Gritstone

Corporate Presentation

JUNE 2020

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, and our bispecific antibody program. All statements other than statements of historical facts contained in this presentation, including statements regarding the timing of immunogenicity and clinical data for GRANITE and SLATE, identification of development candidate for our bispecific antibody program, our 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 May 7, 2020 and any current and periodic reports filed thereafter.

Executive Summary

Phase I Clinical Programs with Neoantigen-based Therapies

Individualized GRANITE

Unprecedented neoantigen-specific CD8+ T cell generation in cancer patients

Off-the-Shelf SLATE

Initial focus on tumors with high frequency of KRAS mutation

Engine for Pipeline & Partnering with Gritstone EDGE™

BiSpecific Antibodies

Tumor-specific binding through identification of HLA-peptide targets and high-quality antibodies

Cell Therapy

Collaboration with bluebird bio for tumor-specific targets and natural T cell receptors for cellular-based therapies

Operational Strength

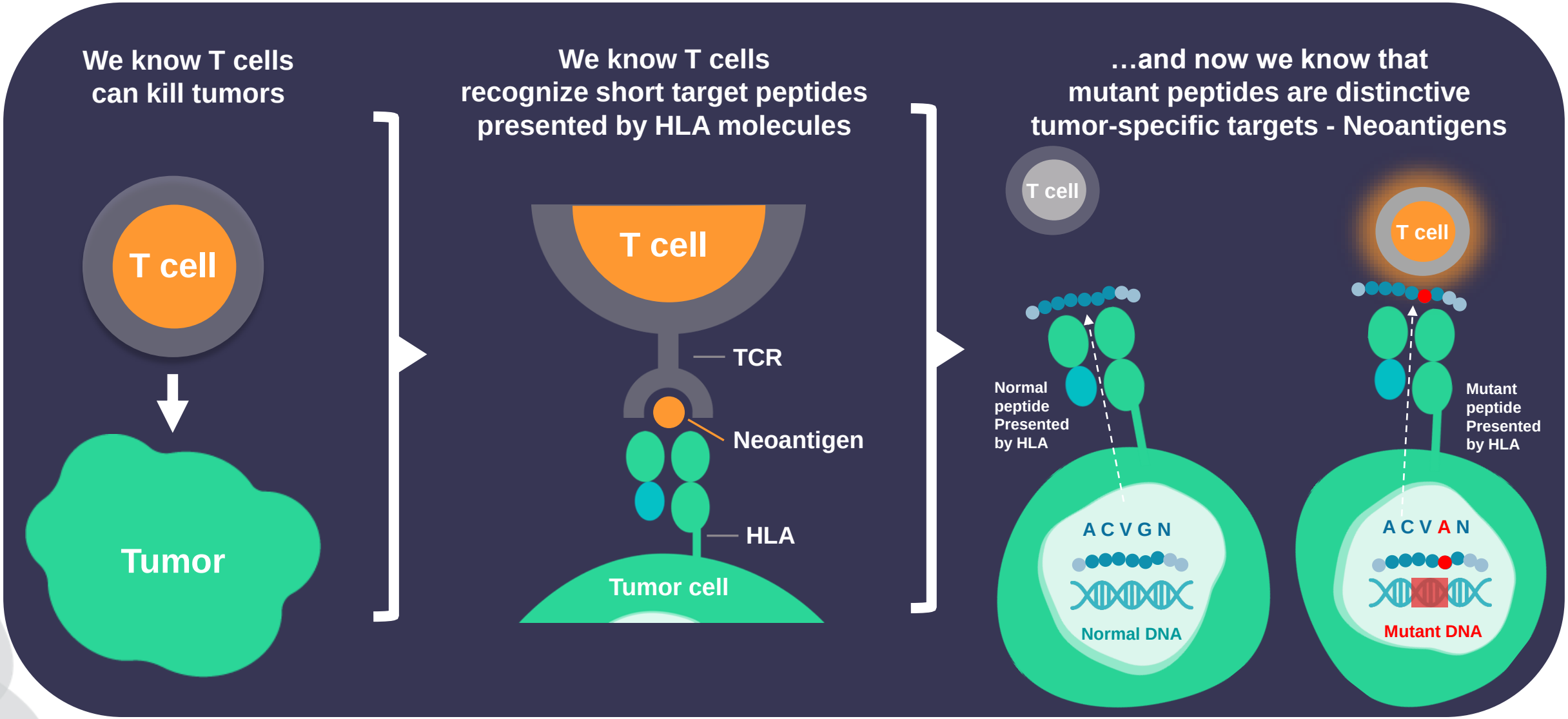
Manufacturing and Testing Facility

~43,000 sq. ft. fully integrated GMP biomanufacturing facility with QC testing

~$109.9MM* in cash at 3/31/20

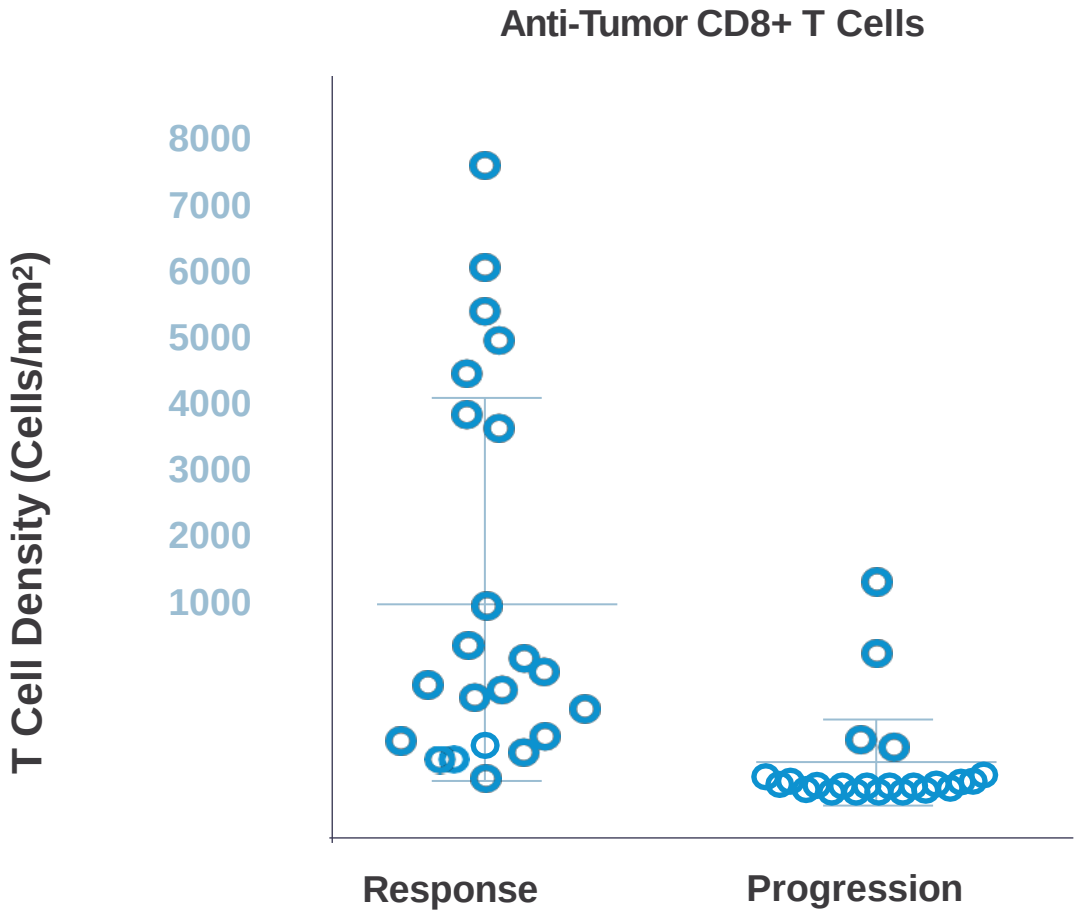
**Cash, cash equivalents, marketable securities and restricted cash as of March 31, 2020*

Tumor Neoantigens are Specific to Tumors and Readily Recognized by Normal T Cells



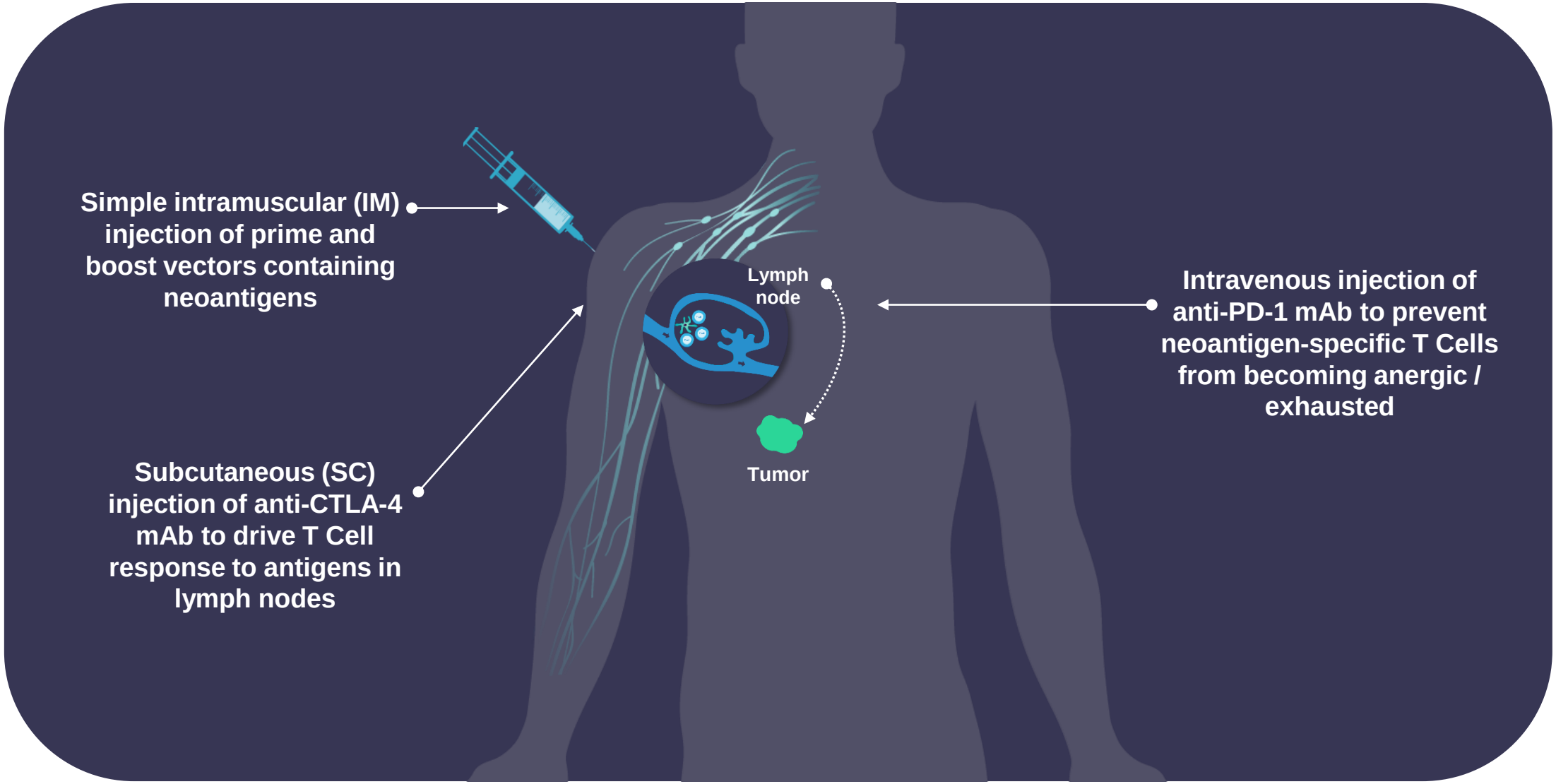
Unfortunately, Many Solid Tumor Patients Lack Neoantigen-Specific T Cells and Will Not Respond to Checkpoint Inhibitor (CPI) Alone

