



gritstone
ONCOLOGY

Gritstone COVID-19 Vaccine Introduction

January 2021



Safe Harbor and Forward-Looking Statements

This presentation contains forward-looking statements including, but not limited to, statements related to our preclinical and clinical product candidates, GRANITE, SLATE, CORAL and bispecific antibody 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, identification of development candidate for our bispecific antibody program, collaborations surrounding our infectious disease program, 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. 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.

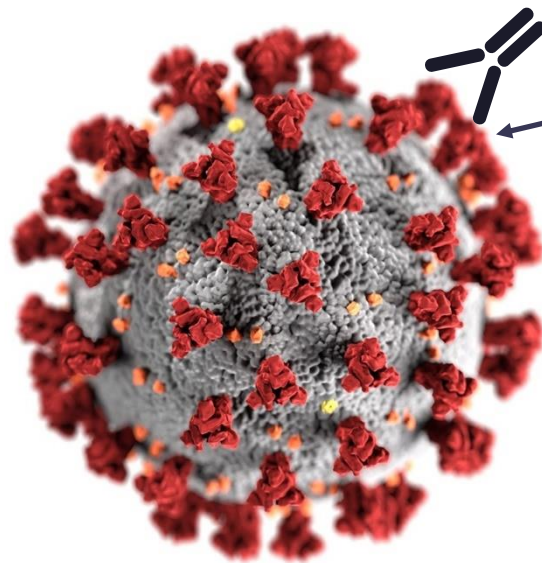
Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. For a further description of the risks and uncertainties that could cause actual 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 5, 2020 and any current and periodic reports filed thereafter.

Gritstone Second Generation COVID-19 Vaccine Program Named CORAL

- First generation COVID-19 vaccines elicit a strong antibody response against SARS-CoV-2 and offer initial protection, but durability of protection is unknown and may be affected by mutations
- CD8 T cells offer a key second layer of defense and may provide longer, more robust immunity
- Through a license agreement with the La Jolla Institute for Immunology, Gritstone gains access to validated CD8 T cell epitopes in Spike and other viral genes that have been identified through studies of COVID-19 patients
- Using these epitopes and its EDGE™ prediction and vaccine platform technologies, Gritstone is developing a vaccine against COVID-19 that has the potential to maximize CD8 T cell and antibody responses and protect against new Spike mutant strains
- The Bill & Melinda Gates Foundation is supporting the preclinical evaluation of the vaccine
- The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, have entered into a clinical trials agreement with Gritstone to initiate clinical testing, expected to start in 1Q21

First Generation COVID-19 Vaccines Elicit a Strong Antibody Response Against SARS-CoV-2 and Offer Convincing Evidence of Initial Protection

Vaccines elicit antibodies that recognize the virus when it enters the body, and prevents it from infecting cells



Surface protein called Spike protein

Neutralizing Antibodies (nAb)
Identify Viruses By
Their Surface Proteins

FDA NEWS RELEASE

FDA Takes Key Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for First COVID-19 Vaccine

Action Follows Thorough Evaluation of Available Safety, Effectiveness, and Manufacturing Quality Information by FDA Career Scientists, Input from Independent Experts

For Immediate Release:

December 11, 2020

FDA NEWS RELEASE

FDA Takes Additional Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for Second COVID-19 Vaccine

Action Follows Thorough Evaluation of Available Safety, Effectiveness, and Manufacturing Quality Information by FDA Career Scientists, Input from Independent Experts

For Immediate Release:

December 18, 2020

However, Antibody Responses are Expected to Wane Over Time and Long-Term Durability of Protection Remains Unknown

The NEW ENGLAND JOURNAL of MEDICINE

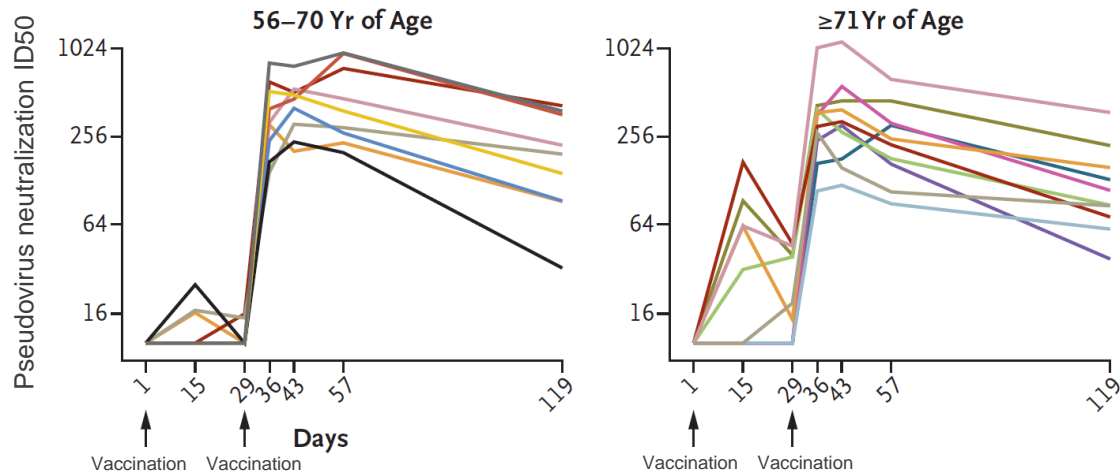
CORRESPONDENCE

Durability of Responses after SARS-CoV-2 mRNA-1273 Vaccination

The NEW ENGLAND JOURNAL of MEDICINE

Rapid Decay of Anti-SARS-CoV-2 Antibodies in Persons with Mild Covid-19
Ibarondo, et al. *NEJM*, 2020

