Optimization of shared neoantigen vaccine design to increase vaccine potency: 
*From bench to bedside and back*

Christine D Palmer, PhD
Gritstone bio, Inc., CA, USA
Disclosure Information

Christine D Palmer

I have the following relevant financial relationships to disclose:

Employee of: Gritstone bio, Inc.
Stockholder in: Gritstone bio, Inc.

I have no additional financial relationships to disclose.
Safe Harbor and Forward-Looking Statements

This presentation contains 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 Annual Report (10K) filed on March 10, 2022, and any current and periodic reports filed thereafter.
SLATE Delivers Shared Neoantigens to Selected Patients Using Gritstone’s Prime/Boost Platform – Off-the-Shelf Therapy

Prime

ChAd Vector

Boost

samRNA Vector

SLATE v1 Shared Neoantigen Cassette
- “Off-the-shelf” Neoantigen Immunotherapy
- 20 cancer driver mutations
- Efficient patient selection via gene panels

G12V, G12D, G12C, Q61H, R213L, R249M, S127Y, K132N/E, +11 other mutations

KRAS

TP53

KRAS, TP53 & other mutations delivered as 25 aa sequences
SLATE Phase 1 Study Design

**SLATE off-the-shelf**

High Frequency KRAS Mutation
- Lung
- Pancreatic
- Colorectal (MSS)
- Mutation Positive Tumors

**PHASE 1**

Objectives:
- Safety and RP2D
- Immunogenicity

Dose Level 1:
- ChAdV 1x10^12 vp
- samRNA 30 µg
- Nivolumab 480 mg IV

Dose Level 2:
- Increasing doses of samRNA
- Nivolumab 480 mg IV

Dose Level 3:
- with 30 mg SC ipilimumab

Dose Level 4:
- ChAdV 1x10^12 vp
- samRNA 30 µg
- Nivolumab 480 mg IV

Nivolumab 480 mg IV

ChAdV 1x10^12 vp

samRNA 30 µg

ipilimumab

30 mg SC
Safety: Immunotherapy Well-Tolerated In Patients with Previously Treated Metastatic Solid Tumors

### SLATE Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Description</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age:</strong> mean (range)</td>
<td>57 (33-86)</td>
<td></td>
</tr>
<tr>
<td><strong>Gender:</strong></td>
<td>Female/Male 22/14</td>
<td></td>
</tr>
<tr>
<td><strong>Tumor Types</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-small cell lung cancer</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Median number of prior therapies (range)</td>
<td>2 (1-4)</td>
<td></td>
</tr>
<tr>
<td>Prior anti-PD-(L)1 therapy</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Microsatellite-stable (MSS) Colorectal Cancer</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Median number of prior therapies (range)</td>
<td>2 (1-3)</td>
<td></td>
</tr>
<tr>
<td>Pancreatic ductal adenocarcinoma (PDA)</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Median number of prior therapies (range)</td>
<td>1 (1-3)</td>
<td></td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Number of prior therapies</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Ampullary adenocarcinoma</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Number of prior therapies</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

Data cut-off: 30 Nov 2021

### Safety

#### n = 36
(all treated with concurrent nivolumab)

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1/2</th>
<th>Grade 3/4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment-related adverse events ≥ 5%</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Nausea</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Injection site reaction</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>ALT increased</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>AST increased</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Anorexia</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Chills</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Generalized weakness</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Myalgia</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

#### Treatment-related SAEs

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>2</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>1</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>1</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>1</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1</td>
</tr>
</tbody>
</table>
### Efficacy: Several NSCLC Patients Who Progressed on Prior IO Have Experienced Decrease in ctDNA Including Patient with High Baseline Levels

<table>
<thead>
<tr>
<th>Patient</th>
<th>Mutation</th>
<th>Baseline ctDNA (mutated hGE/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>G12C</td>
<td>124.64</td>
</tr>
<tr>
<td>S2</td>
<td>G12C</td>
<td>26.92</td>
</tr>
<tr>
<td>S3</td>
<td>G12C</td>
<td>Not detectable</td>
</tr>
<tr>
<td>S10</td>
<td>Q61H</td>
<td>77.23</td>
</tr>
<tr>
<td>S14</td>
<td>G12D</td>
<td>Not detectable</td>
</tr>
<tr>
<td>S26</td>
<td>G12C</td>
<td>3386.05</td>
</tr>
</tbody>
</table>

![Graph showing % change from baseline (mutated hGE/mL)](image)

**Legend:**
- **Blue:** Treatment ≥ 12 weeks
- **Red:** Treatment ≤ 8 weeks

The graph illustrates the % change from baseline (mutated hGE/mL) for NSCLC SLATE Patients, comparing treatments of ≥ 12 weeks and ≤ 8 weeks.
S3: Prolonged Disease Control in a Patient with NSCLC

Longer than disease control on prior anti-PD-1 mAb therapy

55-year-old male with metastatic NSCLC  
KRAS G12C

Prior Therapy
Pembrolizumab + carboplatin + pemetrexed (8 months)

Completed 2 years of study treatment (per protocol) with sustained lesion shrinkage, currently off treatment

Target Lesions

% Change in Target Lesions

<table>
<thead>
<tr>
<th>Weeks post Prime</th>
<th>0</th>
<th>20</th>
<th>40</th>
<th>60</th>
<th>80</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Change</td>
<td>0</td>
<td>-20</td>
<td>-20</td>
<td>-20</td>
<td>-20</td>
<td>-20</td>
</tr>
</tbody>
</table>