Response in Melanoma Patients Treated with Anti-PD-1 Antibody (Pembrolizumab) is Associated with Anti-Tumor CD8+ T Cell Infiltration of the Tumor at Baseline



Adapted from Tumeh, Ribas et al., Nature, 2014

Proposed Solution: Use Neoantigen-Based Immunotherapy to Drive Abundant, Active, Neoantigen-Specific T Cells into Tumors



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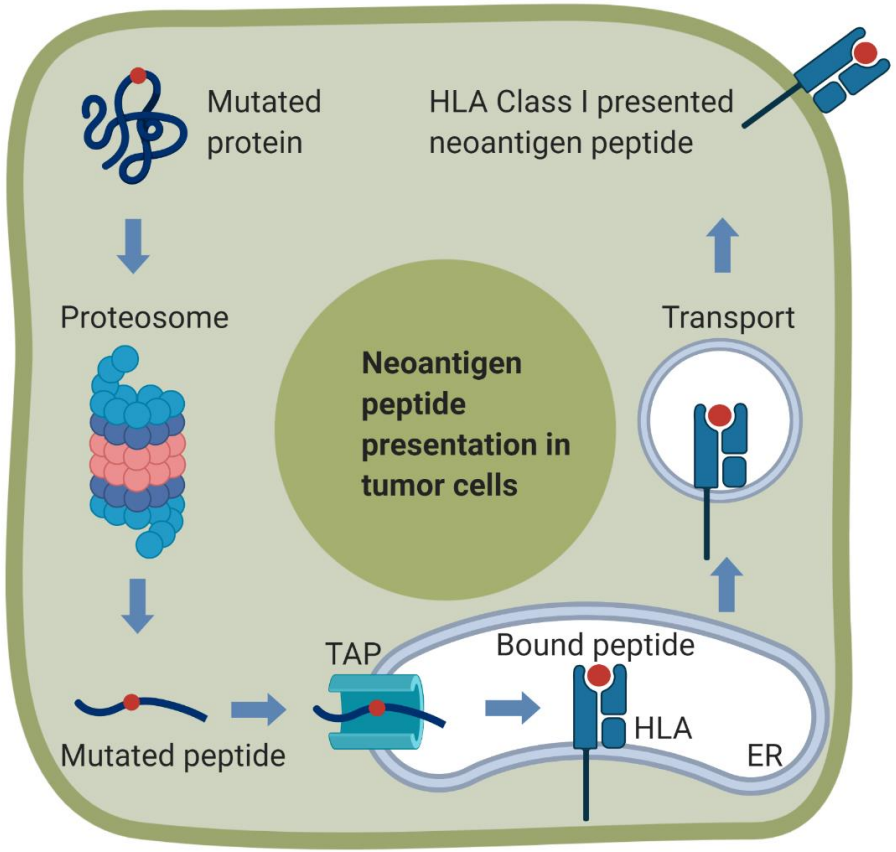
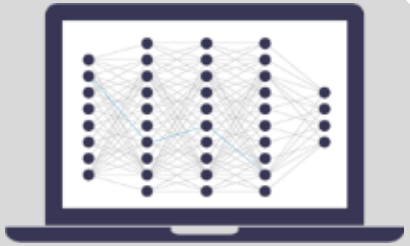
Gritstone's EDGE™ Leads The Field in Neoantigen Identification



EDGE is a neural network model of HLA peptide presentation



nature biotechnology

Deep learning using tumor HLA peptide mass spectrometry datasets improves neoantigen identification

Bulik-Sullivan, et. al. December 2018

(12) **United States Patent**
Yelensky et al.

(10) **Patent No.: US 10,055,540 B2**
(45) **Date of Patent: Aug. 21, 2018**

(54) **NEOANTIGEN IDENTIFICATION, MANUFACTURE, AND USE**

(71) Applicant: **Gritstone Oncology, Inc.**, Emeryville, CA (US)

(72) Inventors: **Roman Yelensky**, Newton, MA (US); **Adnan Derti**, Dedham, MA (US); **Brendan Bulik-Sullivan**, Cambridge, MA (US); **Jennifer Busby**, Burlington, MA (US)

(73) Assignee: **Gritstone Oncology, Inc.**, Emeryville, CA (US)

8,287,883	B2	10/2012	Dubensky, Jr. et al.
8,583,380	B2	11/2013	Stephan et al.
8,680,239	B2	3/2014	Mueller et al.
8,741,556	B2	6/2014	Mann et al.
8,768,629	B2	7/2014	Von Hoff et al.
8,796,414	B2	8/2014	Johnston
8,821,864	B2	9/2014	Von Knebel-Doeberitz et al.
8,840,881	B2	9/2014	Jooss et al.
8,926,993	B2	1/2015	Dubensky, Jr. et al.
9,017,660	B2	4/2015	Shahabi et al.
9,063,149	B2	6/2015	Mann et al.
9,084,747	B2	7/2015	Shahabi et al.
9,115,402	B2	8/2015	Hacohen et al.
9,161,974	B2	10/2015	Dubensky et al.
9,175,088	B2	11/2015	Sahin et al.
9,194,004	B2	11/2015	Sahin et al.
9,198,960	B2	12/2015	Dubensky, Jr. et al.

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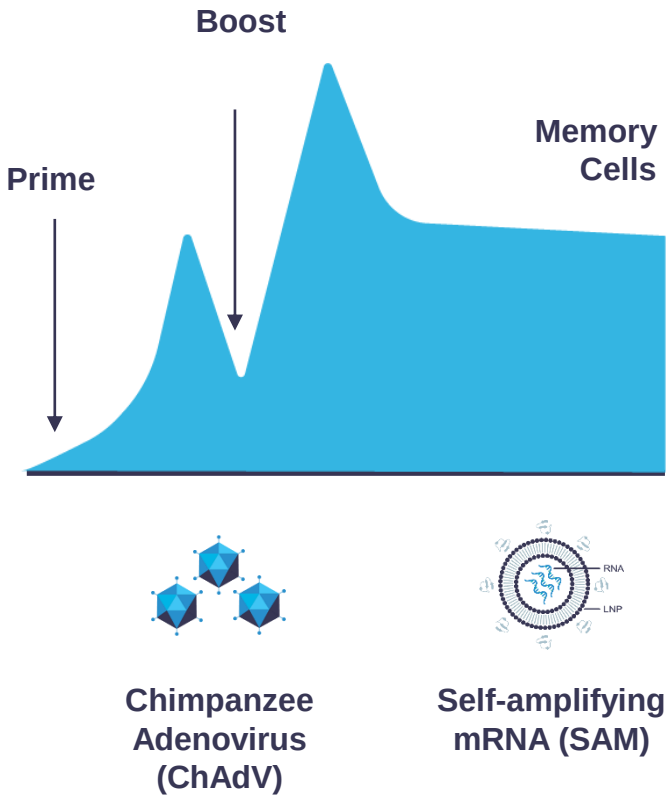
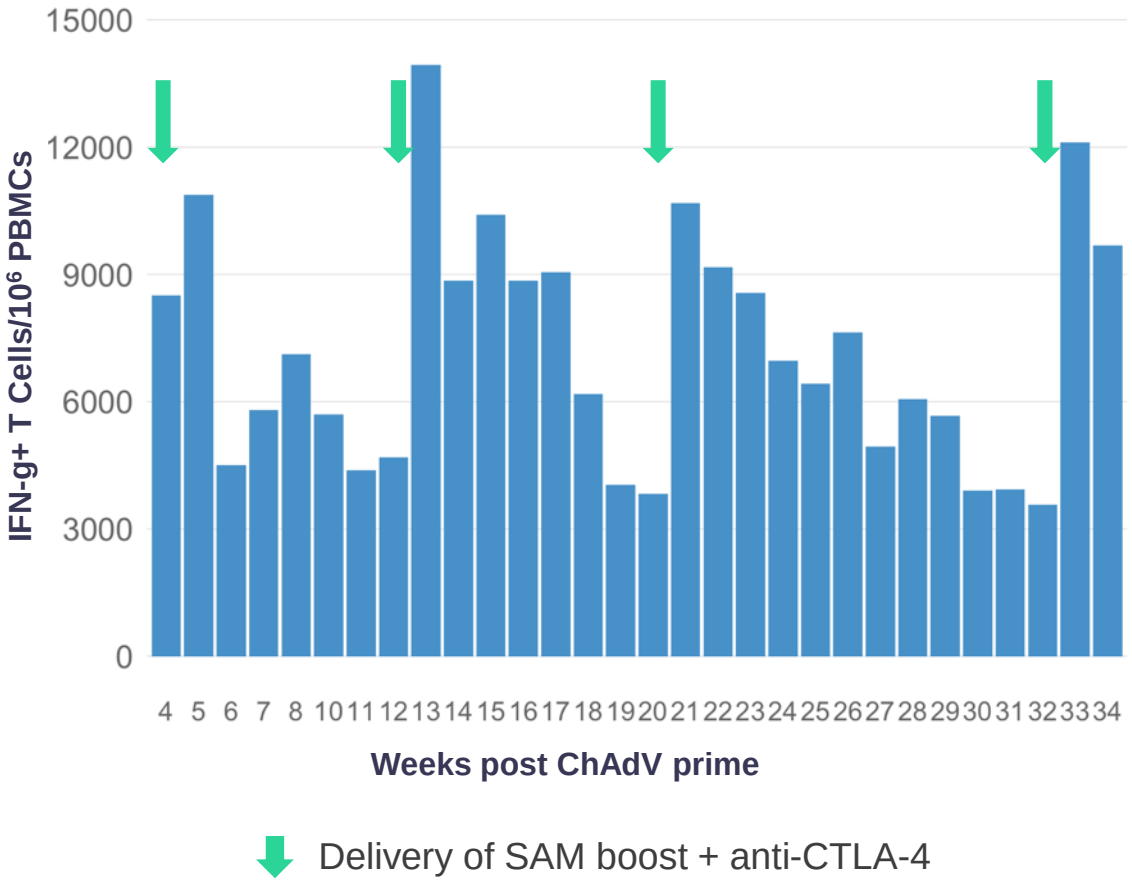
Gritstone Has Developed a Unique, Potent Platform for Delivering Antigens to the Immune System to Drive a Strong T Cell Response