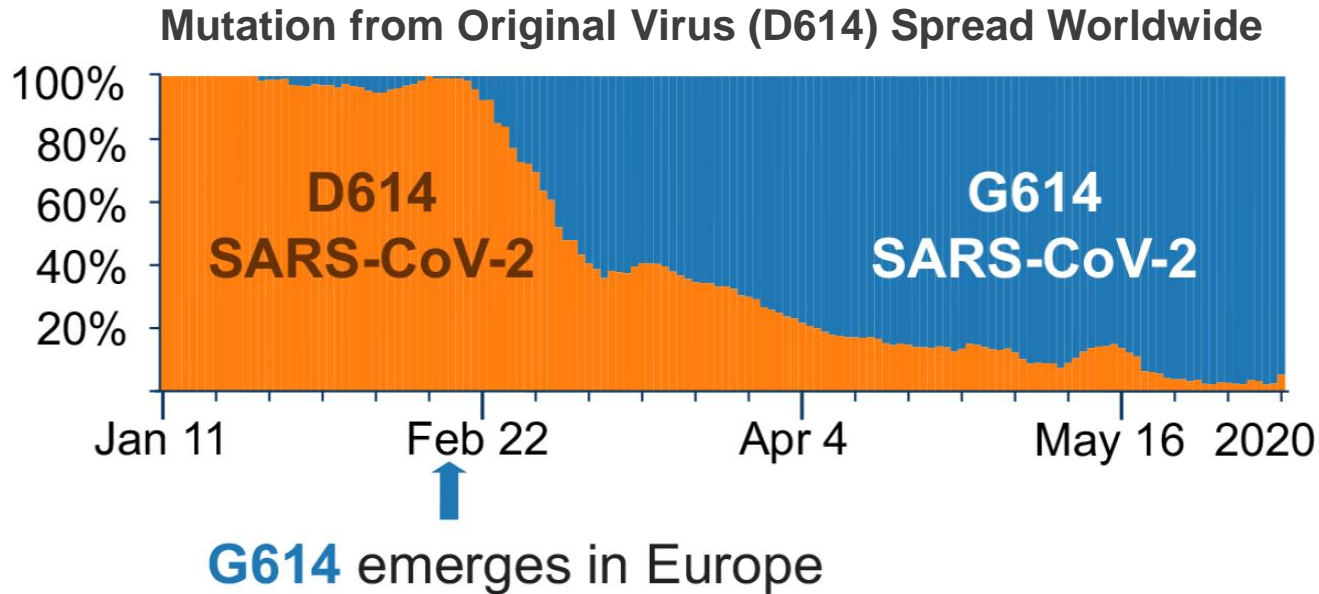
Time course of antibody immune response



nature microbiology

Longitudinal observation and decline of neutralizing antibody responses in the three months following SARS-CoV-2 infection in humans
Seow, et al. *Nature Microbiology*, 2020

Additionally, Mutations in SARS-CoV-2 Continuously Arise and May Further Reduce Neutralizing Antibody Protection



Boris Johnson backtracks on relaxing Christmas rules after scientists warn new Covid-19 strain is spreading faster

By Amy Woodyatt, Lindsay Isaac, [Luke McGee](#) and Arnaud Siad, CNN

Updated 5:13 AM ET, Sun December 20, 2020



bioRxiv

THE PREPRINT SERVER FOR BIOLOGY

Comprehensive mapping of mutations to the SARS-CoV-2 receptor-binding domain that affect recognition by polyclonal human serum antibodies

The most important site is E484, where neutralization by some sera is reduced >10-fold by several mutations, including one in emerging viral lineages in South Africa and Brazil

Cell

Article

Tracking Changes in SARS-CoV-2 Spike: Evidence that D614G Increases Infectivity of the COVID-19 Virus

HEALTH

STAT **Scientists are monitoring a coronavirus mutation that could affect the strength of vaccines**

