IRS Employer Identification Number)** |

**5959 Horton Street, Suite 300**
**Emeryville, California 94608**
**(Address of principal executive offices, including Zip Code)**

**Registrant's telephone number, including area code: (510) 871-6100**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| **Common Stock, par value $0.0001** | **GRTS** | **The Nasdaq Global Select Market** |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

**Item 8.01 Other Events.**

On January 4, 2022, Gritstone bio, Inc. (the "Company" or "Gritstone") announced positive clinical results from the first cohort of its Phase 1 Study (CORAL-BOOST) evaluating a T cell-enhanced self-amplifying mRNA (samRNA) vaccine against COVID-19. A copy of the press release with the foregoing announcement is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

Spokespersons of Gritstone plan to present the information in the presentation slides attached hereto as Exhibit 99.2 at various upcoming investor and analyst meetings previously announced by the Company. A copy of the presentation is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated by reference herein.

**Item 9.01 Financial Statements and Exhibits.**

| Exhibit No. | Description |
|---|---|
| 99.1 | Press Release dated January 4, 2022 |
| 99.2 | Presentation Slides January 2022 |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document). |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**GRITSTONE BIO, INC.**

Date: January 4, 2022

By: /s/ Andrew Allen
Andrew Allen
President and Chief Executive Officer

**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**

*— Single 10 µg dose of samRNA vaccine containing Spike plus additional T cell epitopes (TCE) induced robust neutralizing antibody titers in ten healthy adults ³60yrs 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.** – January 4, 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 ³60 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 ³60 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 $10^6$ cells; assessed by IFNy 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 $ID_{50}$ titer values observed at day 29 against Wild Type variant vs. 108 at treatment day 1 (~20-fold increase)
    - 503 Geomean $ID_{50}$ titer values observed at day 29 against Beta variant vs. 50 at treatment day 1 (~10-fold increase)
    - 525 Geomean $ID_{50}$ 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 ³60 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 µg 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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# Investor Presentation

*January 2022*

# Disclaimer

This presentation and accompanying oral presentation, if any, contain forward-looking statements including, but not limited to, statements related to Gritstone bio, Inc.'s ("Gritstone", "we" or "our") preclinical and clinical product candidates, including GRANITE, SLATE, CORAL, and HIV programs. All statements other than statements of historical facts contained in this presentation, including statements regarding the timing of immunogenicity and clinical data for GRANITE, SLATE, and CORAL, the timing for Gilead's initiation of a Phase 1 in HIV, collaborations surrounding our infectious disease programs, future results of operations and financial position, business strategy, prospective products, availability of funding, clinical trial results, product approvals and regulatory pathways, timing and likelihood of success, plans and objectives of management for future operations, future results of current and anticipated products, and our ability to create value are forward-looking statements. Forward-looking statements generally contain words such as "believes," "expects," "may," "will," "should," "seeks," "approximately," "intends," "plans," "estimates," "anticipates," and other expressions that are predictions of or indicate future events and trends and that do not relate to historical matters. Because forward-looking statements are inherently subject to risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements.

Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. 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 periodic filings with the Securities and Exchange Commission (the "SEC"), including its Quarterly Report filed on November 3, 2021, and any current and periodic reports filed thereafter.

# Gritstone: Taking Immunotherapy to the Next Level

*Leveraging proprietary target identification & vaccine platform technologies*

1
Proprietary Synergistic Technologies + In-House Manufacturing Capabilities

EDGE™ AI Antigen Discovery Platform

Vaccine Delivery Platforms: Viral & Self-amplifying mRNA

2
Differentiated and Expansive Pipeline

Oncology

Infectious Diseases

3
Premier Government and Industry Partnerships

CEPI · GILEAD · BILL & MELINDA GATES foundation · NIH National Institute of Allergy and Infectious Diseases · 2seventybio

4
Multiple Near-Term Catalysts

**CORAL** *(COVID-19)*

**SLATE** *(off-the-shelf neoantigen)*

**GRANITE** *(individualized neoantigen)*

Cash Position* as of Sept 30, 2021

**~$216.4M**

*cash, cash equivalents, marketable securities, and restricted cash

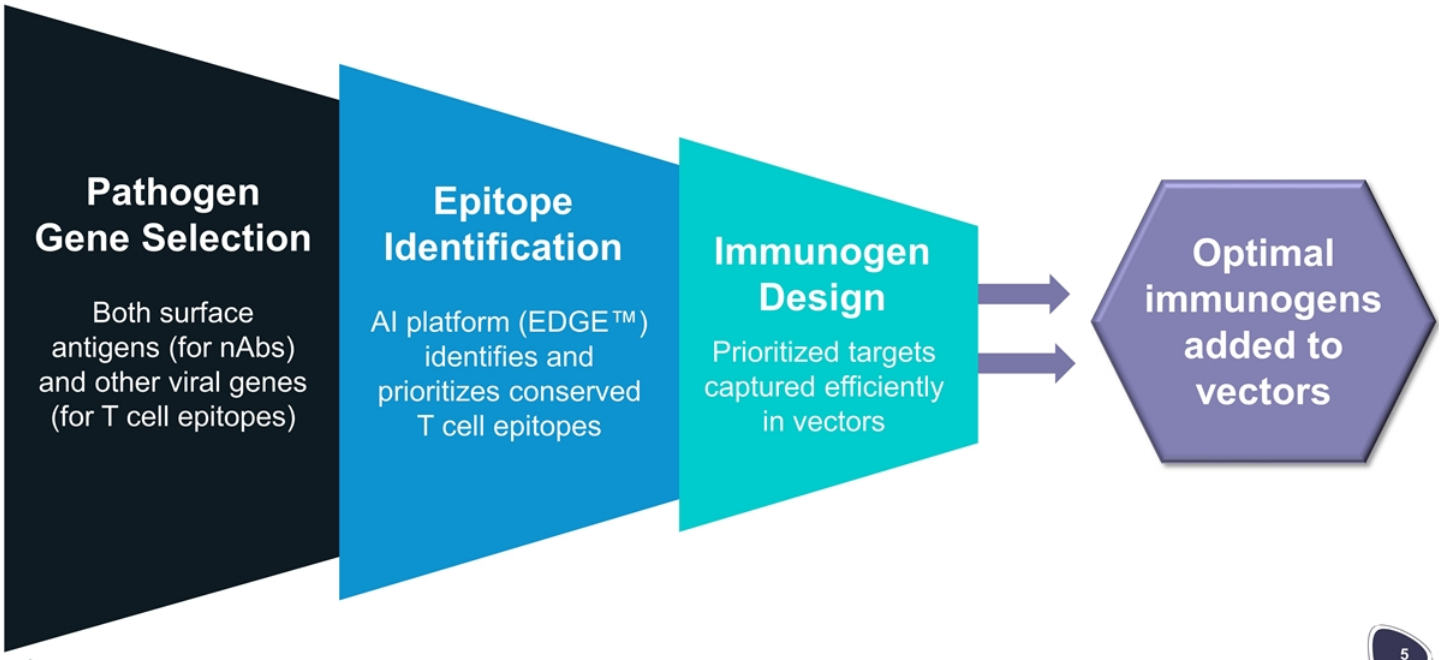
# Dual Platform Approach Generates Distinct Product Candidates

*Novel, proprietary approach enables design of vaccines tailored to clinical need*

| | | Infectious Disease | Oncology |
|---|---|---|---|
| 01 **EDGE™ AI PLATFORM** | EDGE™ AI platform identification and design of antigens that induce robust CD8+ T cell responses  | Highly conserved T cell epitopes for durable protection against emerging variants | Personalized and shared neoantigens for a precision anti-tumor approach |
| 02 **Vaccine Delivery + Manufacturing** | Multi-vector samRNA and ChAd vaccine platform enables flexible, context-specific product development  | Homologous or heterologous vectors for broad, robust and durable immunity (nAb and T cell) | Heterologous vaccine delivery for strong, sustained CD8+ T cell responses |

# Process: Designing Vaccines that Drive Both B and T Cell Immune Responses

*Careful design of the immunogen, the antigenic payload, to optimize the nature of the immune response*

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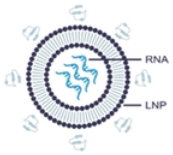
# Two “Mix & Match” Vaccine Platforms in the Clinic with Unique Attributes

*Unique vectors to drive both antibodies and CD8+ T cells*

**samRNA**
**(self-amplifying mRNA)**

*Replicon RNA Based on Venezuelan Equine Encephalitis (VEE) Alphavirus*




- Extended duration and magnitude of antigen expression
- Strong & potentially durable induction of neutralizing antibody & T cell immunity (CD4+ and CD8+)
- Dose sparing potential: Equivalent neutralizing antibody (nAb) induction at up to ~1/10 dose of approved mRNA vaccines
- Potential for refrigerator stable product

**ChAd**
**(Chimpanzee Adenovirus 68)**

*Replication-Defective Virus Based on Chimpanzee Adenovirus 68*

- Drives rapid and substantial CD8+ T cell response
- Induces high, sustained levels of antibodies (as demonstrated by anti-Spike antibodies)
- Simple mass scale production, lyophilized formulation and potential to lower COGS

# Differentiated Clinical Assets Across Technologies & Therapeutic Areas

| | Program | Target | Indication | Pre-clinical | Phase 1 | Phase 2 | Phase 3 | Anticipated Milestones | Commercial Rights |
|---|---|---|---|---|---|---|---|---|---|
| INFECTIOUS DISEASE | CORAL | SARS-CoV-2 Spike + TCE* | COVID-19 BOOST (60+) | | | | | *1Q2022 Data* | gritstone |
| | | | COVID-19 naïve & booster | | NIH NIAID | | | *1H2022 Data* | gritstone |
| | | | COVID-19 Immunocompromised | | | | | *Mid-2022 Data* | gritstone |
| | | | COVID-19 in South Africa naive, convalescent, HIV+ | | CEPI | | | *Mid-2022 Data* | gritstone |
| | HIV | HIV | HIV treatment/cure | | | | | *4Q2021 IND cleared* | GILEAD |
| ONCOLOGY | GRANITE | Individualized neoantigen | Early Stage & Advanced Solid Tumors | | | | | *3Q2021 Data presented* | gritstone |
| | | | MSS-CRC (1L maintenance) | | Randomized | | | *4Q2021 Trial initiated* | gritstone |
| | | | MSS-CRC (adjuvant) | | Randomized | | | *2Q2022 Trial initiation* | gritstone |
| | SLATE | Shared Neoantigens | p53, KRAS Advanced Solid Tumors | | | | | *3Q2021 Data presented* | gritstone |
| | | | $KRAS^{mut}$ Solid Tumors | | | | | *Mid-2022 data* | gritstone |

**CORAL next-generation COVID-19 vaccines includes Spike protein and additional T cell epitopes (TCE) from the SARS-CoV-2 virus; there are 5 different investigational COVID-19 product candidates testing/planned in clinical trials with various antigenic cassettes targeting Wild Type, Beta and Omicron variants*