Heterologous Prime/Boost



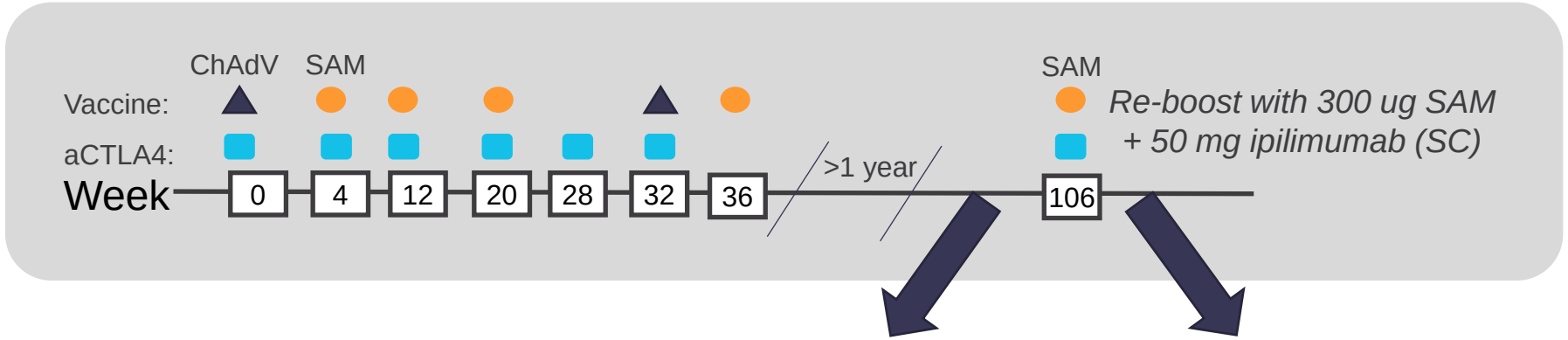
Non-Human Primate Experiment: 6 SIV antigens
ChAdV + SAM + anti-CTLA-4



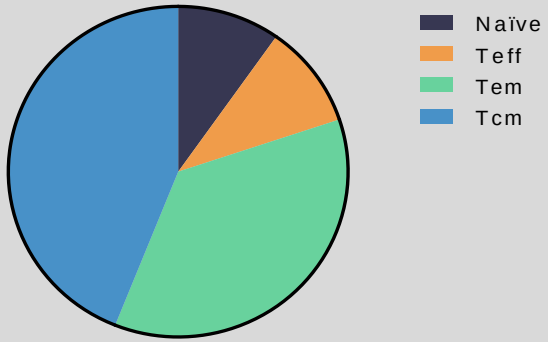
Up to 8% of peripheral CD8+ T cells are antigen-specific

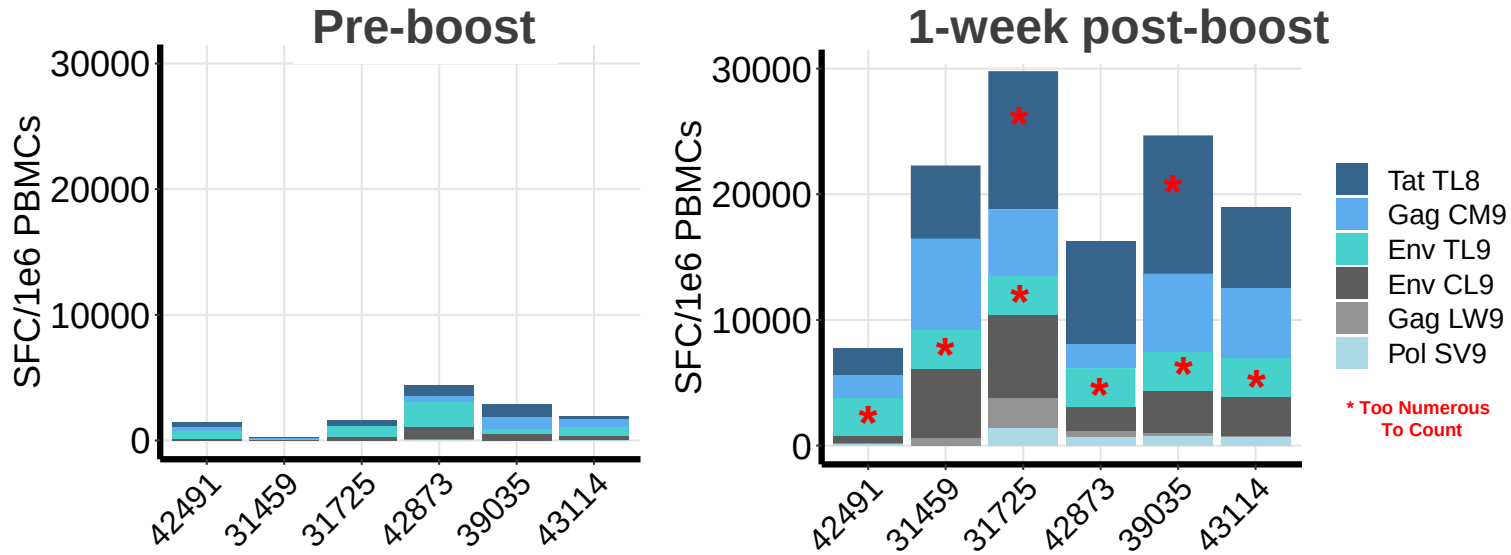
PBMC: peripheral blood mononuclear cell
CD8+ specific T cell responses (overnight stimulation with short peptides of 8-12 amino acids)

Durable T Cell Memory Population Elicited: Very Strong Boost of NHP Immune Response Observed 2 Years After Initial Prime



Antigen-Specific Memory T-cell Populations Pre-Boost





5 – 18% (mean - 12%) of CD8 T Cells are antigen-specific post boost

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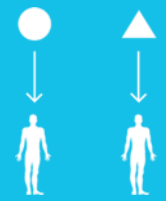
GRANITE

Many Solid Tumor Patients Will Have Their Own Unique Neoantigens Enabling Individualized Immunotherapy

Individualized GRANITE



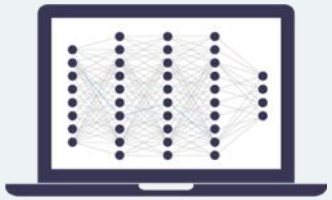
1. Routine Biopsy

Routine clinical biopsy as input material

2. Sequencing

Tumor DNA
Tumor RNA
Normal DNA

3. Neoantigen Prediction



Gritstone EDGE™ AI model for tumor antigen prediction trained on human tumor data

4. Personalized Immunotherapy

Patient-specific predicted neoantigens inserted into viral and RNA vectors

5. Simple Injection

Immunotherapy administered in conjunction with checkpoint inhibitors

Oncologist | **Gritstone** | **Oncologist**

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GRANITE Phase 1: Dosing, Safety and Immunogenicity

Rapid assessment of early clinical activity across advanced tumor types in combination with checkpoint inhibitors

All patients receive nivolumab (anti-PD-1)

- **Lung**
- **Gastric**
- **Colorectal (MSS)**
- **Bladder**

ChAdV prime IM: 10^{12} vp	→	SAM boosts (x8) IM: 300 μg	
SC: 30 mg ipilimumab		*SC: 30 mg ipilimumab*	

ChAdV prime IM: 10^{12} vp	→	SAM boosts (x8) IM: 100 μg	
SC: 30 mg ipilimumab		*SC: 30 mg ipilimumab*	

ChAdV prime IM: 10^{12} vp	→	SAM boosts (x8) IM: 100 μg

ChAdV prime IM: 10^{12} vp	→	SAM boosts (x8) IM: 30 μg

Note: IM = intramuscular; SC = subcutaneous; vp = viral particles

GRANITE Prime/Boost Immunotherapy in Combination with Nivolumab is Well Tolerated with AEs Indicative of an Inflammatory Response

Demographics	n = 6
Age (mean, range)	66 (50-76)
Gender (Female/Male)	2/4
# of doses	
ChAdV	6
SAM	20
Nivolumab (IV)	24
Ipilimumab (SC)	1
Tumor Types	
NSCLC	1
Microsatellite stable (MSS)-CRC	2
Gastroesophageal adenocarcinoma (GEA)	3
Prior anti-PD-(L)1 therapy	1

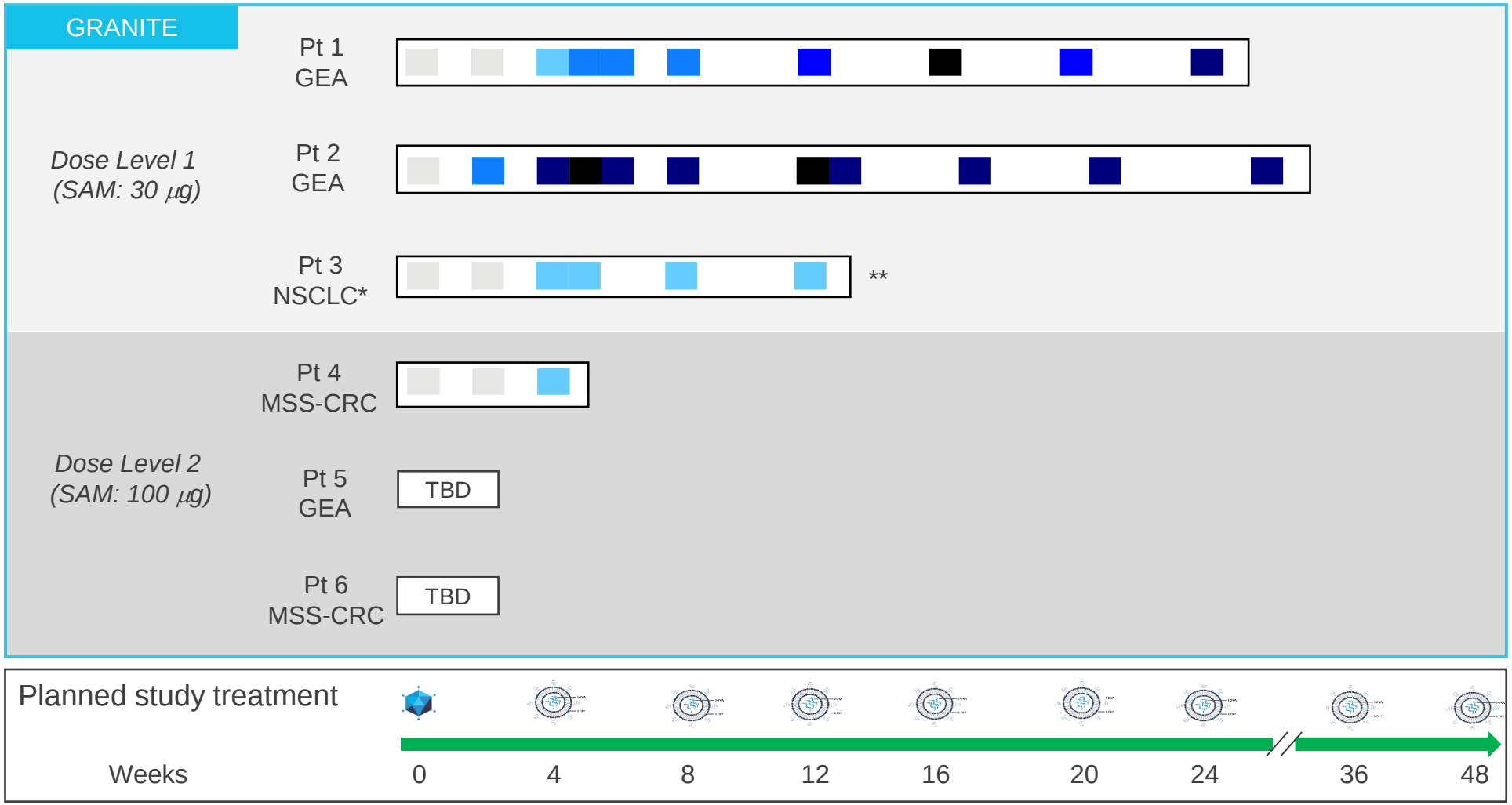
Safety	n = 6	
	Grade 1/2	Grade 3/4
Treatment-related adverse events		
Fever	7	0
Skin rash	2	0
Diarrhea	2	0
Fatigue	2	0
CK Elevation	0	1[a]
Injection-site reactions	1	0
SAEs		
Fever	2[b]	0
Heart Failure	0	1[c]