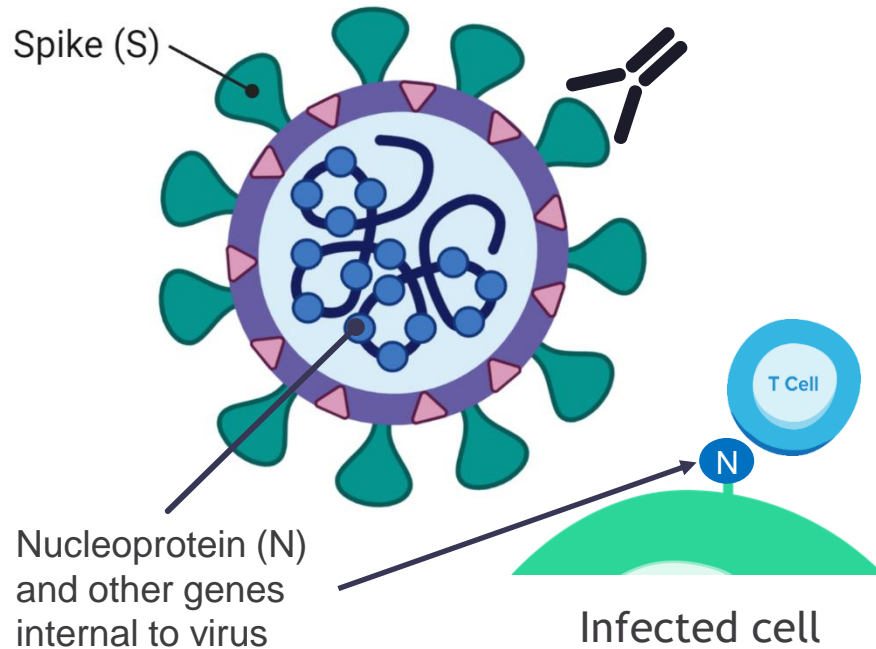
By ANDREW JOSEPH @DrewJoseph / JANUARY 7, 2021

Reprint

CD8 T Cells Offer Second Layer of Defense and May Provide Longer Immunity

Analysis of blood from convalescent COVID-19 patients exhibit both T cell and antibody immune responses

T Cells Can Identify Virus Protein Fragments From Within The Virus



Killer T cells (CD8+ T cells)

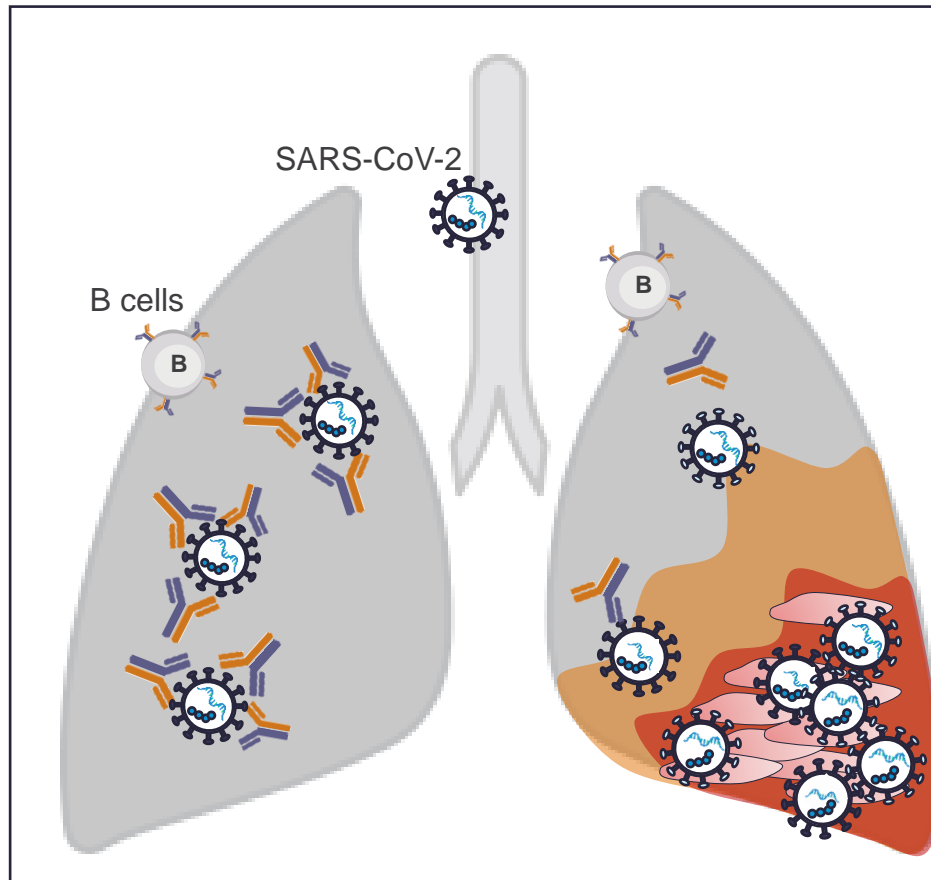


Once the virus has infected a cell, the cell displays pieces from inside the virus on its surface, which T cells can recognize