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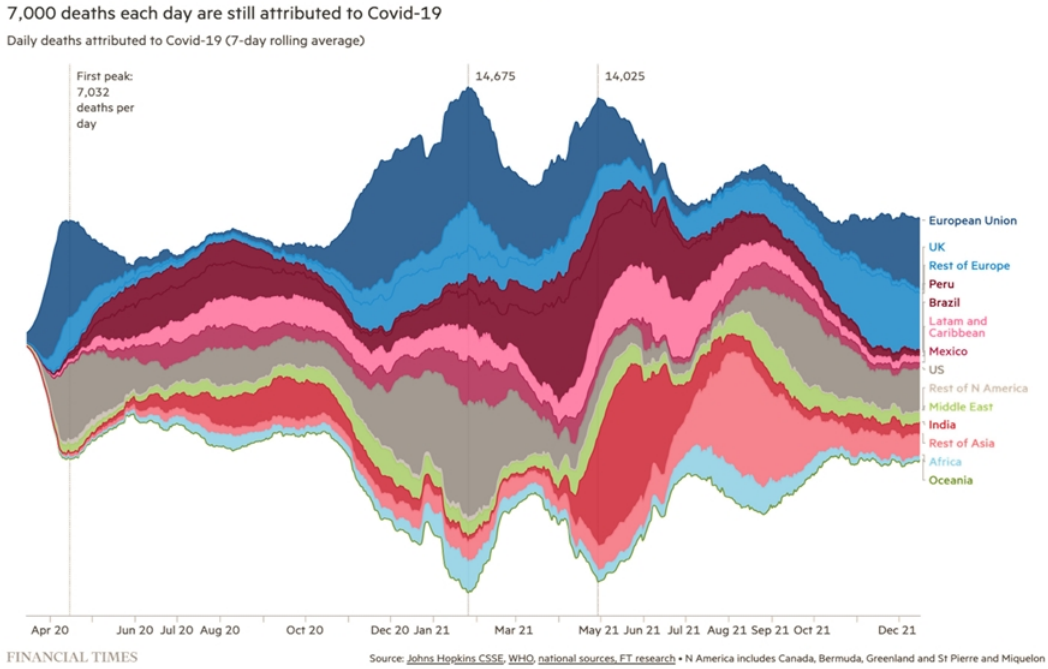
To be initiated


Infectious Disease
COVID-19 (CORAL)
HIV

# COVID-19 Remains a Global Pandemic

*Omicron is now the globally dominant variant; what's next?*

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**Adapted from Financial Times Coronavirus Tracker, Jan 2, 2022*

# Omicron Mutations Are Centered on Spike….

Comparison of Mutations Within Variants to the Original SARS-CoV-2 Wild Type Strain

| Variant | Spike (1273AA) | Orf1ab (7096AA) | Orf3a (275AA) | E (77AA) | M (222AA) | Orf7a (121AA) | N (419AA) |
|---|---|---|---|---|---|---|---|
| Beta | 7 | 7 | 2 | 1 | 0 | 0 | 1 |
| Delta | 10 | 3 | 1 | 0 | 1 | 2 | 3 |
| Omicron | 37 | 12 | 3 | 1 | 3 | 1 | 6 |

*E=Envelope*
*M=Membrane*
*N=Nucleoprotein*

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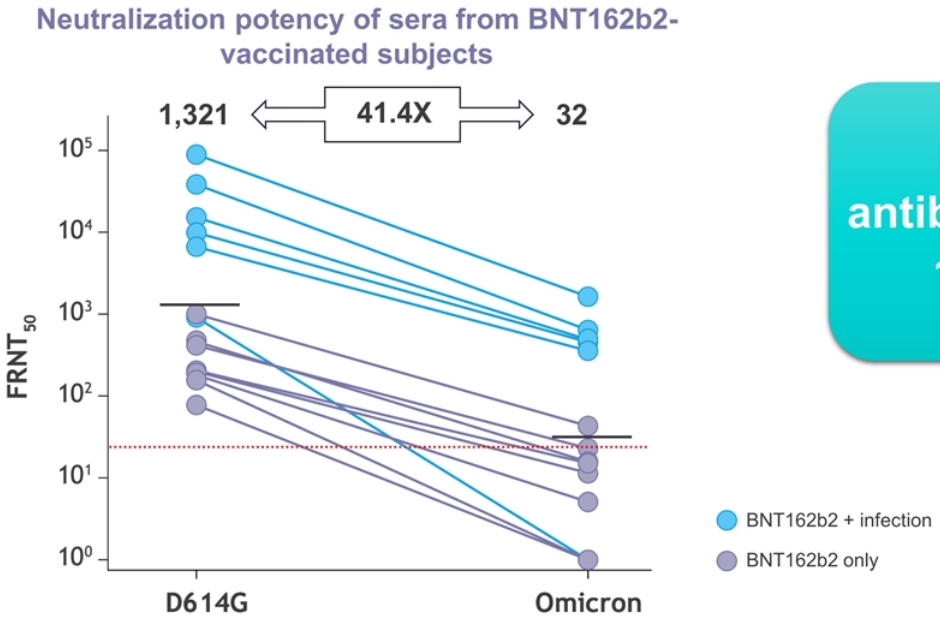
*Sources: outbreak.org & cov-lineages.org*

# …And Reduce The Neutralizing Potency of Reference-Strain Spike Vaccine-Elicited Antibodies




**Potency of antibodies reduced ~20-40 fold**

gritstone bio *Cele, et. al., medRxiv, 2021; Sources: outbreak.org & cov-lineages.org*

# New Vaccine Approach is Desired to Achieve Durable Immunity

*Existing vaccine solutions have limitations as Spike rapidly mutates and variants of concern (VoC) emerge*

| Vaccination Approach to VoC | Limitations |
|---|---|
| **Re-boost** | • Requires repeated vaccinations<br>• Protection is often less complete than against reference strain[1]<br>• Protection reduces as nAb titers wane |
| **Variant-specific** | • Longer production cycle<br>• Expensive<br>• Production required for each variant<br>• Potential loss of efficacy over time* |

**Ideal Solution**

Protection across current and future variants

Favorable dosing and administration

Rapid and scalable production

Potential pan-corona virus protection

[1]*Hansen et al. medRxiv 12/22/2021*

# T Cells Offer Potential Path to More Robust and Durable Immunity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Dates of articles above: "The T-Cell Covid Cavalry", Dec 30, 2021; "Beyond the spike…", Dec 20, 2021; "T Cells Might Be Our Bodies….", Dec 14, 2021; "Covid-resistant people…", Nov 10, 2021.

# samRNA: A Second-Generation mRNA Platform with Unique Attributes

*Differentiated vector that drives robust antibody and CD8+ T cell responses*

**samRNA**
**self-amplifying mRNA**

- Extended duration and magnitude of antigen expression
- Strong & potentially durable induction of neutralizing antibody & T cell immunity (CD4+ and CD8+)
- Dose sparing potential: Equivalent neutralizing antibody (nAb) induction at up to ~1/10 dose of approved mRNA vaccines
- Potential for refrigerator stable product

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- First to put samRNA into humans*
- Ongoing vector innovations to increase immunogenicity/efficacy, tolerability, and manufacturability
- Extensive clinical and regulatory experience
- INDs (or equivalent) and trials for 7 products in oncology and SARS-CoV-2 across four continents



*first to introduce samRNA + LNP into clinical trials

# CORAL Clinical Development Strategy Designed to Answer Key Questions Concerning Dose, Regimen and Patient Population

*Optimized construct and dose to be identified to enable pivotal trial initiation*

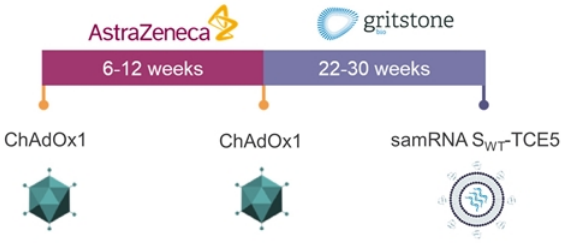
| Study | Population | Vaccine | Location | Construct | n |
|---|---|---|---|---|---|
| **CORAL - BOOST** | Healthy volunteers ≥60 years previously vaccinated | samRNA<br>samRNA/samRNA | UK & US | $S_{WT}$-TCE5 | 120 |
| **CORAL - IMMUNO-COMPROMISED** | B-cell deficient (hematologic malignancies, MS), previously vaccinated | ChAd/samRNA<br>ChAd/ChAd | UK | $S_{WT}$-TCE5 | 20-30 |
| **CORAL - CEPI** | Healthy volunteers (naïve or convalescent; including PLWH) | samRNA<br>samRNA/samRNA | S. Africa | $S_{beta}$-TCE9<br>$S_{beta}$-N-TCE11<br>$S_{omicron}$-N-TCE11 | 320 |
| **CORAL - NIH** | Healthy volunteers previously vaccinated | samRNA<br>ChAd<br>samRNA/samRNA | U.S. | $S_{WT}$<br>$S_{WT}$-TCE5 | 150 |

*$S_{WT}$ – Wild Type variant Spike; $S_{beta}$ – Beta variant Spike (B.1.351); $S_{omicron}$ – Omicron variant Spike (B.1.1.529); TCE – T-cell epitopes; N – Nucleocapsid; PLWH – People Living with HIV; ChAd – Chimpanzee adenovirus*

# CORAL-BOOST: samRNA as Boost Following Approved COVID-19 Vaccination

*Single dose of samRNA CORAL vaccine containing T cell epitopes and WT Strain Spike antigen*

| CORAL-BOOST | |
|---|---|
| Vaccine Candidate | **CORAL samRNA-$S_{WT}$-TCE5 (GRT-R910)** |
| Population | Healthy volunteers ≥60 years<br>Previously vaccinated with 2 doses of ChAdOx1 ≥ 4 months prior |
| Timing | • Vaccination initiated in September 2021<br>• Cohort 1 (10 µg) fully enrolled; n = 10<br>• Cohort 2 (30 µg) currently enrolling; n =10 |
| Sites | University of Manchester (UK) - Prof Andy Ustianowski (PI) |