The graph shows the % change in target lesions over weeks post prime treatment.
S26: Molecular Response and Unconfirmed Partial Radiologic Response in a Patient with NSCLC

53-year-old male with metastatic NSCLC
KRAS G12C

Prior Therapy
Pembrolizumab + carboplatin + pemetrexed (3 months)

Began SLATE immunotherapy in Jan 2021

PD

Spinal compression fracture at site of pre-existing vertebral bodies in month 5

PD

Tumor tissue from vertebral lesion showed increased IFN and immune infiltrate expression signatures and increased HLA expression

% Change in mutated hGE/mL

Weeks post Prime

0 4 8 12 16

0 20 40 60 80 100

-100 -80 -60 -40 -20 0

Neoantigen ctDNA

% Change in Target Lesions

Weeks post Prime

0 4 8 12 16

-100 -80 -60 -40 -20 0 20

Target Lesions

IFN to increase?
S26: Unconfirmed Partial Response with Clear Reduction in Liver and Lung Lesions

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 8</th>
<th>Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>113 mm*</td>
<td>95 mm* (-16% relative to baseline)</td>
<td>61 mm* (-46% relative to baseline)</td>
</tr>
</tbody>
</table>

*Sum of longest diameters of two target lesions
SLATE V1: CD8+ T Cells Consistently Induced Against Multiple KRAS Driver Mutations but ex vivo ELISpot Positive in Subset of Patients Only

SLATE drives detectable CD8+ T cell responses against single neoantigens

**Ex vivo ELISpot**

- **S2 KRAS G12C**
  - Weeks post Prime: 0, 2, 4, 5, 6, 8, 12, 16, 20, 24
  - SFU per 1e6 cells: 0, 200, 400, 600, 800, 1000

- **S4 KRAS Q61H**
  - Weeks post Prime: 0, 2, 4, 5, 6
  - SFU per 1e6 cells: 0, 50, 100, 150

**CD8+ T cell responses against single neoantigens from multiple KRAS driver mutations detectable in post IVS* ELISpot**

- Patient ID/KRAS mutation:
  - S2 KRAS G12C
  - S3 KRAS...
  - S4 KRAS Q61H
  - S7...
  - S11 KRAS...
  - S15 KRAS G12V

*IVS – In vitro stimulation
SLATE V1: TP53\textsuperscript{mut} Neoantigens Seem Immunodominant – Although Rarer than KRAS\textsuperscript{mut} Neoantigens, they Drive Strong CD8\textsuperscript{+} T Cell Responses

Responses to 3/3 TP53 mutations tested to date; mutations presented by 3 different Class I HLA alleles

- TP53\textsuperscript{R213L} pool
- TP53\textsuperscript{S127Y} pool
- TP53\textsuperscript{R249M} pool

Ex vivo ELISpot graphs for different TP53 mutations:

- **S2**: TP53\textsuperscript{R213L} pool
- **S3**: TP53\textsuperscript{R213L} pool
- **S9**: TP53\textsuperscript{S127Y} pool
- **S11**: TP53\textsuperscript{R213L} pool, TP53\textsuperscript{S127Y} pool
- **S13**: TP53\textsuperscript{R249M} pool

SFU per 10^6 cells vs. Weeks post Prime
Optimizing Cassette to Mitigate TP53 Immunodominance and Enhance KRAS Immunogenicity

“version 1”
\[n=26\]

“version 2”
\[n=11\]

Repeat KRAS mutations delivered as 25 aa sequences

KRAS, TP53 & other mutations delivered as 25 aa sequences
SLATE: Version 2 of the $\text{KRAS}^{\text{mut}}$ Antigenic Cassette Induces Stronger T-Cell Responses to Multiple KRAS Neoantigens in Both Mice and Patients

No ex vivo T-cell responses observed in transgenic mice or representative patient with SLATE v1 cassette.
**S31: Partial Response at First Scan at 8 Weeks with Shrinkage in Both Target Lesions**

Durable tumor shrinkage with decrease of 28% on confirmatory scan at 18 weeks (scan delayed due to COVID infection)

- **41-year-old male with metastatic NSCLC**
  - KRAS G12V

**Prior Therapy**
- Pembrolizumab/carboplatin/pemetrexed (16 months)

**Began SLATE immunotherapy in Oct 2021**

| Baseline | 8 weeks (-37%) |

**Neoantigen ctDNA**

**Target Lesions**

Weeks Post Prime:
- 0
- 4
- 5
- 6
- 7
- 8

Weeks post Prime:
- 0
- 4
- 8
- 12
- 16

% Change in Target Lesions:
- $-20$
- $-40$
- $-60$
- $-80$
- $-100$

- **Neonantigen ctDNA**
- **Target Lesions**
SLATE Highlights

Safety & Tolerability
- Neoantigen immunotherapy appears to have a favorable safety and tolerability profile

Efficacy
- Even in advanced NSCLC patients who have progressed on prior chemo-immunotherapy we observe molecular responses and tumor shrinkage in patients with durable clinical benefit
- One patient completed two years on study treatment and now off all treatment

Translational approach
- An emerging hierarchy of neoantigen immunodominance is emerging that may be related to peptide-HLA complex density on tumor cell surface

Clinical Development Strategy
- We aim to move into earlier disease settings to amplify efficacy signals and drive the survival curve plateau higher
ACKNOWLEDGEMENTS

• Patients and their families
• SLATE Investigators, research nurses, study coordinators, and site staff
• Gritstone bio staff supporting the study
• Bristol-Myers Squibb for supply of nivolumab and ipilimumab

Thank you!