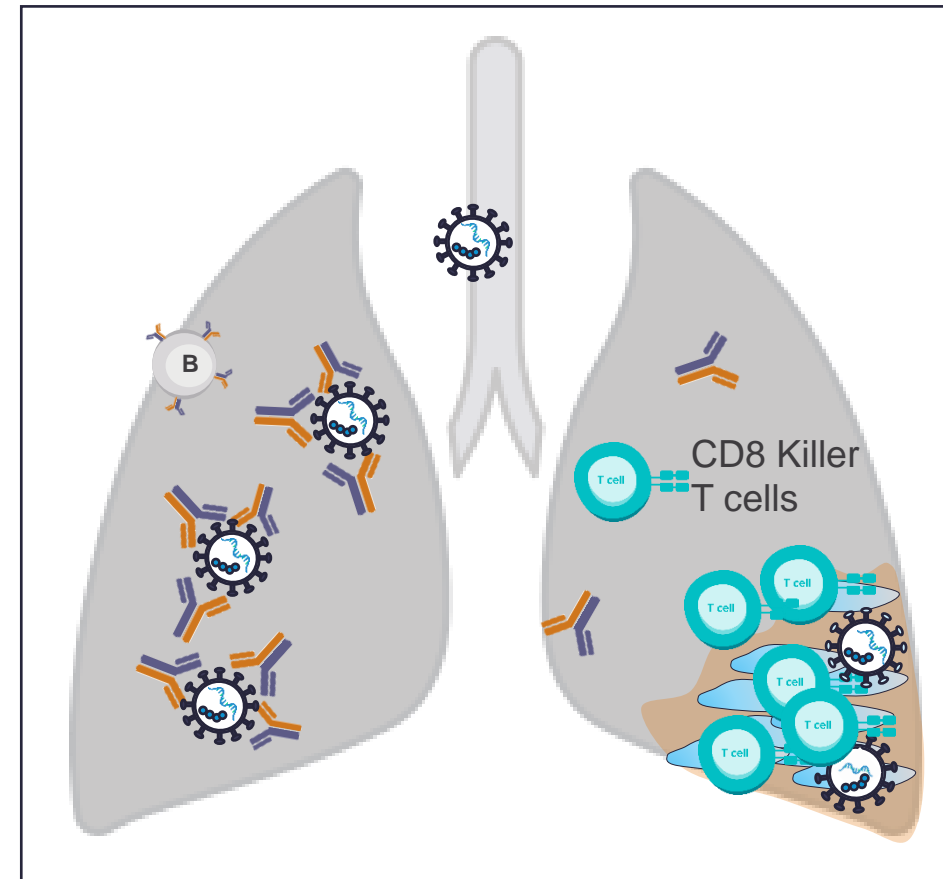
T cells remember what viruses look like, providing longer immunity

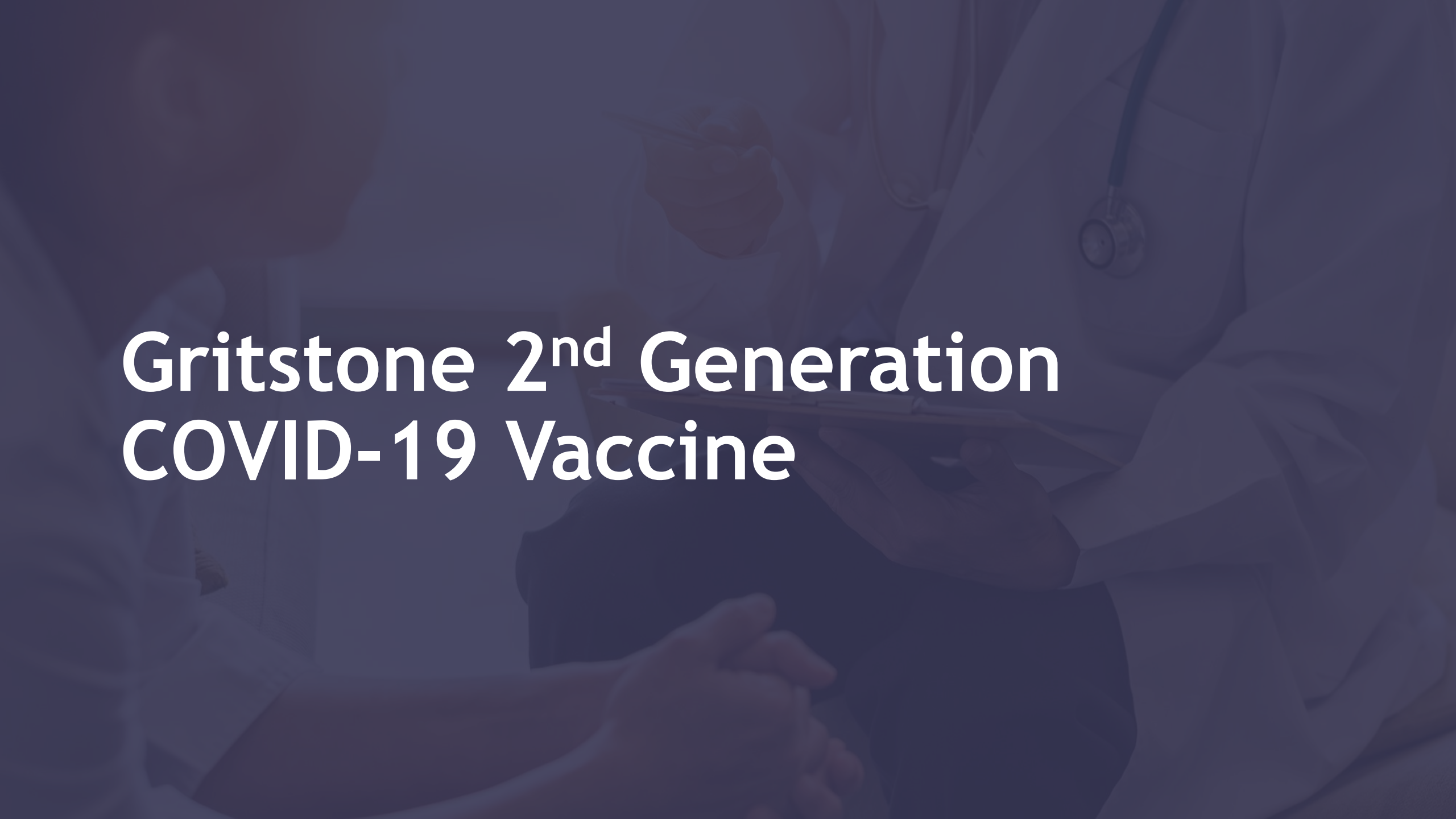
CORAL Program Seeks to Maximize CD8 T Cell Response in Addition to nAb Response for 2nd Layer of Protection if/when nAb Protection Wanes