No DLTs to date

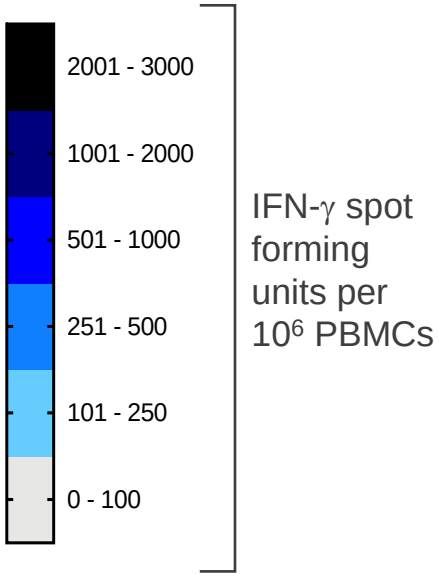
[a] Self-limiting, asymptomatic increase in creatine kinase
[b] Both SAEs of fever occurring in the same patient
[c] Not treatment-related

Data cut-off 06 Jan 2020

Priming with ChAdV Induces Rapid CD8+ T Cell Response and SAM Boosts Further Increase CD8+ T Cell Levels



***Ex vivo* (overnight) ELISpot for CD8+ T Cell responses**



**Patient progressed on prior anti-PD-(L)1 antibody*
***Patient had high pre-existing cross-reactive immunity to ChAdV Hexon*
vp, viral particles

As presented at JPM 1/16/20

GRANITE Patient 1, Dose Level 1: Stable Disease for 6 Months

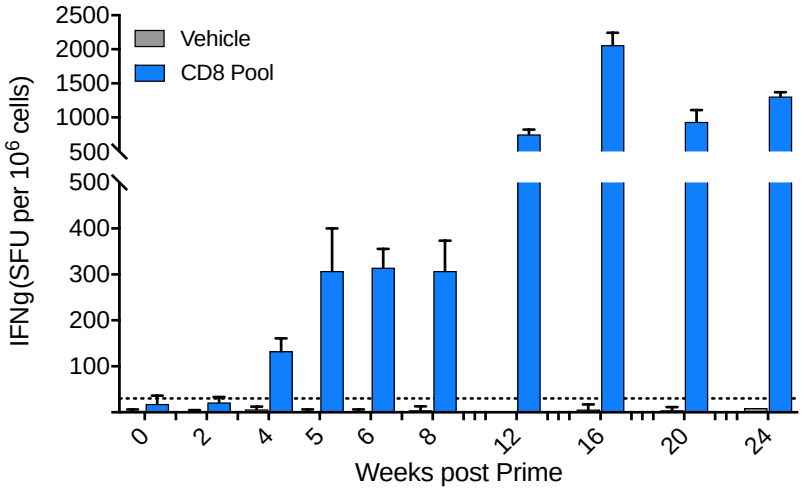
76-year old male with metastatic gastroesophageal junctional adenocarcinoma

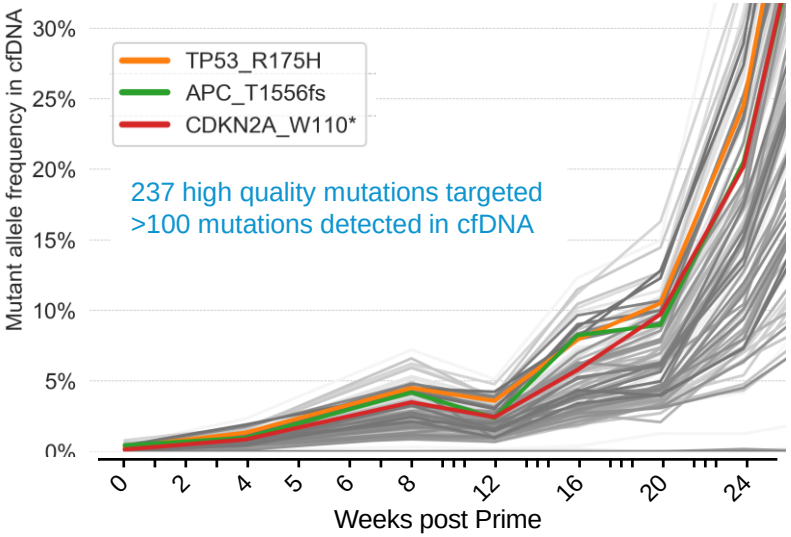
Prior Therapy

- Partial response to 1st Line FOLFOX
- Received concomitant 5-FU with first two doses of study treatment

GRANITE Response

- Best overall response: stable disease
- Progressive disease at week 24
- Grade 2 skin rash requiring holding nivolumab for boosts 5 and 6 and introducing IV steroids after boost 5





As presented at JPM 1/16/20

5-FU = 5-fluorouracil; SFU = spot-forming unit; cfDNA = cell-free DNA

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GRANITE Patient 2, Dose Level 1: Disease Control for 8 Months So Far

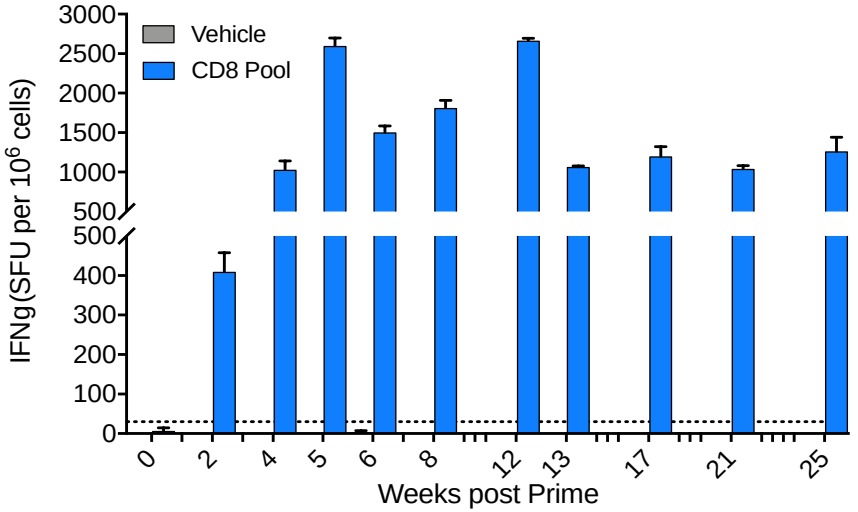
60-year old male with metastatic gastroesophageal junctional adenocarcinoma

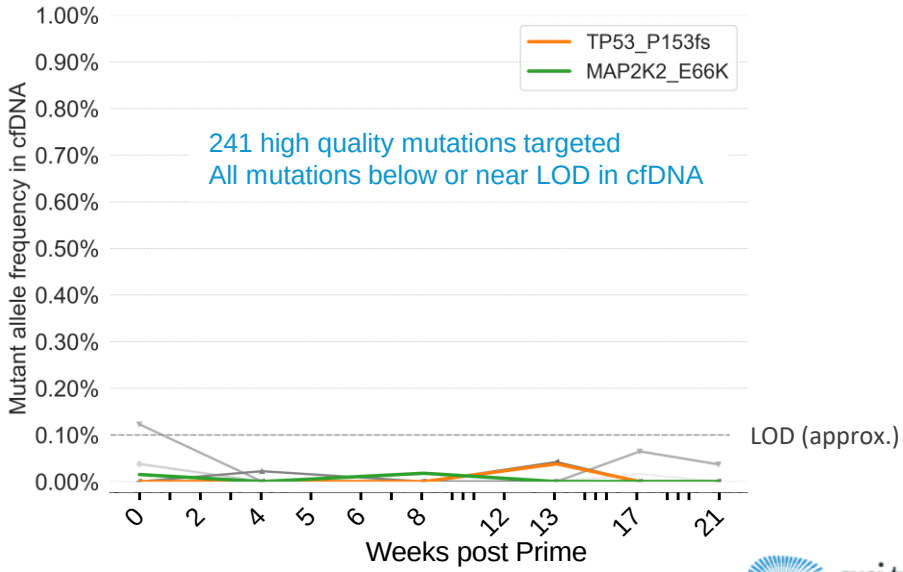
Prior Therapy

- Partial response to 1st Line FOLFOX followed by complete surgical resection of previously inoperable tumor followed by 3 months of FOLFOX
- No radiologic evidence of disease at study entry

GRANITE Response

- Best overall response: no evidence of disease
- Asymptomatic grade 3/4 CK elevation and thrombocytopenia (from pre-existing condition) resulted in 9-week delay between boosts 1 and 2





As presented at JPM 1/16/20

SFU = spot-forming unit; cfDNA = cell-free DNA; CK, creatinine kinase

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GRANITE Patient 3, Dose Level 1: Unconfirmed PD; Treated Beyond Progression with Apparent Lesion Cavitation