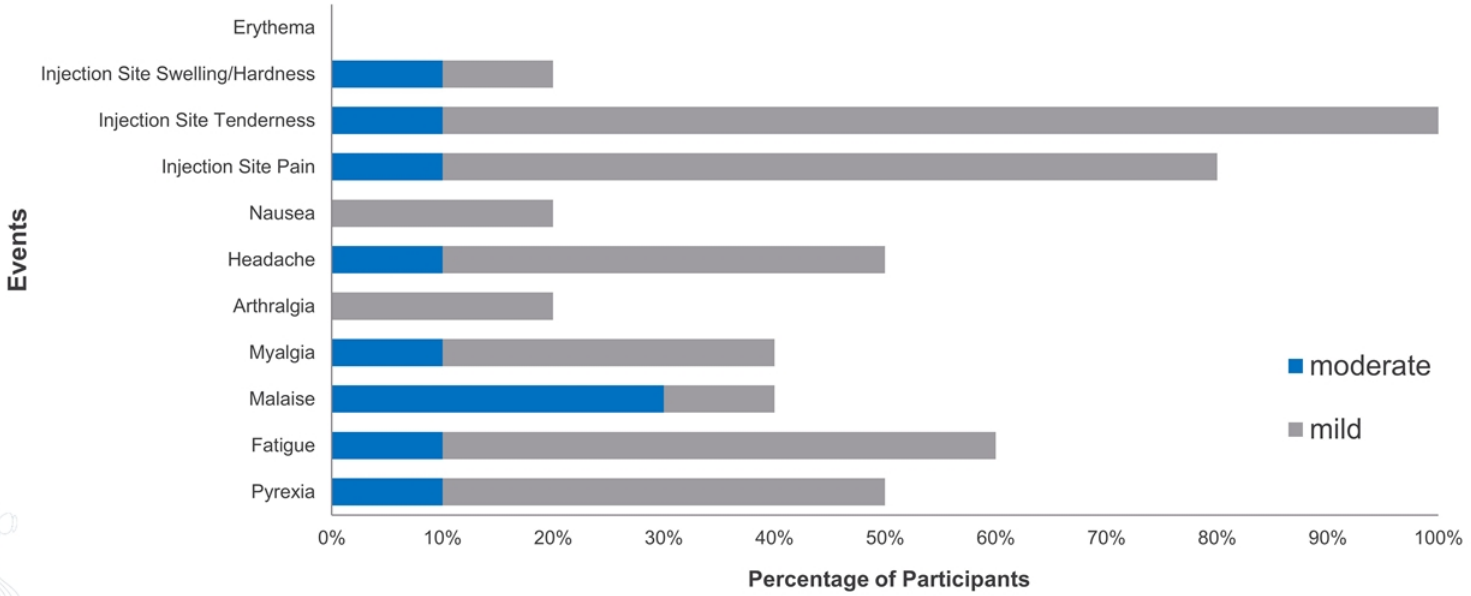

| Immunogenicity Endpoints | |
|---|---|
| Neutralizing Antibodies and IgG Titers | Pseudovirus neutralizing antibody and IgG titers assessed against multiple Spike variants |
| CD8+ T Cell Priming vs Novel T Cell Epitopes | In vitro stimulated ELISpot assay using overlapping peptide pools derived from TCE5-included target gene regions (ORF3a, N, M) |
| T Cell Boosting vs Spike Epitopes | Ex vivo ELISpot assay using overlapping peptide pools derived from Spike |

# Cohort 1: Subject Demographics

| Subject ID | Gender | Age | Weeks post 2nd Vaxzevria dose |
|---|---|---|---|
| 0001 | M | 63 | 30 |
| 0002 | F | 64 | 30 |
| 0003 | F | 63 | 22 |
| 0004 | M | 63 | 22 |
| 0005 | M | 69 | 25 |
| 0007 | F | 63 | 24 |
| 0008 | M | 81 | 25 |
| 0009 | F | 75 | 23 |
| 0014 | M | 75 | 27 |
| 0015 | M | 72 | 22 |

# samRNA Boost was Shown to Have a Favorable Safety and Tolerability Profile at 10µg in Healthy Volunteers ≥60 yrs

*No unexpected reactogenicity or safety events*



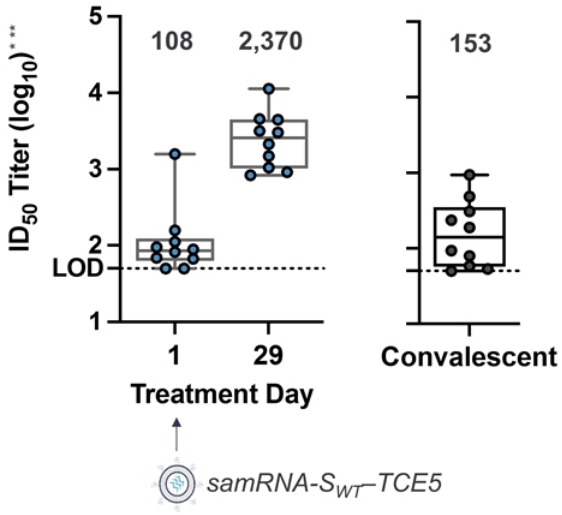

1 AE of recurrence of asthma and 1 AE of recurrence of muscle spasm in 10 µg dose cohort

*Database snapshot as of 11/29/2021*

gritstone bio

# Single 10µg samRNA Boost Dose Post Vaxzevria Two Dose Series Induced Potent Neutralizing Antibody Response Against SARS-CoV-2

Neutralizing antibodies (geomean) against
**Wild Type Variant**

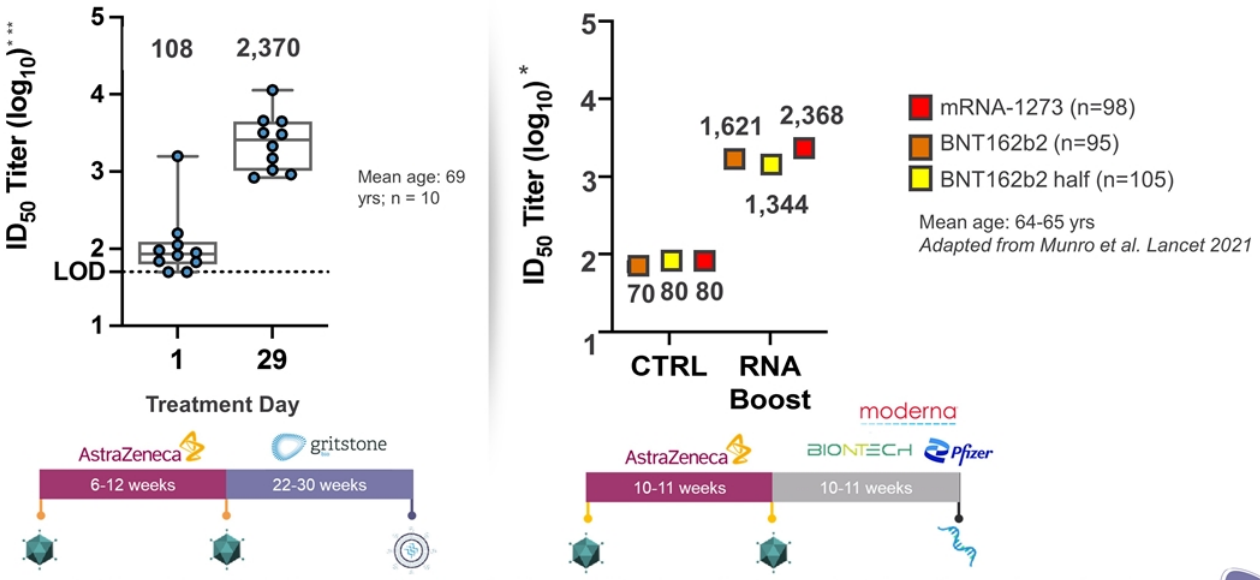



*$ID_{50}$ = Median infective dose; **Geomean $ID_{50}$ titer values notated; Assays conducted using WHO international standards
Treatment day = day 1 GRTS samRNA boost dose was administered. Boxes and horizontal bars denote interquartile range (IQR) and median neutralization, respectively. Whisker endpoints are equal to the maximum and minimum values below or above the median +/- 1.5 x IQR.*

gritstone bio

# Comparison Across Studies: 10µg samRNA Boost Elicited Similar, Potent nAb Response to 100µg of Moderna (mRNA-1273) after AZ Primary Series

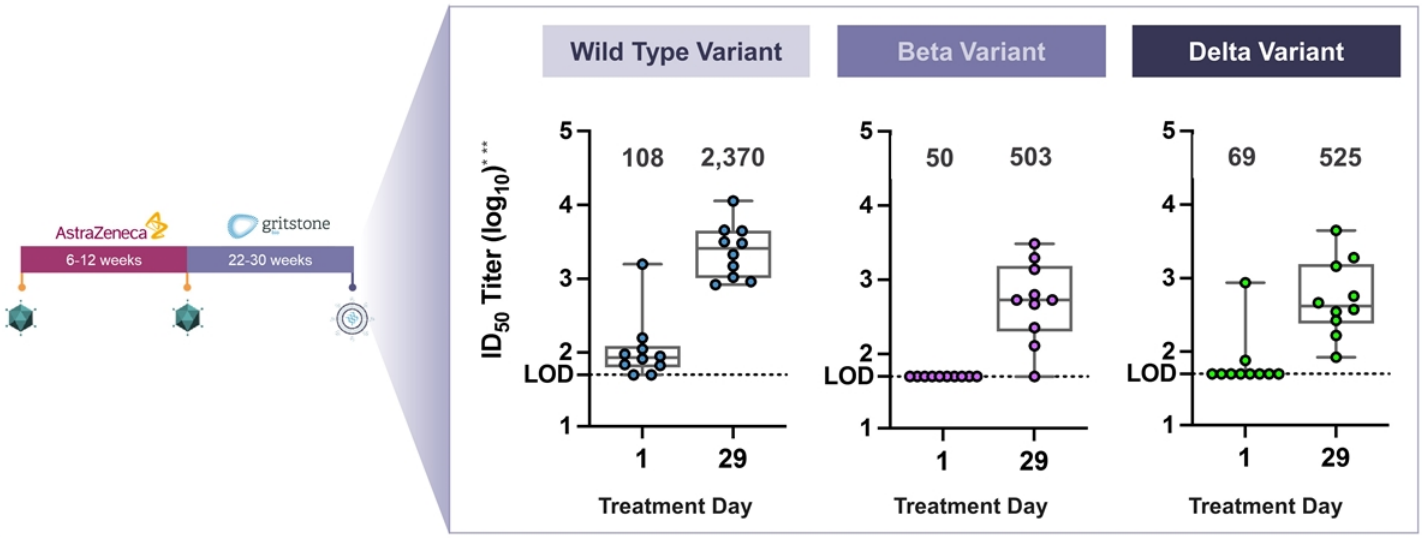
Neutralizing antibodies (geomean) against **Wild Type Variant**




*$ID_{50}$ = Median infective dose; **Geomean $ID_{50}$ titer values notated – not studied head-to-head directly; CTRL: Equivalent meningococcal conjugate vaccine; Treatment day = day 1 GRTS samRNA boost dose was administered. Boxes and horizontal bars denote interquartile range (IQR) and median neutralization, respectively. Whisker endpoints are equal to the maximum and minimum values below or above the median +/- 1.5 x IQR.*

# Single 10µg samRNA Boost Dose Induced a Broad, Potent nAb Response

*nAbs induced against Wild Type, Beta, and Delta variants of SARS-CoV-2*

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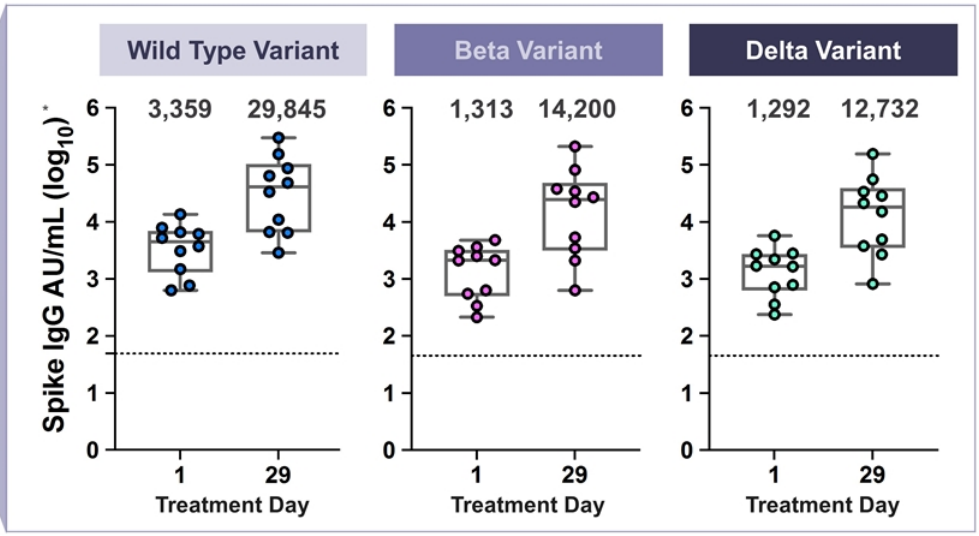
*$ID_{50}$ = Median infective dose, **Geomean $ID_{50}$ titer values notated – not studied head-to-head directly.
Treatment day = day 1 GRTS samRNA boost dose was administered. Boxes and horizontal bars denote interquartile range (IQR) and median neutralization, respectively. Whisker endpoints are equal to the maximum and minimum values below or above the median +/- 1.5 x IQR.