Neutralization of the incoming virus by antibodies can be incomplete. Free virus infects lung cells and starts replicating and inflicting organ damage.



If neutralization by antibodies is incomplete, memory CD8 T cells expand rapidly upon virus infection, clear virus from infected cells and reduce/prevent organ damage





Gritstone 2nd Generation COVID-19 Vaccine

Gritstone's COVID-19 Vaccine Platform Combines Two Potent Vaccine Vectors to Elicit Strong CD8 T cell and Antibody Response

GRITSTONE APPROACH

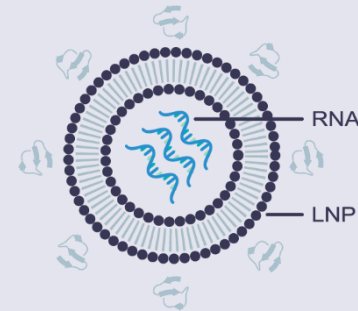
Two Vaccine Vectors Given Sequentially

Prime



Chimpanzee
Adenovirus (ChAd)
Based Vaccine

Boost

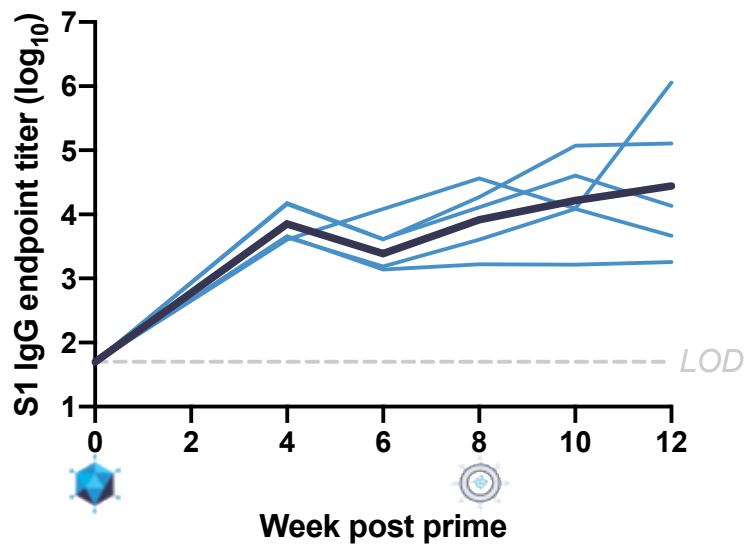


Self Amplifying
RNA (SAM)
Based Vaccine

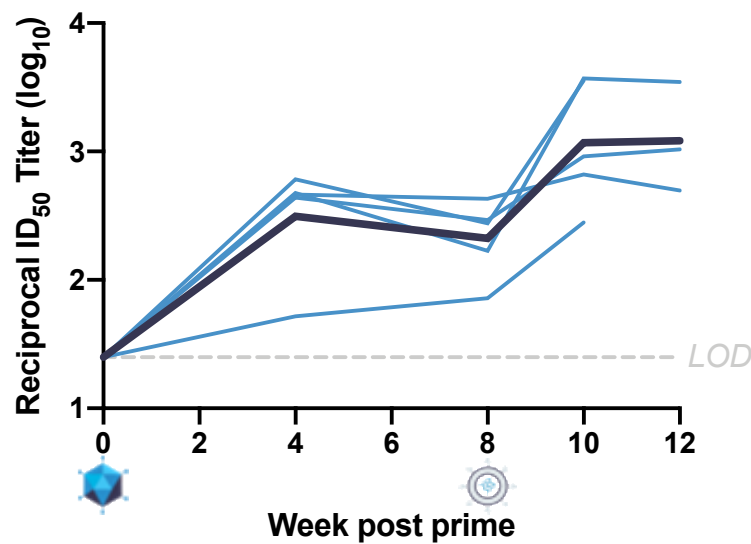
Approach also known as heterologous prime / boost

Gritstone's Heterologous Platform Drives a High Neutralizing Antibody Response in Non-Human Primates (NHPs)