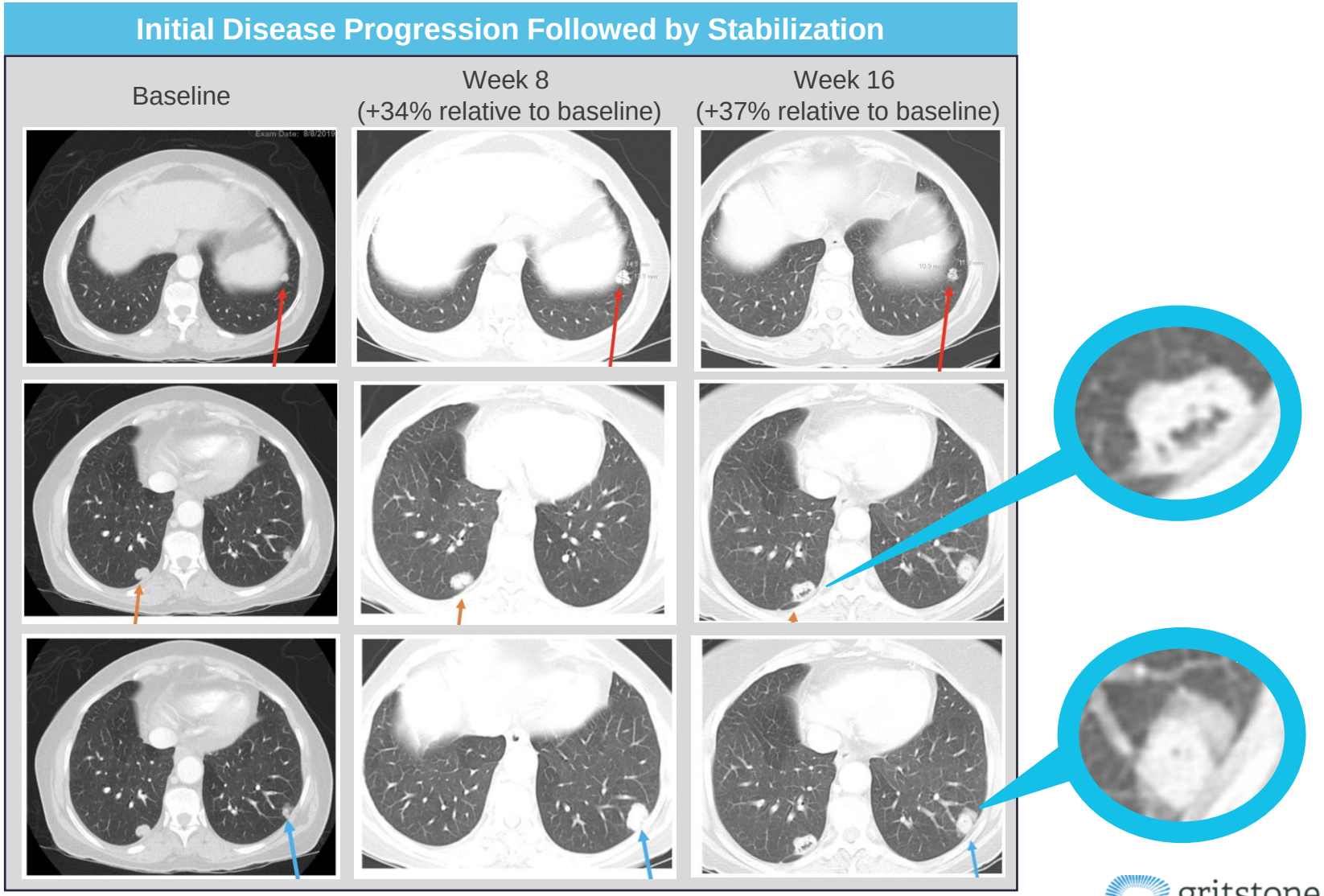
72-year old female diagnosed with Stage IIIB NSCLC and progression following chemoradiation and durvalumab

Prior Therapy

- Received subsequent carboplatin/gemcitabine, commenced study treatment upon progression

GRANITE Response

- Progressive disease at week 8, but clinically stable and was treated beyond progression with only further increase of 3% at week 16
- Grade 2 fever related to ChAdV and nivolumab



As presented at JPM 1/16/20

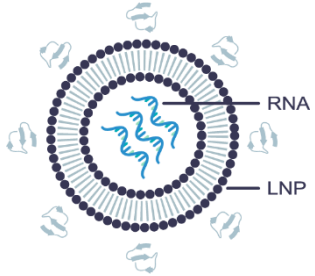
SLATE

SLATE Delivers Shared Neoantigens Using Gritstone's Prime/Boost Platform

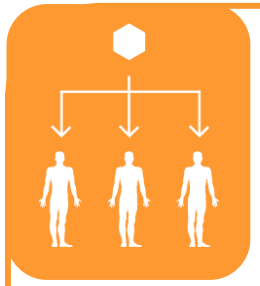
Prime

ChAdV Vector

Boost



SAM Vector



SLATE Shared Neoantigen Cassette

- "Off-the-shelf" Neoantigen Immunotherapy
- 20 cancer driver mutations
- Efficient patient selection via gene panels

G12V **G12D** **G12C** **x 20 total** **mutations**

KRAS and other mutations delivered as 25 aa sequences

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SLATE Product Concept

One Product – Many Selected Patients

Common Driver Mutation

KRAS

- G12 D
- G12 A
- G12 C
- G12 V

β-CATENIN

TP53

Other genes

×

Class I HLA Molecule

HLA - A

- A* 01:01
- A* 02:01
- A* 11:01

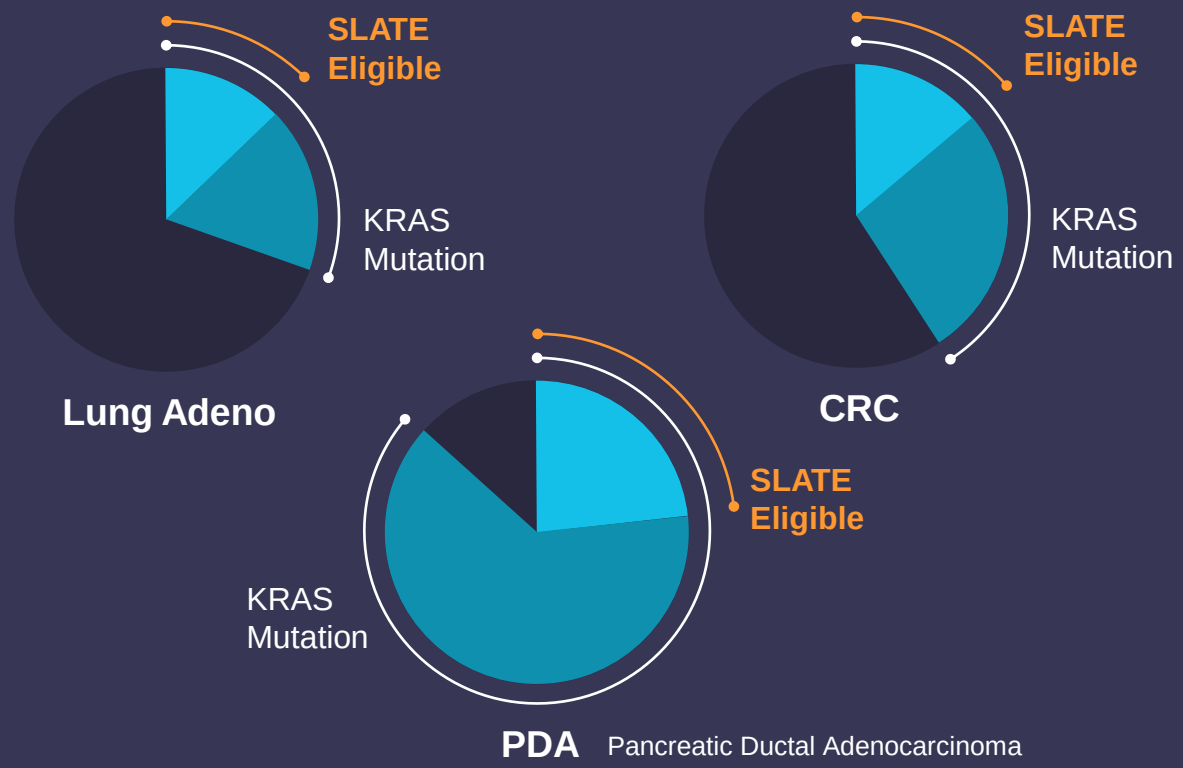
HLA - B

- B* 08:01
- B* 35:01

HLA - C

- C* 01:02
- C* 08:02

SLATE Patient Selection for KRAS mutations



Exemplary matches only shown

Projected approximate total coverage

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SLATE Phase 1: Dosing, Safety and Immunogenicity

Rapid assessment of early clinical activity with potential for quick to registration path in Phase 2 expansion cohorts

All patients receive nivolumab (anti-PD-1)

High Frequency KRAS Mutation:

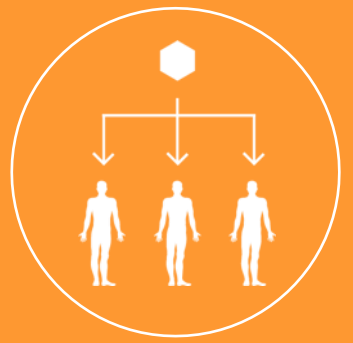
- Lung
- Pancreatic
- Colorectal (MSS)
- Mutation Positive Tumors

ChAdV prime IM: 10^{12} vp → **SAM boosts (x8)** IM: 300 μg
SC: 30 mg ipilimumab → *SC: 30 mg ipilimumab*

ChAdV prime IM: 10^{12} vp → **SAM boosts (x8)** IM: 100 μg
SC: 30 mg ipilimumab → *SC: 30 mg ipilimumab*

ChAdV prime IM: 10^{12} vp → **SAM boosts (x8)** IM: 30 μg
SC: 30 mg ipilimumab → *SC: 30 mg ipilimumab*

ChAdV prime IM: 10^{12} vp → **SAM boosts (x8)** IM: 30 μg



Note: IM refers to intramuscular, SC refers to subcutaneous and vp refers to viral particles

SLATE Prime/Boost Immunotherapy in Combination with Nivolumab and Ipilimumab Well Tolerated To Date

Demographics	n = 4
Age (mean, range)	62 (33-83)
Gender (Female/Male)	2/2
# of doses	
ChAdV	4
SAM	6
Nivolumab (IV)	10
Ipilimumab (SC)	4
Tumor and Mutation Types	
NSCLC • KRAS G12C	3
MSS-CRC • KRAS Q61H	1
Prior anti-PD-(L)1 therapy	3

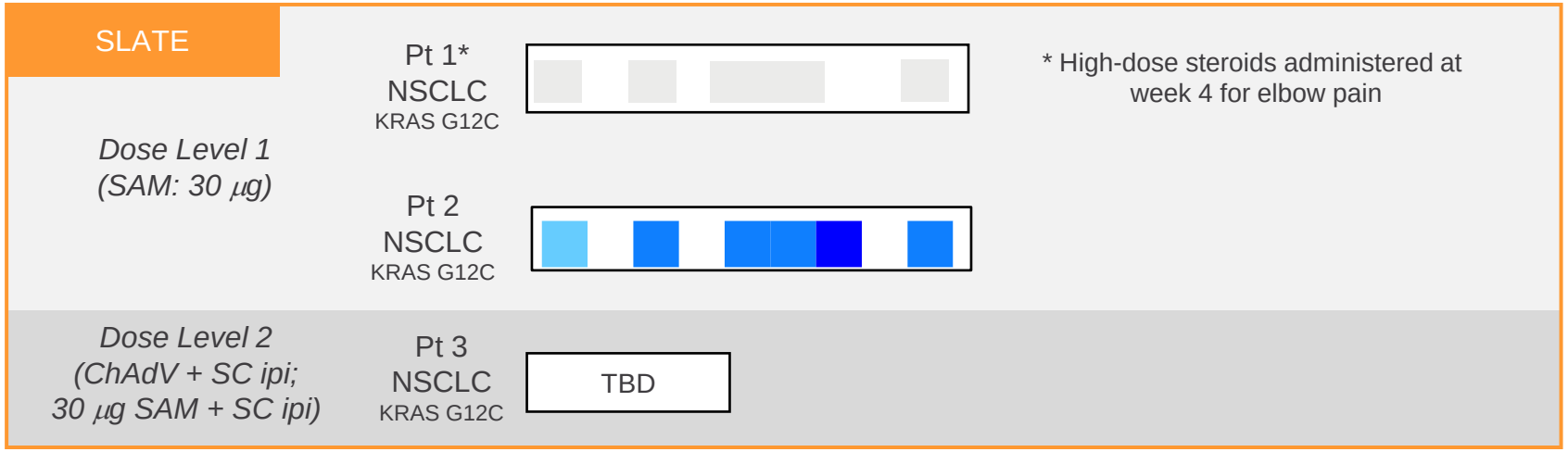
Safety	n = 4	
	Grade 1/2	Grade 3/4
Treatment-related adverse events		
Myalgia	1	0
Pruritus	1	0
SAEs		
Anemia	0	1[a]
Cervical Fracture	0	1[a]