# Single 10µg samRNA Boost Dose Induced Broad Anti-Spike IgG Response

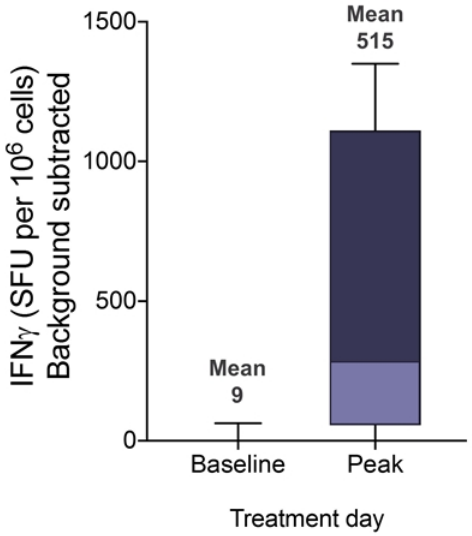
*ELISA-based assay assessing anti-Spike IgG concentration in arbitrary units (AU) per mL*


*Geomean AU/ml indicated*
*Treatment day = day 1 GRTS samRNA boost dose was administered. Boxes and horizontal bars denote interquartile range (IQR) and median neutralization, respectively. Whisker endpoints are equal to the maximum and minimum values below or above the median +/- 1.5 x IQR.*

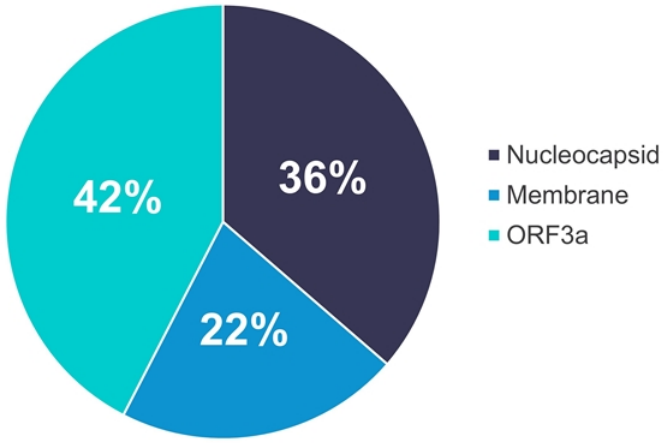
# Single 10µg samRNA Boost was Shown to Drive Significant CD8+ T Cell Responses to Non-Spike Epitopes - Potential for Variant-Proof Immunity

*Post-IVS ELISPOT*




Minimal TCE5 epitope pools (stacked); background subtracted
Box and whisker plot: 90% CI and median shown

*Proportion of responses to TCE5 regions assessed by post-IVS ELISpot*




TCE5 overlapping peptide (OLP) pools to TCE5 Nucleocapsid, Membrane and ORF3a regions assessed by post-IVS ELISpot (post-treatment timepoint)

# As Expected, Variant Mutations Had Minimal Impact on Gritstone Vaccine T Cell Epitopes (TCE)

**Comparison of Mutations within Variants to the Original SARS-CoV-2 Wild Type Strain**

| Variant | Spike (1273AA) | Orf1ab (7096AA) | Orf3a (275AA) | E (75AA) | M (222AA) | Orf7a (121AA) | N (419AA) |
|---|---|---|---|---|---|---|---|
| Beta | 7 | 7 | 2 | 1 | 0 | 0 | 1 |
| Delta | 10 | 3 | 1 | 0 | 1 | 2 | 3 |
| Omicron | 37 | 12 | 3 | 1 | 3 | 1 | 6 |

**Impact of Omicron Mutations on Gritstone TCE Cassettes***

| Gritstone Construct | # of Epitopes Impacted | Total # of Epitopes | % of Epitopes Impacted |
|---|---|---|---|
| TCE5 | **3** | 146 | 2.1% |
| TCE9 | **2*** | 72 | 2.8% |
| TCE11** | **0** | 25 | 0% |

**analyses for the table above were executed Nov 28, 2021*

*E=Envelope*
*M=Membrane*
*N=Nucleoprotein*
**2 epitopes impacted in 10% of Omicron isolates; 0 epitopes impacted in other isolates*
*** N-TCE11: no epitopes impacted in TCE but 6 Omicron mutations in 419 AA Nucleoprotein <1.5% of total protein*

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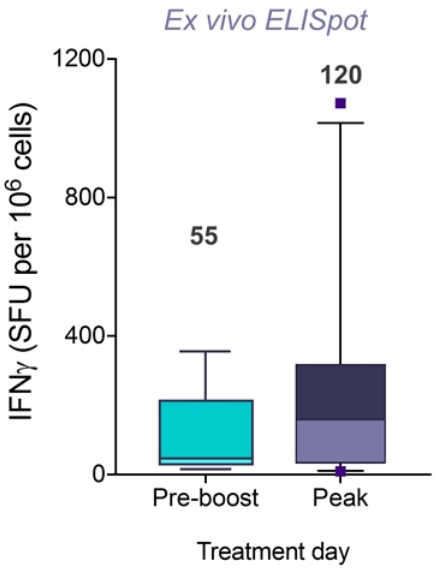
# Spike-Specific T Cell Responses Boosted after Single 10µg Dose of samRNA

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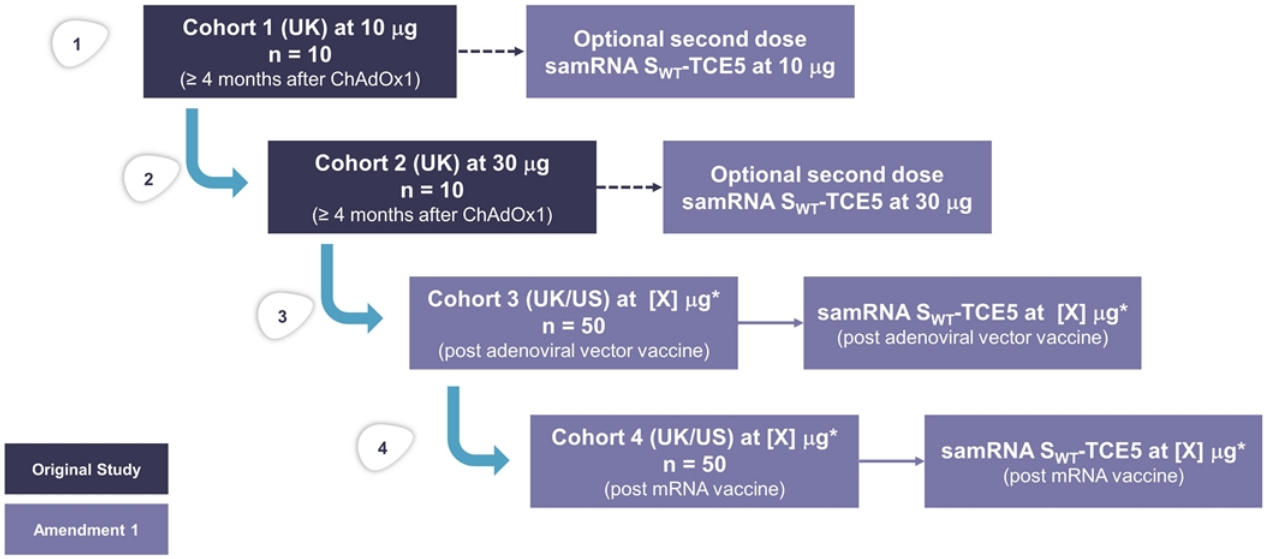
*Spike overlapping peptide pools (stacked)*

**Geometric mean is indicated*
*Box and whisker plot: 90% CI and median shown*

# CORAL-BOOST: Planned Study Expansion

*Expanded study intended to explore effects of 2nd samRNA dose and assess different primary vaccine series*

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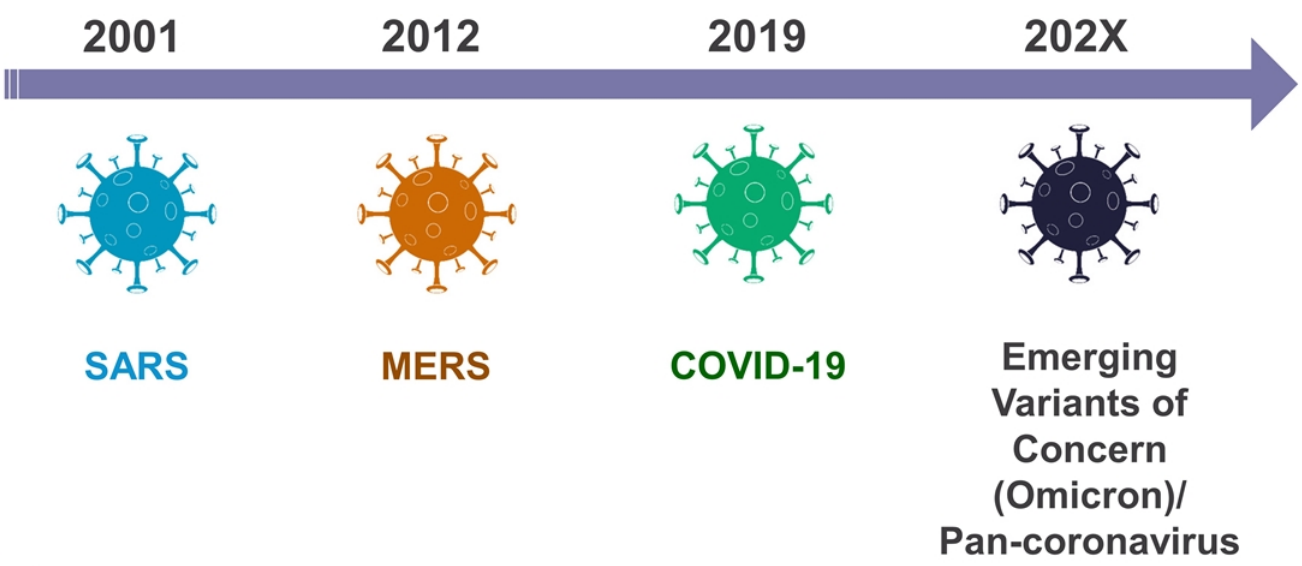
**Dose to be determined by immune and safety data from Cohorts 1&2*