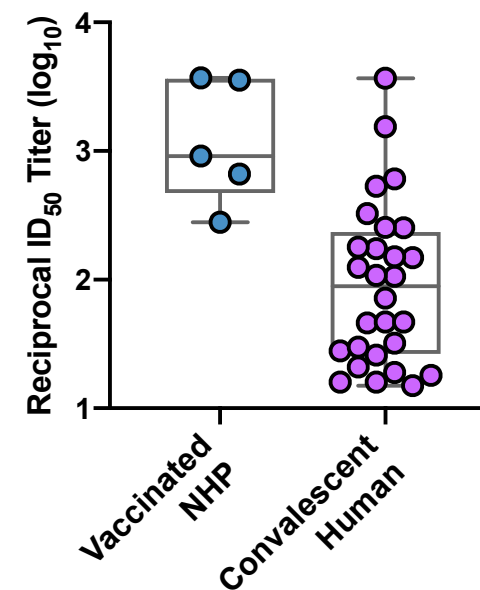
SARS-CoV-2 Total Antibody Response



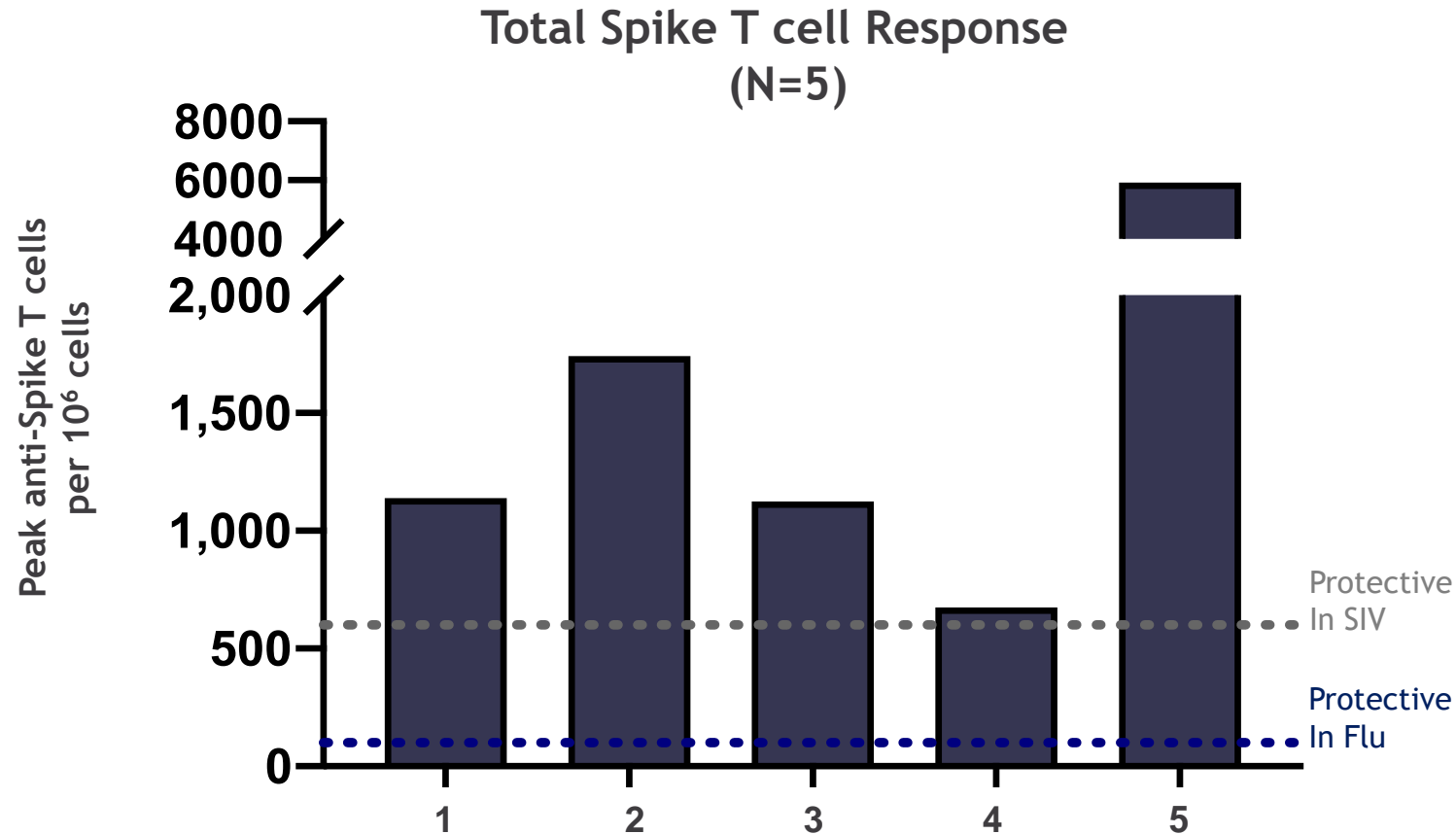
SARS-CoV-2 Neutralizing Antibody Response