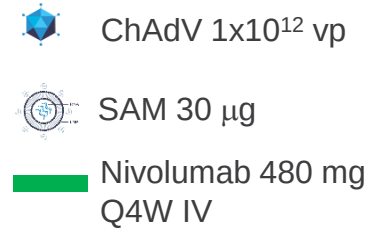
[a] Not treatment-related

No DLTs to date

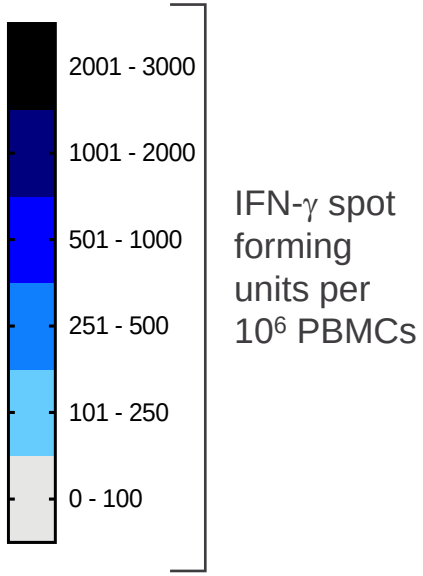
Data cut-off 14 Jan 2020

SLATE: Single Neoantigen Capable of Driving Strong CD8+ T Cell Response





Ex vivo (overnight) ELISpot for $CD8^+$ T cell responses



As presented at JPM 1/16/20

SLATE Patient 2, Dose Level 1: ChAdV Prime Induces Strong ex vivo CD8+ T Cell Responses Boosted by 30µg Dose of SAM Correlating with Drop in Circulating Neoantigen DNA

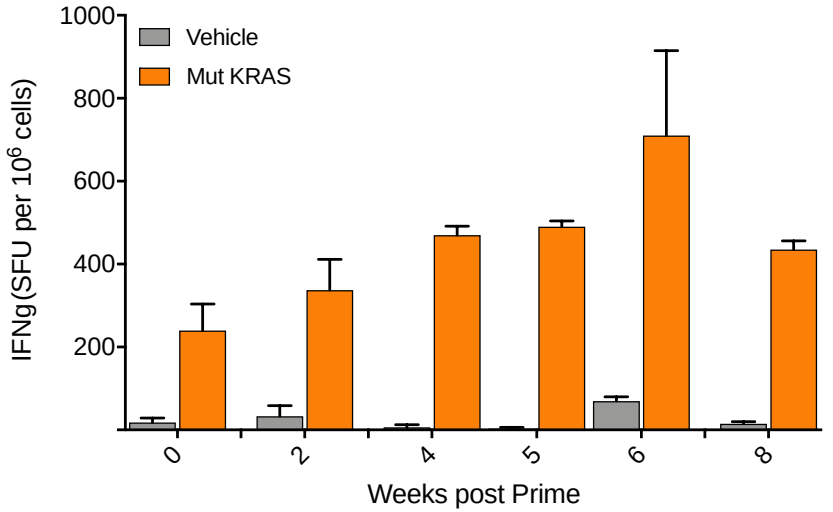
84-year old female with stage IV NSCLC; *KRAS* G12C

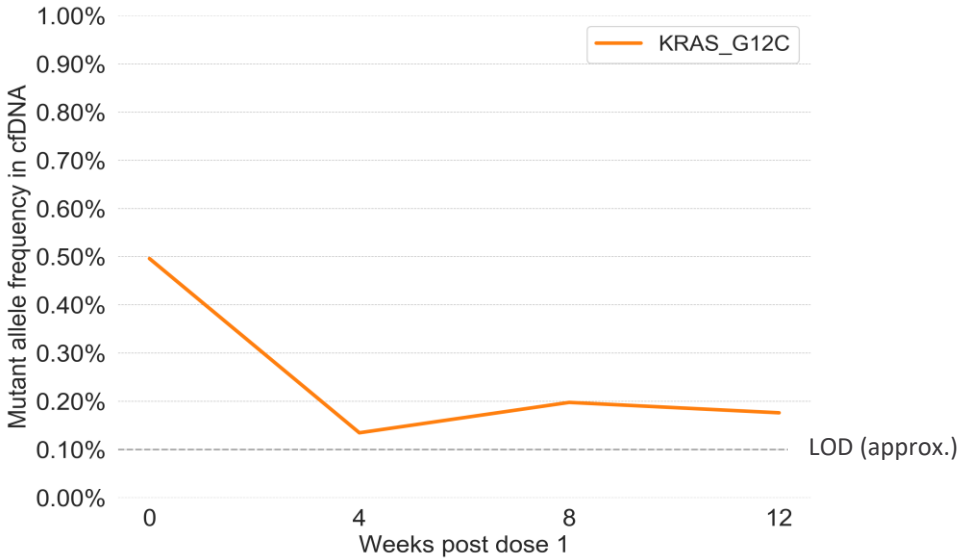
Prior Therapy

- Pembrolizumab (best response = PD)
- Anti-TIGIT (best response = SD)
- Carboplatin/pemetrexed/SBRT (best response = PR)
- Disease progression following chemotherapy

SLATE Response

- Drop in ctDNA* correlates with 20% tumor reduction at week 8 by CT scan
- Grade 2 pruritis





**cfDNA monitoring for target mutation in SLATE cassette*
Additional data not shown for Pt 1 due to lack of T cell response and progression at first scan (day 56)
NSCLC, non-small cell lung carcinoma; SFU, spot-forming unit

As presented at JPM 1/16/20

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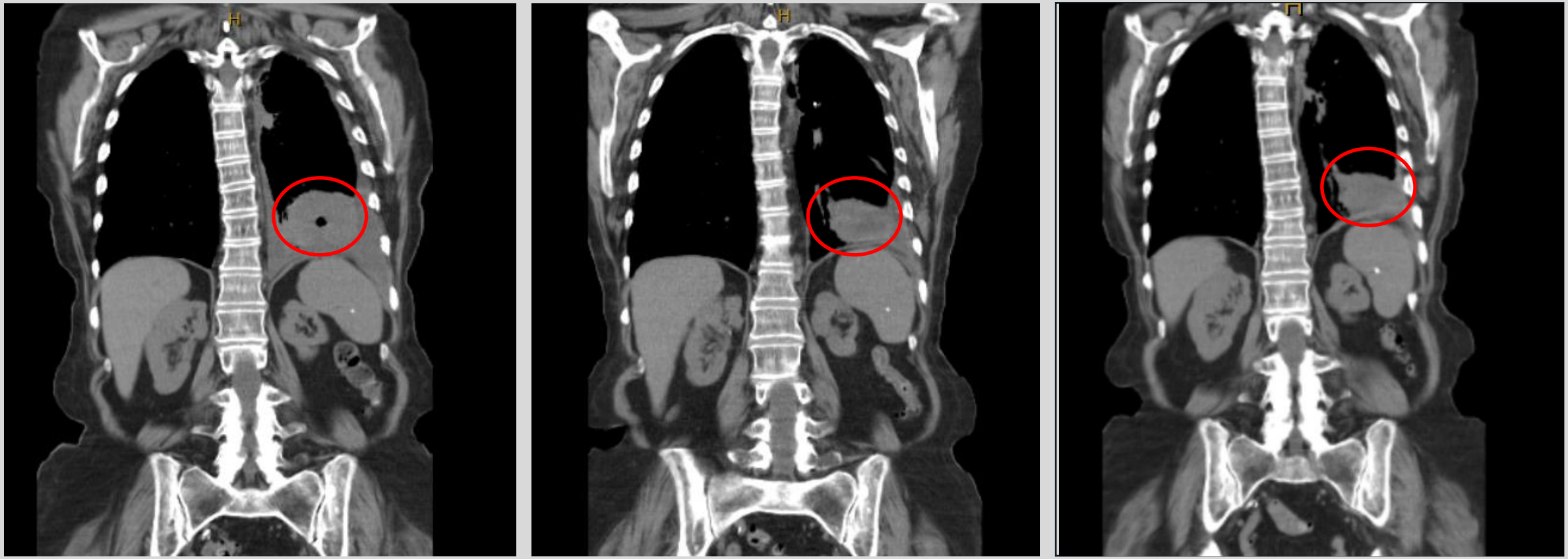
SLATE Patient 2, Dose Level 1: ~20% Sustained Tumor Shrinkage

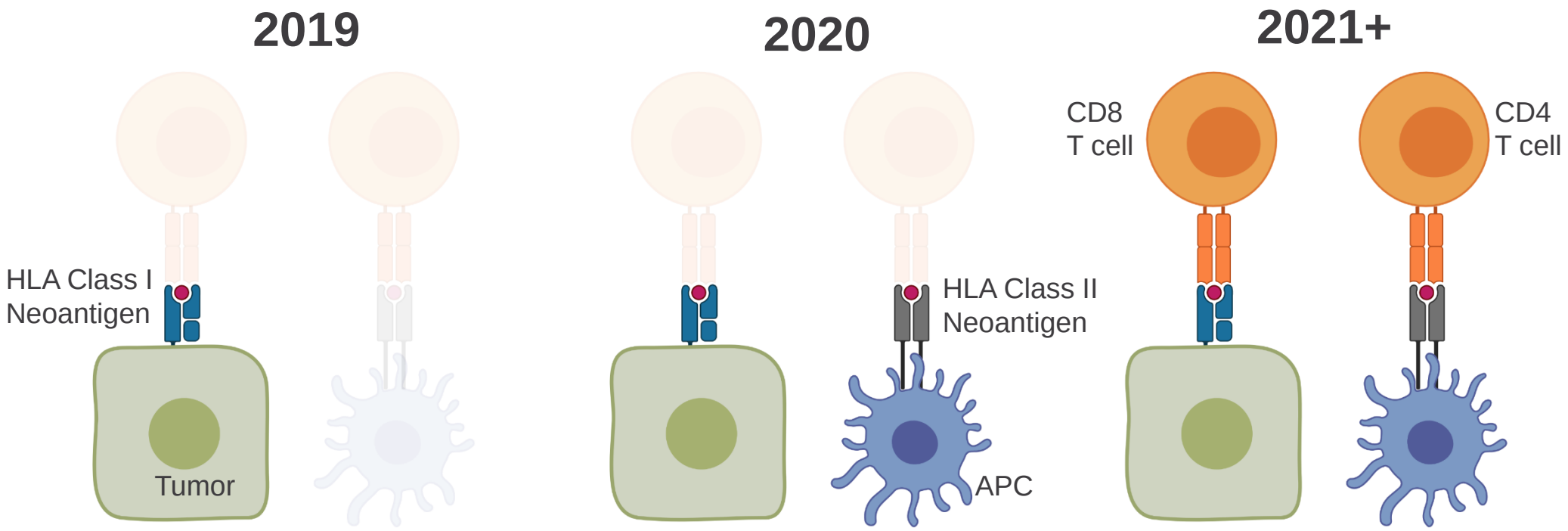
Baseline	Week 8	Week 16
95 mm*	76 mm* (-20% relative to baseline)	77 mm* (-19% relative to baseline)