# Gritstone's Platform is Highly Adaptable to Protect Against Variants

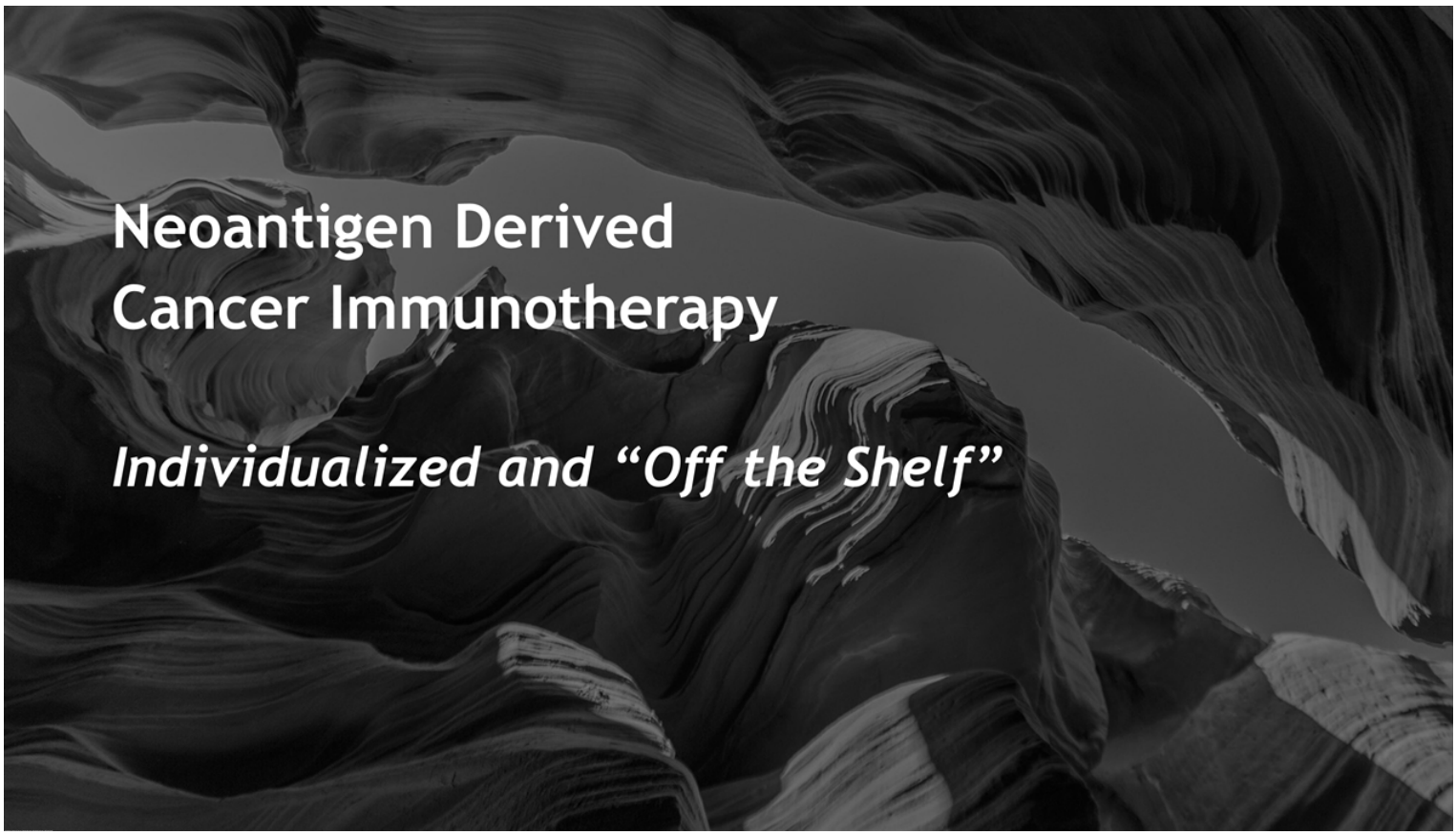
*Coronavirus evolution may give rise to additional pandemic strains*



# Collaboration with Gilead Under their HIV Cure Program to Research and Develop Vaccine-based HIV Immunotherapy Treatment

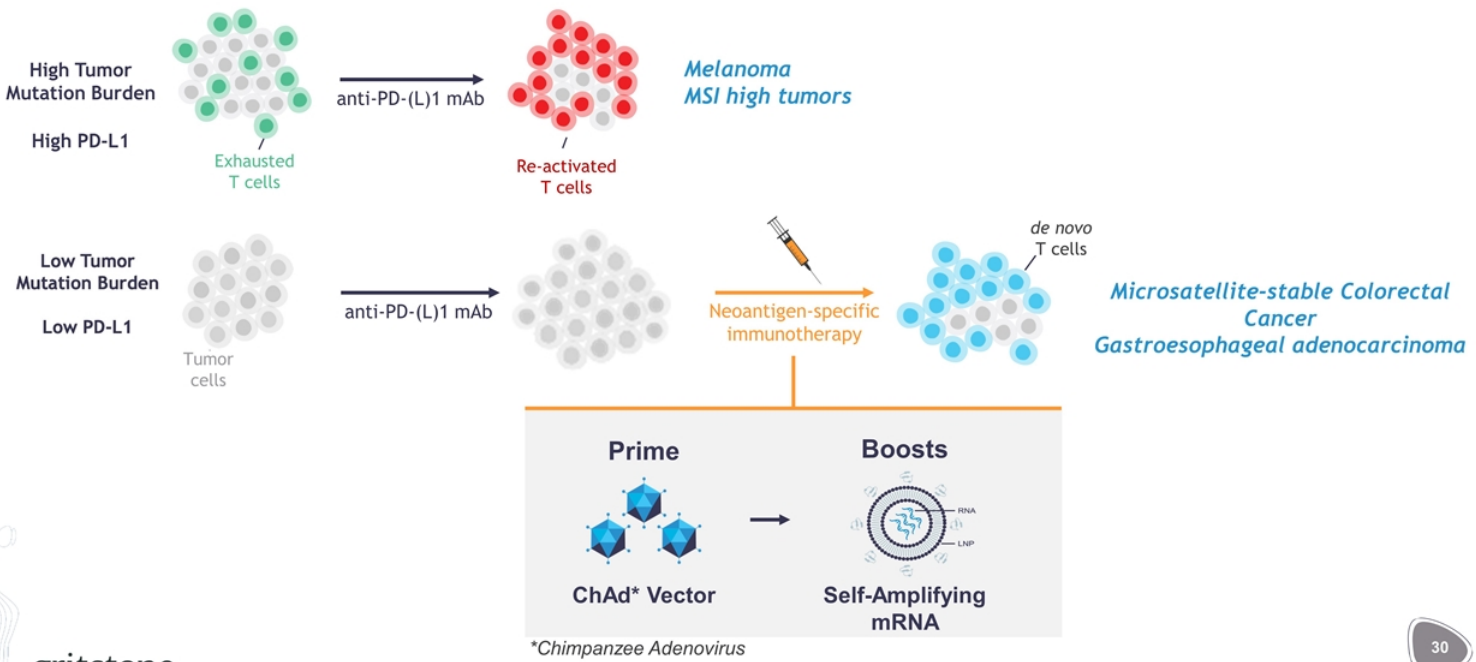
*Deal value of up to $785 million plus royalties*

- Gilead and Gritstone to develop an HIV-specific therapeutic vaccine
  - Gritstone's vaccine platform technology: adenoviral and self-amplifying mRNA vectors
- Based on preclinical data demonstrating strong, durable and broad anti-SIV CD8+ T cell responses and T cell memory data
- Gilead responsible for conducting Phase 1 study
  - IND cleared in December 2021; phase 1 to begin imminently
  - Option to obtain an exclusive license to develop and commercialize beyond Phase 1
- $60 million upfront; total deal value of up to $785 million
  - $60 million upfront: $30 million cash and $30 million in equity at a premium
  - Up to an additional $725 million if option exercised and certain clinical, regulatory and commercial milestones are achieved
  - Mid single-digit to low double-digit tiered royalties on net sales upon commercialization


Neoantigen Derived
Cancer Immunotherapy
*Individualized and "Off the Shelf"*

# Therapeutic Hypothesis: Many Solid Tumors Contain Neoantigens, but May Require Vaccine-Induction of Neoantigen-Specific CD8+ T Cells for Successful Immunotherapy

*This approach could enable immunotherapy in tumors where anti-PD-(L)1 antibodies are ineffective*




*Chimpanzee Adenovirus

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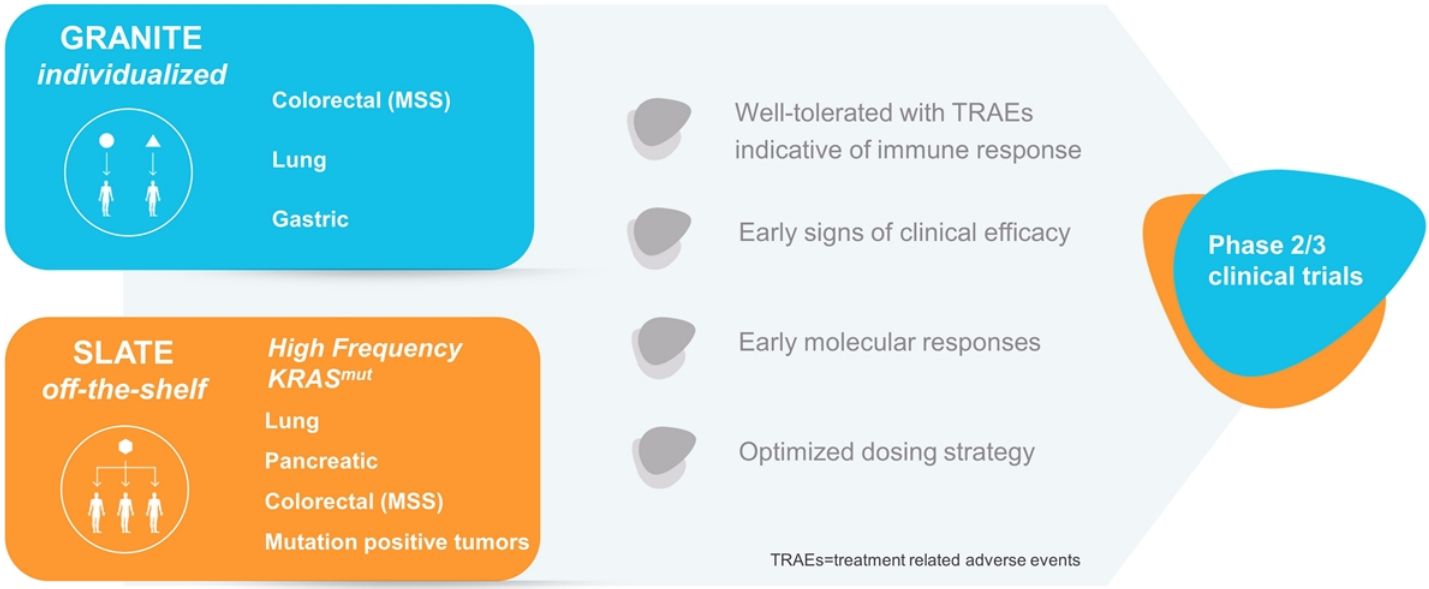
# GRANITE and SLATE Phase 1/2 Studies Support Advancement into Randomized Phase 2 Trials