Neutralizing Antibodies 2 Weeks Post-boost

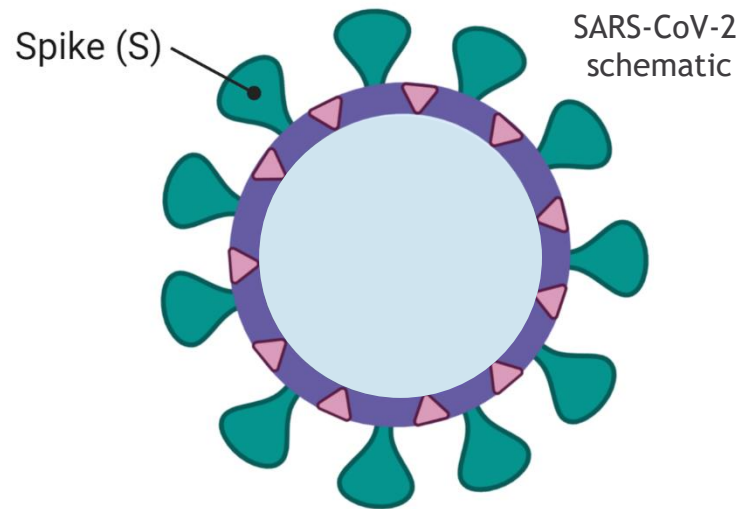


T Cell Responses in NHPs Vaccinated with Gritstone's SARS-CoV-2 Vaccine Reach Levels Known to be Protective Against Other Viruses



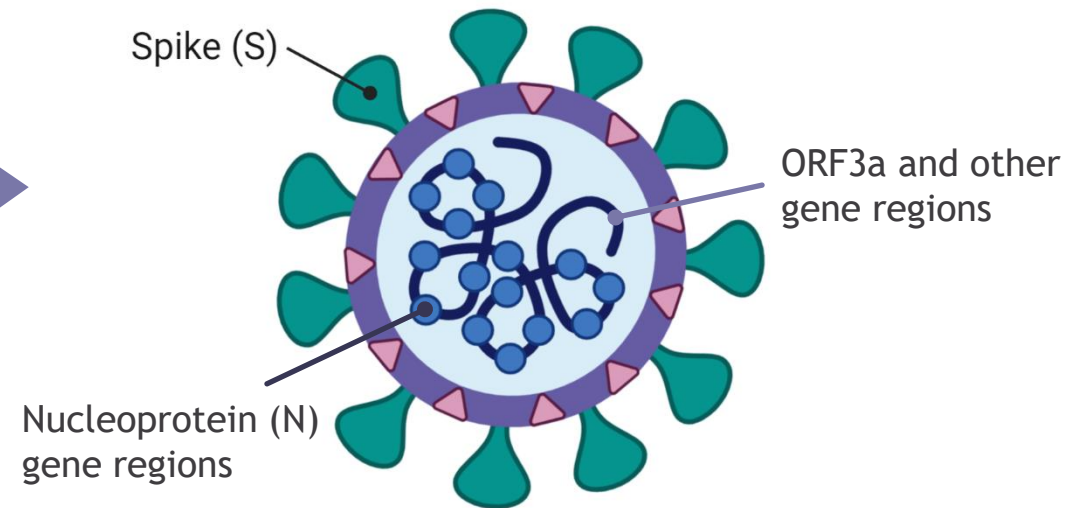
Gritstone Adds Targets From Multiple Viral Genes to Maximize Likelihood of an Effective Killer CD8 T Cell Response Against SARS-CoV-2

1st generation vaccines:
Spike (S) protein only



- Neutralizing antibodies (S)
- Limited CD8 T cells against S in some individuals
- No CD8 response against other highly expressed genes

2nd generation Gritstone vaccine:
S + additional gene regions



- Neutralizing antibodies (S)
- Strong CD8 T cell response in most individuals targeted against S and other highly expressed viral genes

T Cell Responses Against Highly Expressed Coronavirus Proteins Such as Nucleoprotein (N) Can Last For Over a Decade

nature

*“...we showed that patients ... who recovered from SARS (the disease associated with SARS-CoV infection) possess long-lasting memory T cells that are reactive to the N protein of SARS-CoV **17 years after** the outbreak of SARS in 2003.”*

Le Bert, et al, *Nature*, 2020



Gritstone COVID-19 Vaccine Path to Clinic

Gritstone's Biomanufacturing and Clinical Capabilities are Established

Gritstone vaccines have been manufactured and administered to cancer patients in the U.S.

Fully Integrated Manufacturing and Testing Facility in Pleasanton, CA



Biomanufacturing Processes Established.
Formulation Optimization and Scale Up Underway



Gritstone's CORAL Program is Supported by Key Relationships



- License agreement
- Supplying Gritstone validated SARS-CoV-2 epitopes identified through studies of hundreds of patients recovering from COVID-19



- Research grant
- Collaboration for pre-clinical studies of Gritstone's vaccine
- Gritstone conducts all studies