As presented at JPM 1/16/20

**Sum of longest diameters of two target lesions*

EDGE Development Continues and is Identifying Novel Neoantigens



EDGE I

- HLA Class I presented peptides
- Published in Nature Biotechnology
- Issued U.S. Patent

EDGE II

- HLA Class I and Class II presented peptides
- Application in SLATE and GRANITE programs

Next Gen EDGE

- Incorporate modeling of immunogenicity / T cell recognition
- Novel antigen class identification

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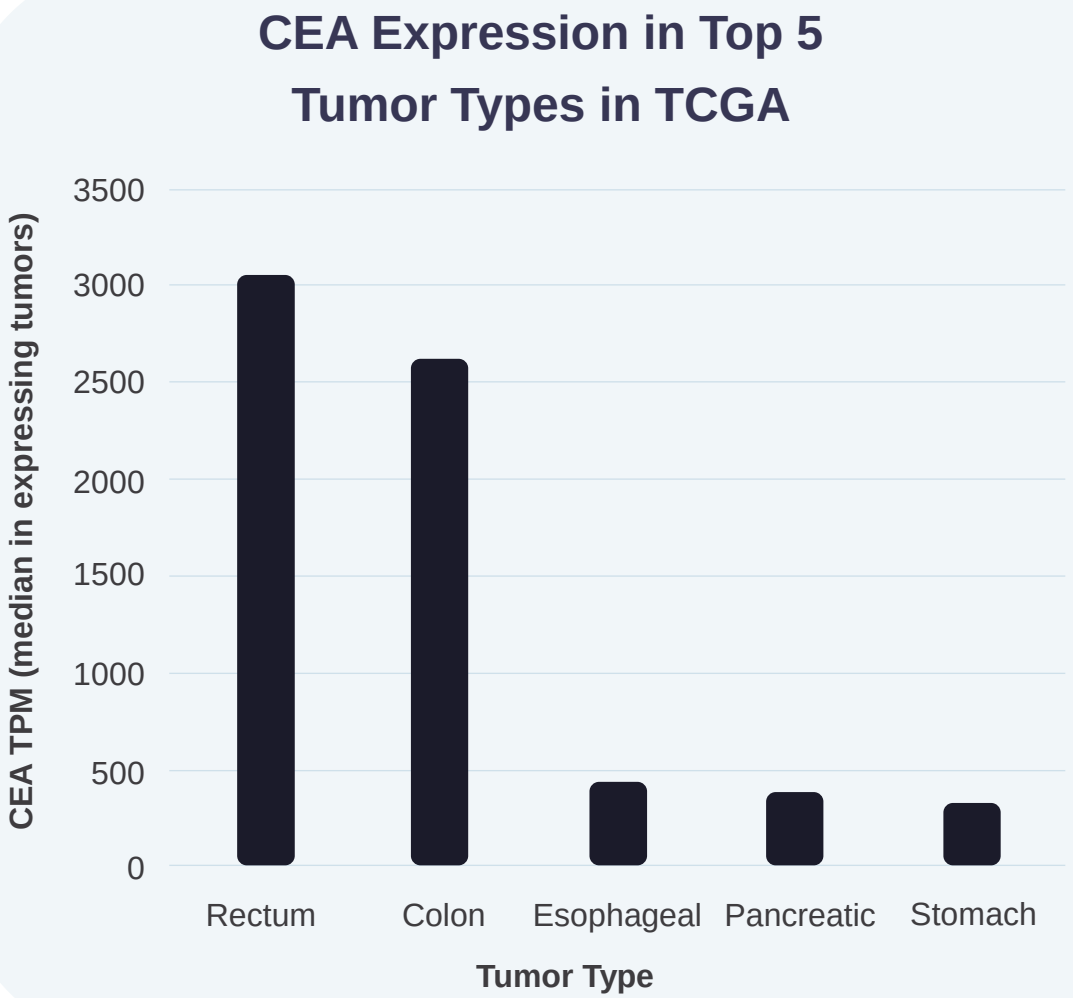
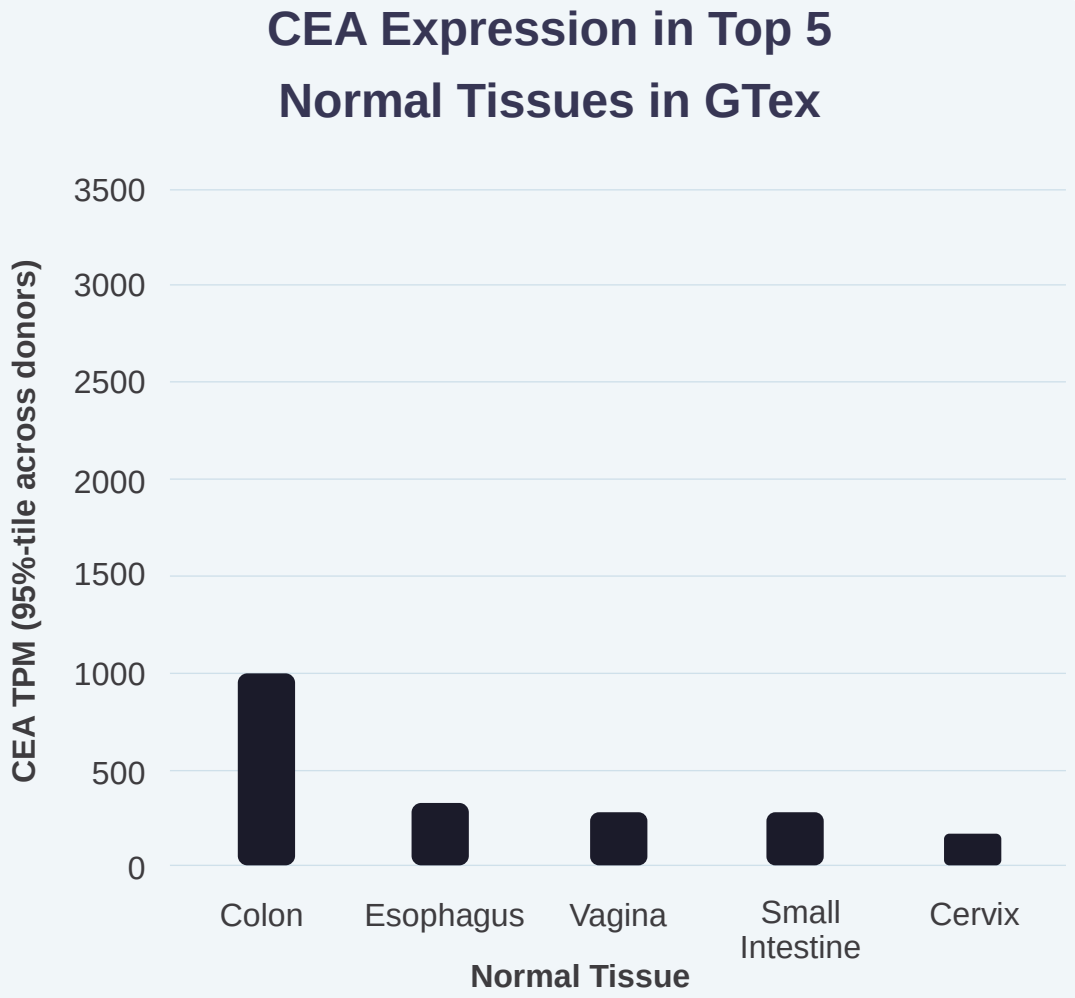
TUMOR-SPECIFIC BISPECIFIC ANTIBODIES (BiSAb)

First Generation of Solid Tumor BiSAb Targets May Have a Limited Therapeutic Window Due To High Expression in Normal Tissues





TPM= Transcripts per million

Bispecific Antibody Therapy for Solid Tumors May be Enhanced with Superior Tumor-Specific Target Selection

Identify High Quality Tumor-Specific HLA-Peptide Targets

- Validate on primary human tumors
- Determine surface density

Predict Potential Off-Target Binding of Ab

Overall target health-check:

- How many similar peptides exist?
- How similar are they?
- Where are they expressed?

Employ target and off-target analyses in optimized discovery

Prioritize targets with ideal characteristics: uniqueness, validation, density, prevalence

Utilize off-target information throughout discovery and optimization to drive high specificity

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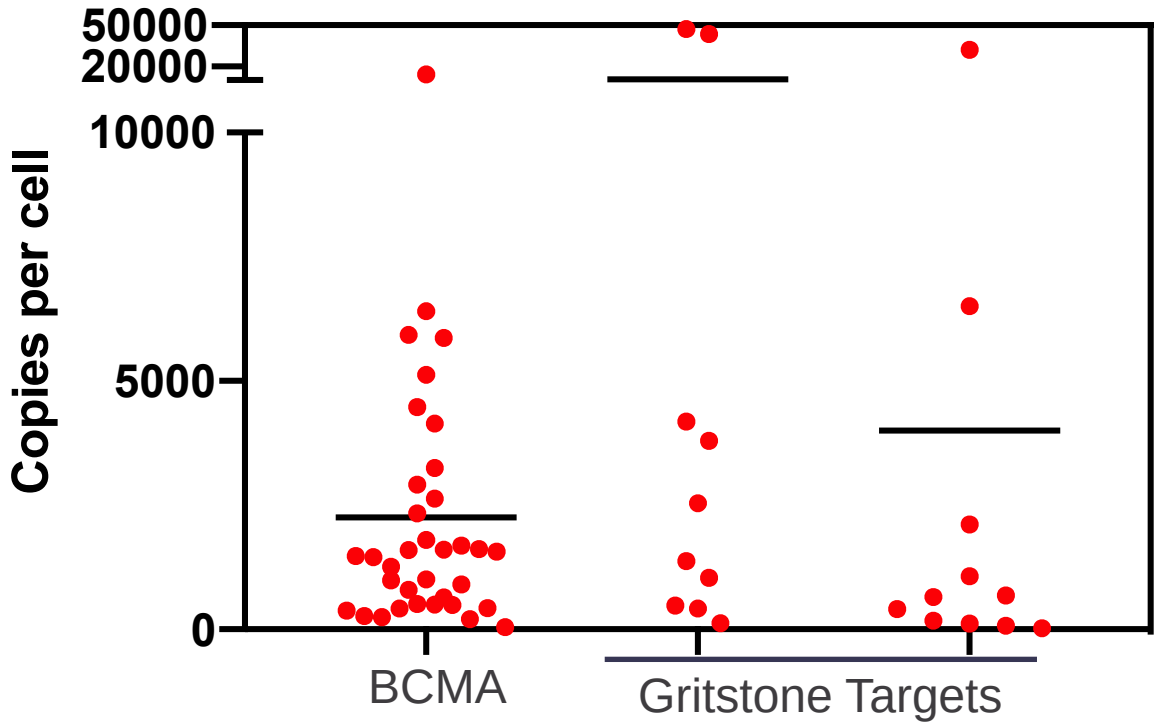
Select HLA-Peptide Complexes are as Densely Expressed on Cancer Cells as on Validated B Cell Targets, Offering Novel Solid Tumor Targets