*GRANITE & SLATE programs demonstrated promising efficacy with tolerable safety across solid tumors*




TRAEs=treatment related adverse events

# Phase 1/2 Study Evaluating the Safety, Immunogenicity, and Clinical Activity of GRANITE in Combination with Checkpoint Blockade

| | | Phase 1<br>Dose Escalation<br>N=14 | | | | Phase 2<br>Efficacy Evaluation in Tumor-Specific Expansion Cohorts<br>N=12 (treated to date) | Primary Objective |
|---|---|---|---|---|---|---|---|
| | | Dose Level 1<br>N=3 | Dose Level 2<br>N=3 | Dose Level 3<br>N=2 | Dose Level 4<br>N=6 | | |
| Prime |  ChAd Vector | GRT-C901 | | | | **Cohort 1:**<br>*Microsatellite-stable Colorectal Cancer (MSS-CRC)* | Safety and Tolerability |
| Boost |  Self-Amplifying RNA | GRT-R902<br>(dose escalation) | | | | **Cohort 2:**<br>*Gastroesophageal adenocarcinoma (GEA)* | Phase 2: Overall Response Rate |
| | Ipilimumab (SC) | - | - | 30 mg | 30 mg | **Cohort 3:**<br>*Non-small cell lung cancer* | Recommended Phase 2 Dose |
| | Nivolumab (IV) | 480 mg → | | | | | |

*GRT-C901 = chimpanzee adenovirus encoding 20 neoantigens*
*GRT-R902 = self-amplifying mRNA in lipid nanoparticles encoding same neoantigens as GRT-C901*

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# Safety: Immunotherapy Well-Tolerated In Patients with Previously Treated Metastatic Solid Tumors

*No patients experienced a DLT, no vaccine discontinuations due to TRAEs, and most common AEs comprise low-grade fever and injections site reactions, consistent with potent vaccine*

| Demographics and Tumor Types | n=26 |
|---|---|
| **Age: mean (range)** | **60 (38-77)** |
| **Gender: Female/Male** | **9/17** |
| **Tumor Types** | |
| Microsatellite-stable (MSS) Colorectal Cancer | 12 |
| Median number of prior therapies (range) | 2 (2-3) |
| Gastroesophageal adenocarcinoma (GEA) | 12 |
| Median number of prior therapies (range) | 1 (1-2) |
| Non-small cell lung cancer | 2 |
| Median number of prior therapies (range) | 2 (2) |
| Prior anti-PD(L)1 therapy | 2 |

Abbreviations: DLT=dose-limiting toxicity; TRAE=treatment-related adverse event; ISR=injection-site reaction

*Data cut-off: 05 Aug 2021*

| Safety | n = 26 (all patients treated with concurrent nivolumab) | |
|---|---|---|
| | Grade 1/2 | Grade 3/4 |
| **Treatment-related adverse events ≥ 5%** | | |
| Fever | 15 | - |
| Injection site reaction | 15 | - |
| Fatigue | 7 | - |
| Diarrhea | 6 | - |
| Anorexia | 4 | - |
| Rash | 3 | - |
| Abdominal pain | 2 | - |
| Chills | 3 | - |
| ALT increased | 1 | 1 |
| AST increased | 2 | - |
| CK elevation | 2 | - |
| Hypotension | 2 | - |
| **Treatment-related SAEs** | | |
| Duodenitis | - | 1 |
| Fever | 1 | - |
| Hyperthyroidism | - | 1 |
| Myositis | - | 1 |

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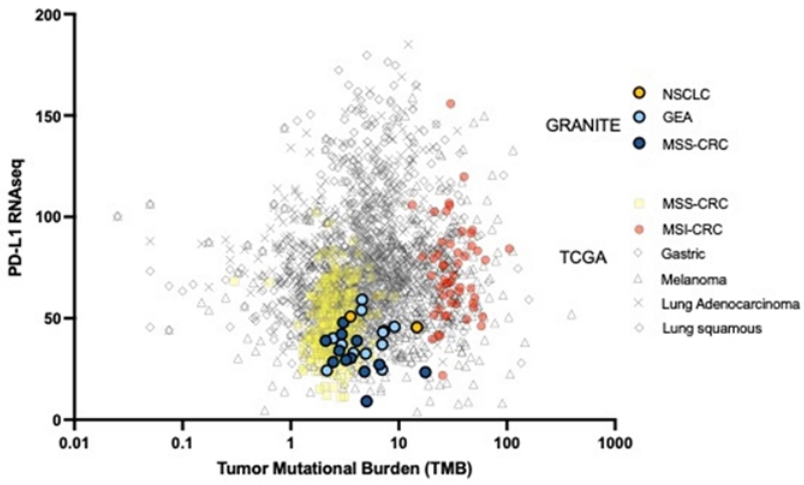
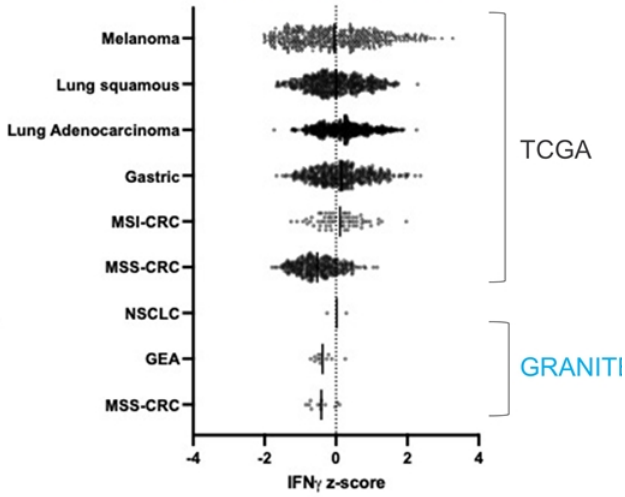
# MSS-CRC & GEA Tumors in GRANITE are “Cold” with No Immune Reactivity

*Low tumor mutational burden, low PD-L1 expression, and low IFN-γ expression signature*

PD-L1 mRNA expression *vs.* Tumor Mutational Burden




Interferon Gamma (IFN-γ) mRNA expression signature




*TMB calculated based on all somatic mutations called divided by WES bait set size*

*IFN-γ score was obtained by averaging IFN-γ established gene set z-scores calculated across GRANITE and relevant PANCAN TCGA tissue types (LUAD, LUSC, COAD, SKCM): J Clin Invest. 2017;127(8):2930-2940*

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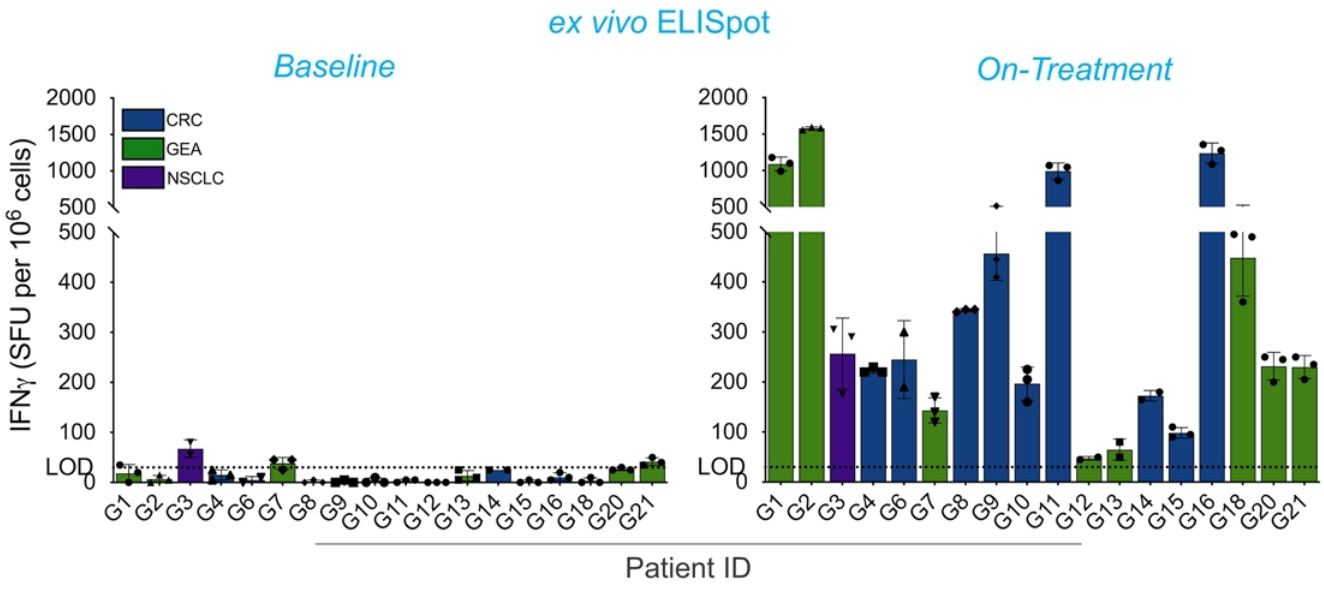
# Immunogenicity: GRANITE Consistently Induces Neoantigen-specific T-cells

*Lack of T cells in patients prior to treatment reflective of poor immunogenicity*

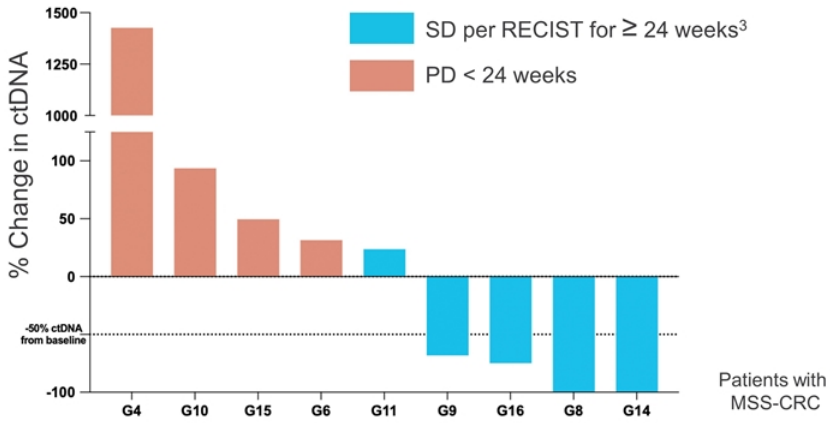



*G5: no samples available (patient died)*

# Efficacy: Clinical Activity in Previously Treated MSS-CRC Based on Partial and Complete Molecular Responses and Associated Prolonged PFS

*Tumor lesion shrinkage also observed in multiple patients - often over many months*

***Best ctDNA molecular response (% ctDNA change from baseline)[1,2]***




1. ctDNA assessment based on Gritstone-developed, tumor-informed assay
2. ctDNA assessment not available for the 3 most recently treated patients
3. Patients G14 and G16 with PD at week 16 and 9 respectively not confirmed on subsequent scans through week 24