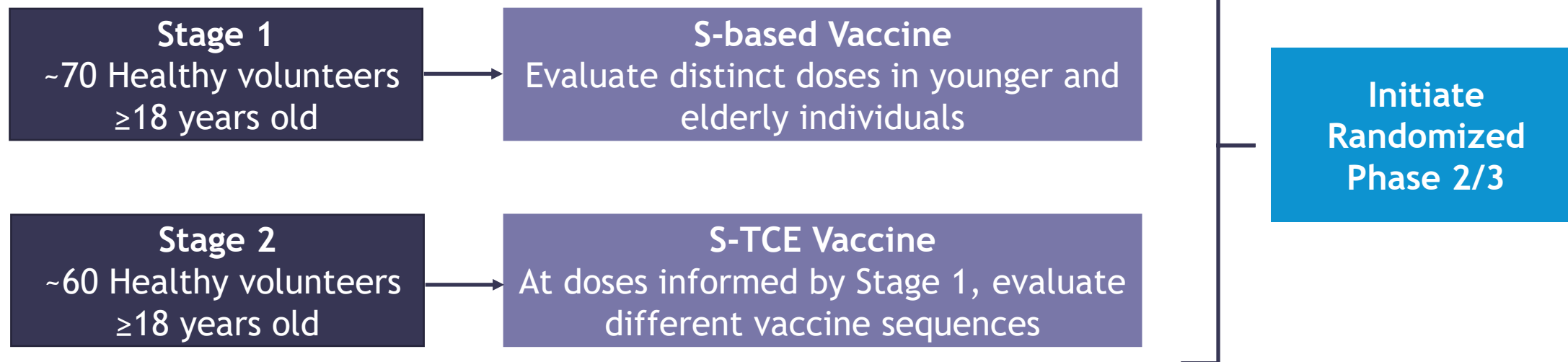
- A Phase 1 clinical trial, expected to be conducted through the NIAID-supported Infectious Diseases Clinical Research Consortium (IDCRC), is in development.

Gritstone Retains all Rights to Asset

CORAL Development Plans: On Track to the Clinic

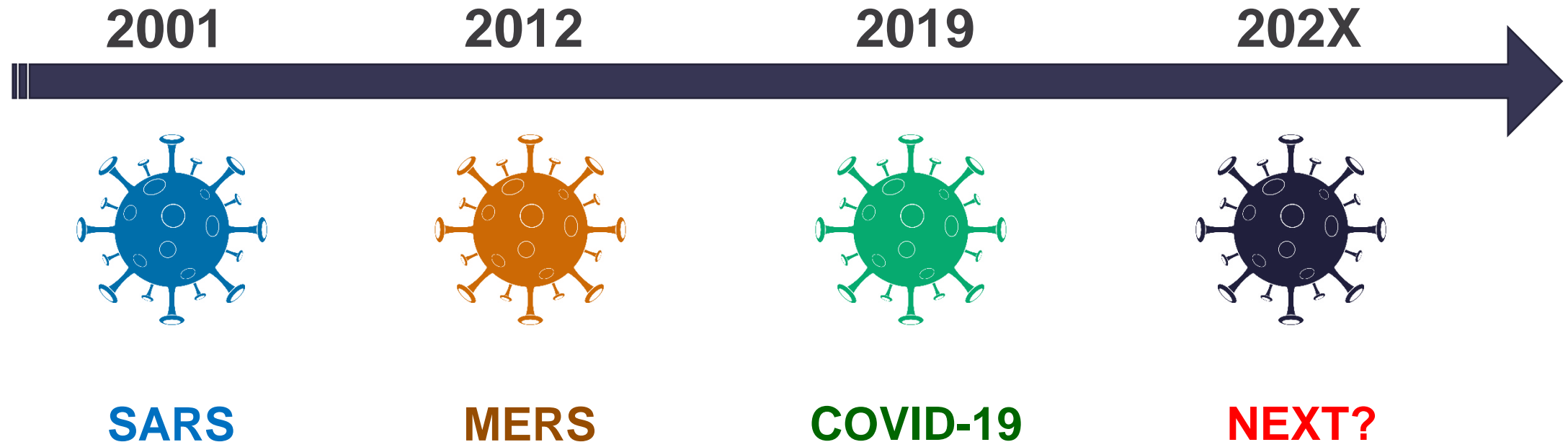
- Two candidates are being tested: Spike-based (S) and Spike + T Cell Epitopes (S-TCE)
- S-based vaccine will allow faster dose evaluation and immunogenicity comparison with S-TCE
- Completed pre-IND interaction with FDA
- Initiate Stage 1 (S) in 1Q2021 and Stage 2 (S-TCE) in 2Q2021
 - Expect preliminary data in mid-2021

Phase 1: Assess Safety and Immunogenicity of a Two-dose Vaccine



Coronavirus Evolution is Continuing and May Give Rise to Additional Pandemic Strains

Gritstone platform well-suited for pan-coronavirus vaccine development to protect against future pandemics



Gritstone's CORAL Program - Advancing the Second Generation of COVID-19 Vaccine Products

BROAD: Multiple viral proteins targeted (not just Spike)

DURABLE: CD8⁺ T cell immunity typically more durable than antibody responses

POWERFUL: Vaccine platform combines two vectors and drives antibody and killer CD8⁺ T cell responses

ESTABLISHED HUMAN SAFETY AND IMMUNE RESPONSES

- Vaccine vectors given at high doses have shown safety and immune responses in completed Phase 1 oncology trials

SUPPORTED BY KEY LEADERS

- La Jolla Institute license agreement
- Bill & Melinda Gates Foundation grant for preclinical development
- NIH/NIAID support of Phase 1 clinical program

CLEAR DEVELOPMENT PATH

- In-house manufacturing
- Product for Phase 1 (FPI 1Q21) currently being manufactured
- Extensive immunologic testing of patients to assess depth, breadth and duration of immune responses to SARS-CoV-2