Target Surface Density on Primary Human Cancer Specimens

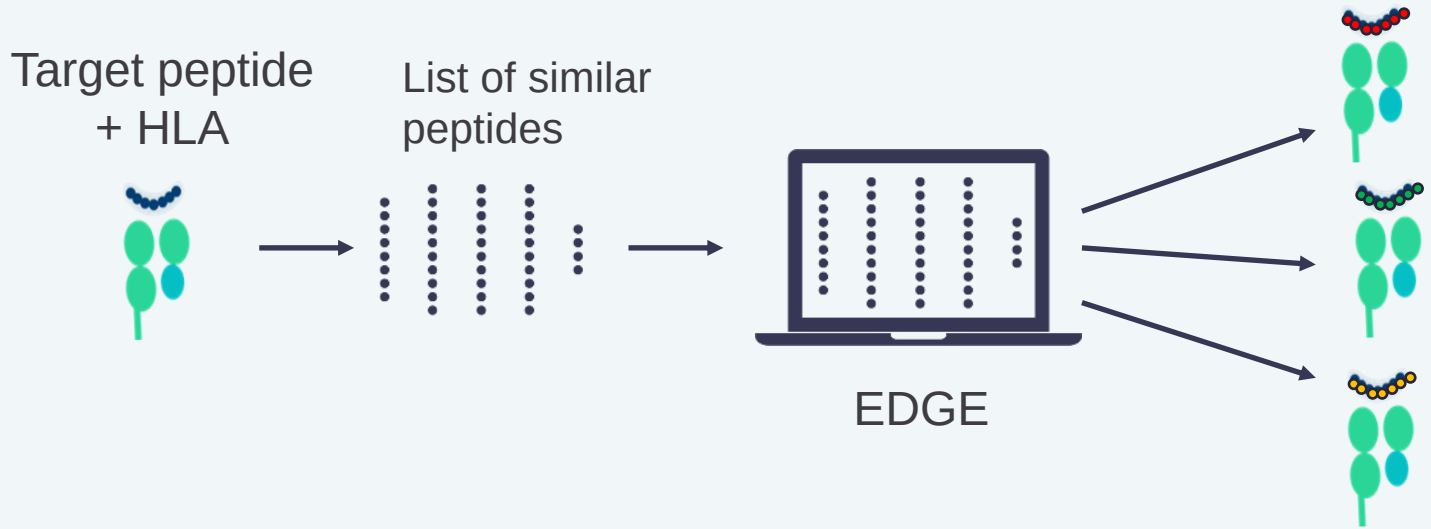


BCMA data from Seckinger et al., 2017, Cancer Cell 31, 396–410 (ABC assay)
Gritstone targets determined by mass spectrometry

Superior Off-Target Liability Prediction Using EDGE

An engineered T cell with a TCR targeting a MAGEA3 peptide resulted in deaths in a clinical study due to cross-reacting with a peptide from an unrelated protein, called titin, expressed in heart muscle

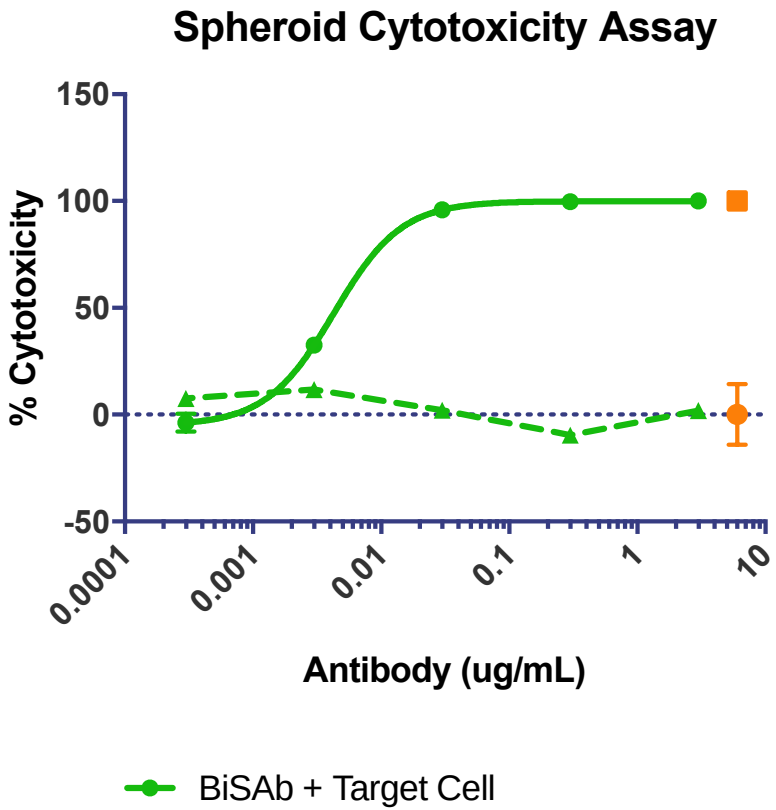
We use EDGE to identify the off-target liabilities that are most likely to be presented:

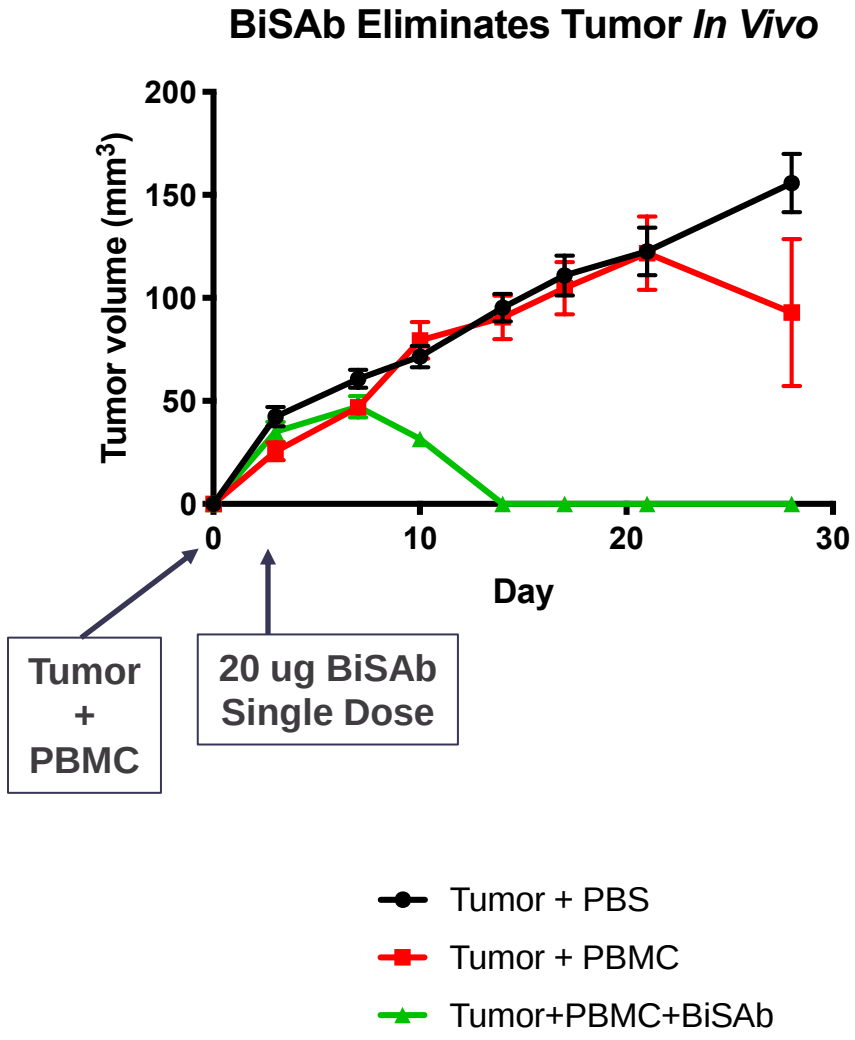


Closest peptides in terms of sequence that are likely to be presented in same HLA as target

While developing a bispecific to a MAGEA3/6 peptide, our methods identified titin as a potential liability. We were able to demonstrate lack of binding & cytotoxicity of the titin target by our bispecific.

Gritstone BiSAb Against HLA-peptide Complexes Can Drive Potent and Efficient Killing *In Vitro* and *In Vivo*





BUSINESS OPERATIONS

Strong U.S. and Global Foundational IP Position

Broad and Deep Intellectual Property Covering:

edge™
EPITOPE DISCOVERY IN CANCER GENOMES

- Issued U.S. Patent
- Class I and Class II prediction
- Patient Selection

GRANITE SLATE

- Vectors including ChAdV and SAM
- Personalized and Shared NeoAg Targets
- Manufacturing
- Exclusive Delivery Technology License

BISPECIFIC ANTIBODIES

- Optimized Bispecific Antibody Platforms
- Cancer-Testis Antigen Targets and Binders
- Shared NeoAg Targets and Binders

CELL THERAPY

- Cancer-Testis Antigen Targets
- Shared NeoAg Targets
- TCRs Binding Targets

130+ Applications Pending Worldwide | **1** Issued U.S. Patent | **2036-2040** Patent Exclusivity

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Gritstone's Bay Area Biomanufacturing Facility Delivers GMP Vaccines for our Clinical Programs

Fully Integrated 43,000 sq. ft. Manufacturing and Testing Facility in Pleasanton, CA

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Key Financial Highlights

3 Months Ended March 31, 2020

Cash, Cash Equivalents, Marketable Securities, Restricted Cash *Expected to support operations into Q3 2021*	**$109.9MM**
Research and Development Expenses	**$22.5MM**
General and Administrative Expenses	**$5.5MM**

Multiple Value-Generating Milestones in Next 12 Months

Anticipated Milestones

	1H-2020	2H-2020	1Q-2021
Neoantigen-based Immunotherapies			
GRANITE Phase 1 Clinical Data	○		
SLATE Phase 1 Clinical Data	○		
Phase 2 Expansion Initiation (advanced disease)		○	
Phase 1 Completed Clinical Data for GRANITE & SLATE		○	
Phase 2 Adjuvant Initiation (early disease)			○
Bispecific Antibodies			
BiSAb Dev. Candidate Nomination (CTA*/KRAS^{mut})		○	

*Cancer testis antigen

Thank you!

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