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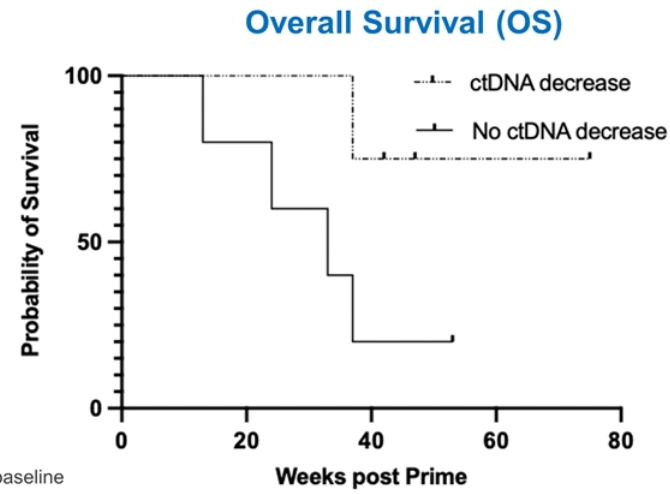
SD=stable disease; PD=progressive disease

# Efficacy: Molecular Response (ctDNA reduction) is Associated with Increased OS (>17 vs 7.8 months)

| 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 |

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

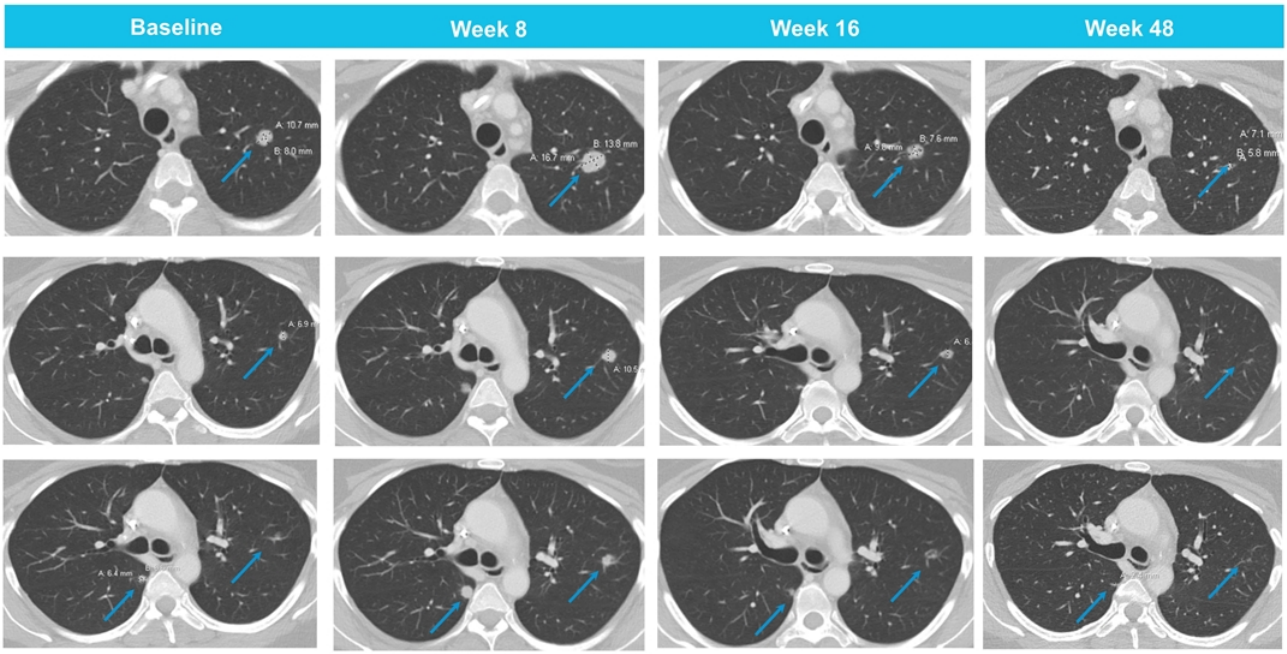



Data cut-off 05 Aug 2021



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

# G8 Case Study: Lung CT Shows Transient Lesion Expansion at Week 8 (T Cell Infiltration?) Then Contraction

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# GRANITE Clinical Development Strategy

*Based on Ph1/2 data, we are advancing GRANITE into 2 randomized, controlled clinical trials in MSS-CRC*

| Study | Phase | N | Population | Induction | Maintenance | | Primary Endpoint |
|---|---|---|---|---|---|---|---|
| | | | | | Control Arm | Treatment Arm | |
| GRANITE - 1L | 2 | 80 | 1st Line MSS-CRC | Oxaliplatin + Fluoropyrimidine + bevacizumab | Fluoropyrimidine + bevacizumab | Vaccine* + anti PD-L1+ Fluoropyrimidine + bevacizumab | Molecular response (ctDNA ↓) |
| | 3 | 200 | | | | | iPFS per independent review |
| GRANITE - adjuvant | 2 | | Adjuvant MSS-CRC | Adjuvant Chemotherapy | Observation | ChAd w/anti-CTLA-4 followed with samRNA Boosts + anti PD-(L)1 | ctDNA ↓<br>DSF<br>OS |

*Vaccine = ChAd prime + anti-CTLA-4 followed by repeat samRNA boosts and single ChAd boost

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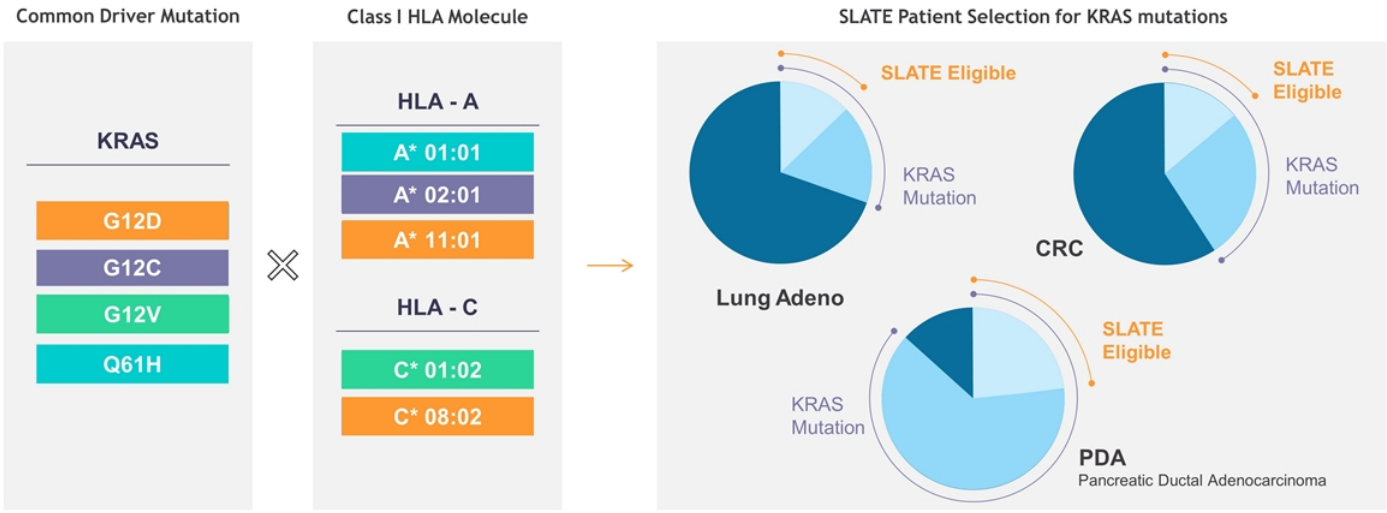
# SLATE Product Targeting *KRAS* Mutants

*One Product - Many Selected Patients*



# Safety: Immunotherapy Well-Tolerated In Patients with Previously Treated Metastatic Solid Tumors

| SLATE Baseline Characteristics | n=26 |
|---|---|
| **Age: mean (range)** | 59 (33-83) |
| Gender: Female/Male | 16/10 |
| **Tumor Types** | |
| Non-small cell lung cancer | 13 |
| Median number of prior therapies (range) | 2 (1-4) |
| Prior anti-PD-(L)1 therapy | 13 |
| Microsatellite-stable (MSS) Colorectal Cancer | 6 |
| Median number of prior therapies (range) | 2 (1-3) |
| Pancreatic ductal adenocarcinoma (PDA) | 5 |
| Median number of prior therapies (range) | 1 (1-3) |
| Ovarian cancer | 1 |
| Median number of prior therapies (range) | 4 |
| Ampullary adenocarcinoma | 1 |
| Prior anti-PD-(L)1 therapy | 5 |

*Data cut-off: 05 Aug 2021*

| Safety | n = 26 (all treated with concurrent nivolumab) | |
|---|---|---|
| | Grade 1/2 | Grade 3/4 |
| **Treatment-related adverse events ≥ 5%** | | |
| Fever | 13 | |
| Fatigue | 8 | |
| Nausea | 7 | |
| Vomiting | 7 | |
| Diarrhea | 5 | |
| Injection site reaction | 5 | |
| Arthralgia | 3 | |
| ALT increased | 1 | 1 |
| AST increased | 1 | 1 |
| Anorexia | 2 | |
| Chills | 2 | |
| Dizziness | 2 | |
| Dyspnea | 2 | |
| Generalized weakness | 2 | |
| Myalgia | 2 | |
| Pruritus | 2 | |
| **Treatment-related SAEs** | | |
| Fever | 2 | |
| Hepatitis | | 1 |
| Neutropenia | | 1 |
| Pneumonitis | | 1 |
| Rhabdomyolysis | | 1 |
| Vomiting | 1 | |

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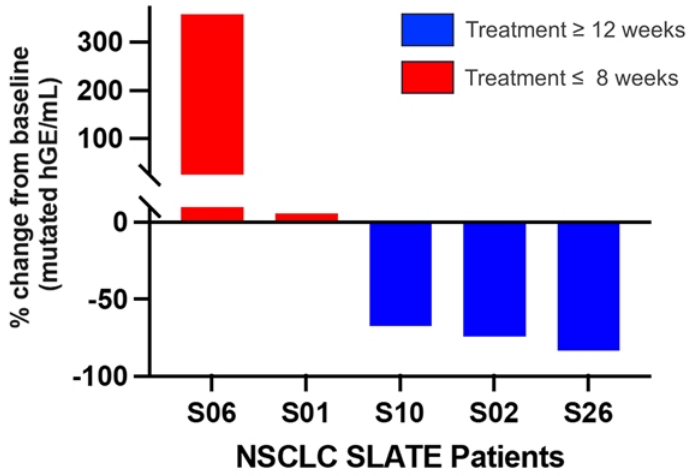
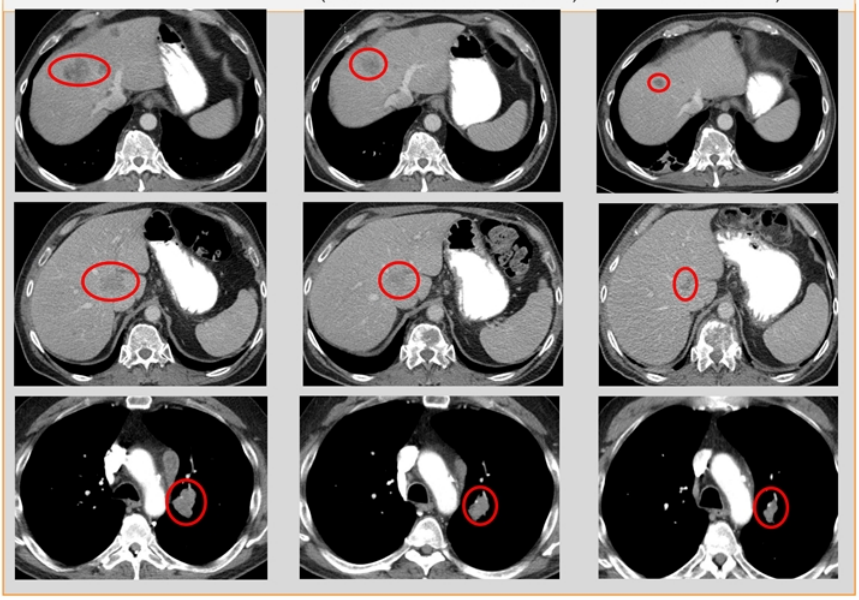
# Efficacy: Several NSCLC Patients Experienced Decrease in ctDNA Including Patient with High Baseline Levels

| Patient | Mutation | Baseline ctDNA (mutated hGE/mL) |
|---|---|---|
| S1 | G12C | 124.64 |
| S2 | G12C | 26.92 |
| S3 | G12C | Not detectable |
| S6 | G12D | 21.12 |
| S10 | Q61H | 77.23 |
| S14 | G12D | Not detectable |
| S26 | G12C | 3386.05 |



# Case Study - S26: Unconfirmed Partial Response with Clear Reduction in Liver and Lung Lesions

| Baseline | Week 8 | Week 16 |
|---|---|---|
| 113 mm* | 95 mm* (-16% relative to baseline) | 61 mm* (-46% relative to baseline) |



**Sum of longest diameters of two target lesions*

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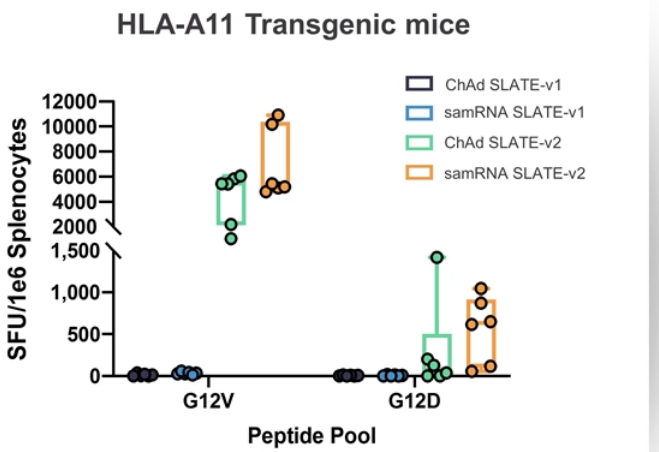
# SLATE: Version 2 of the *KRAS$^{mut}$* Antigenic Cassette Induces Potent T-Cell Responses to Multiple KRAS Neoantigens - Phase 2 Trial Underway

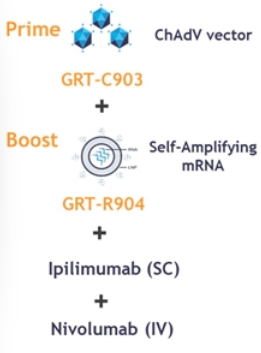
*No T-cell response was observed in these transgenic mice with SLATE cassette version 1*




Overnight stimulation with peptide pool containing 38 minimal epitopes. Background subtracted.

**Phase 2**

Efficacy Evaluation in Tumor-Specific Expansion Cohorts




**Cohort 1:**
*CRC 1L M (n=20)*

**Cohort 2:**
*CRC 3L (n=20)*

**Cohort 3:**
*NSCLC post-IO (n=20)*

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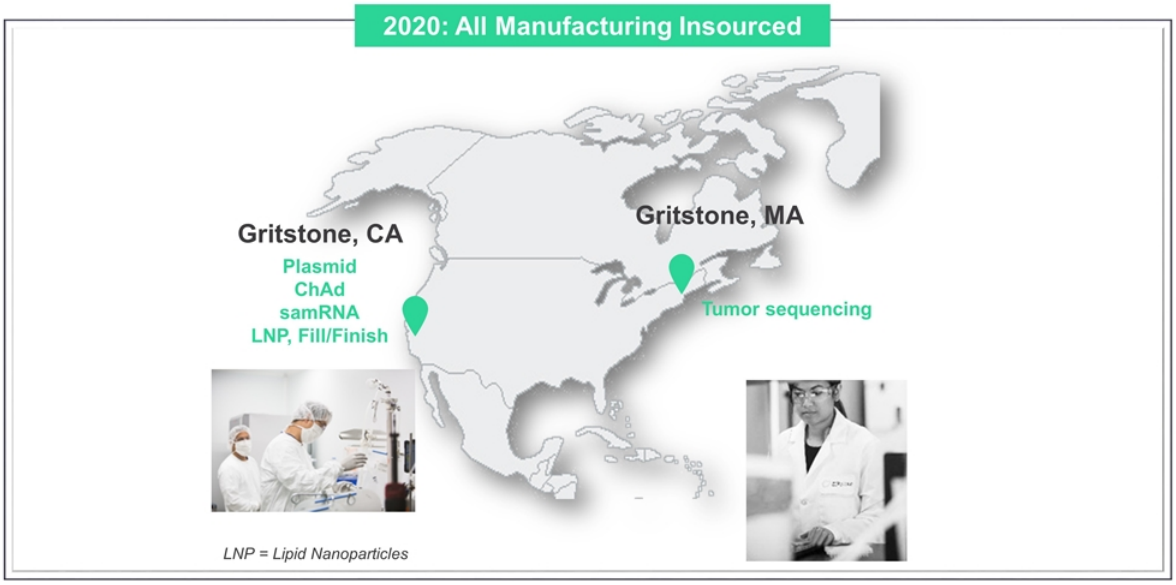
# Gritstone Has its Own Fully Insourced Biomanufacturing Facility

*43,000 sq. ft. manufacturing and testing facility in Pleasanton, CA*



# Key Accomplishments and Anticipated Upcoming Milestones

*Near-term catalysts provide multiple value inflection points for Gritstone*

**4Q 2021**

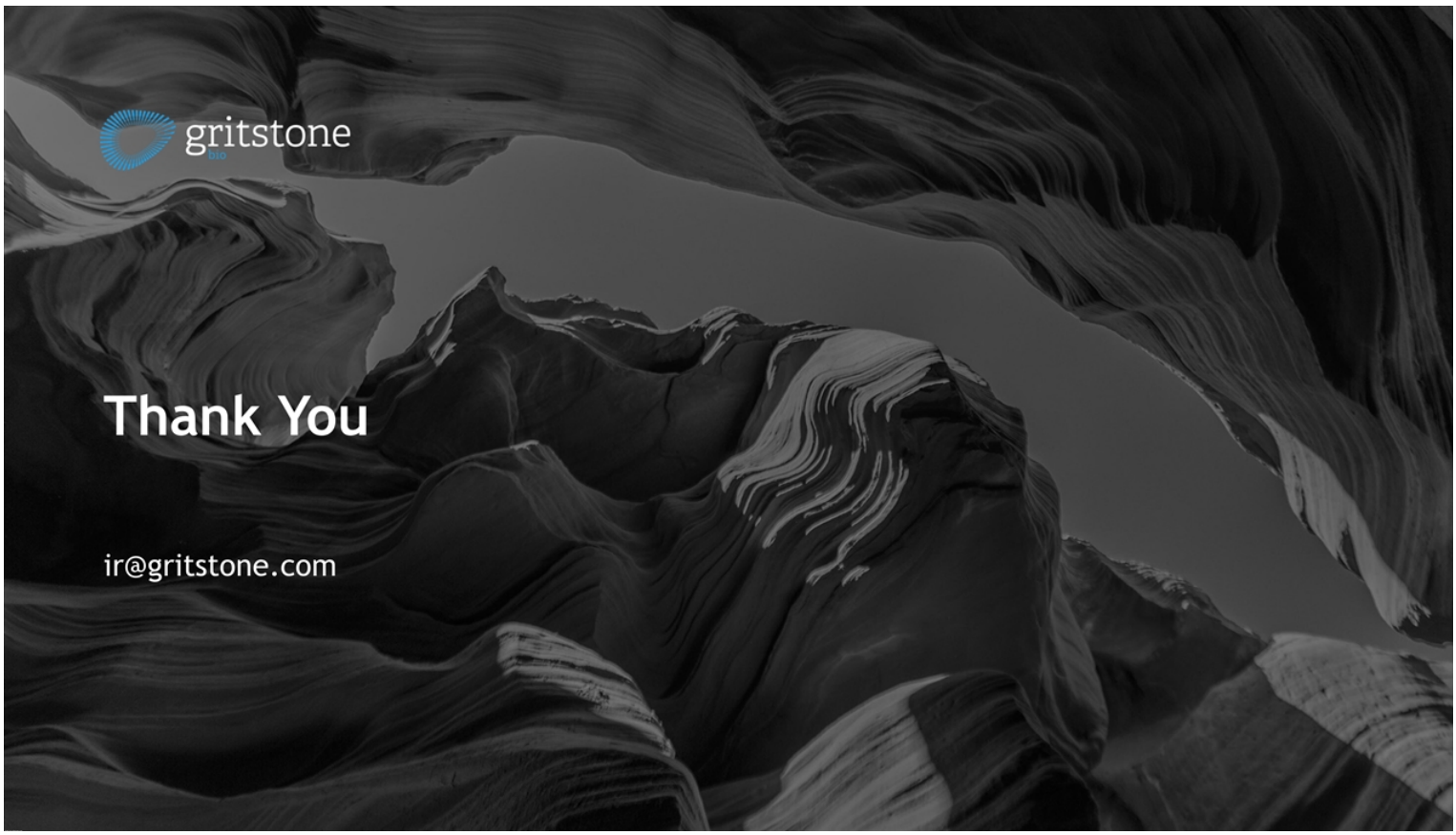
- **Initiate GRANITE Randomized Ph2/3 Trial in 1L maintenance MSS-CRC** ✓
- **Pre-publish non-human primate viral challenge data** ✓
- **CORAL-IMMUNOCOMPROMISED trial – MHRA clearance received Dec 2021** ✓
- **GRTS-GILEAD HIV Collaboration – Phase 1 trial IND cleared** ✓
- **Expand CEPI agreement to address Omicron variant** ✓

**1Q 2022**

- **Initial data from GRTS sponsored CORAL booster trial in 60+ (UK)** ✓
- **CORAL-CEPI trial in South Africa – currently under review by SAHPRA**

**2Q-3Q 2022**

- **Initiate GRANITE Randomized Phase 2 trial in adjuvant setting for Stage II/III MSS-CRC**
- **Prelim data from CORAL-NIH trial (1H2022)**
- **SLATE v2 Preliminary Data (mid-2022)**
- **Prelim data from CORAL-IMMUNOCOMPROMISED trial (mid-2022)**
- **Prelim data from CORAL-CEPI trial in South Africa (mid-2022)**
- **Additional CORAL-BOOST data from 003 and expansion (3Q2022)**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bio
Thank You
ir@gritstone.com