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): July 13, 2020

Gritstone Oncology, 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 July 13, 2020, Gritstone Oncology, Inc. (the "Company") hosted a teleconference and webcast during which it provided a clinical update on its ongoing Phase 1 studies of its immunotherapy product candidates GRANITE and SLATE, as well as discussing its Phase 2 study plans.

A copy of the presentation utilized by the Company during the teleconference and webcast is filed as Exhibit 99.1 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	Presentation, dated July 13, 2020

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 ONCOLOGY, INC.

Date: July 13, 2020

By: /s/ Jean-Marc Bellemin
Jean-Marc Bellemin
Executive Vice President, Chief Financial Officer

Exhibit 99.1


gritstone
ONCOLOGY
Clinical Data Update &
Near-term Phase 2 Plans
13 July 2020
Gritstone

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.

Agenda

- **Gritstone's GRANITE and SLATE product candidates** - Dr Andrew Allen
- **Phase 1 Clinical Trial Data** - Dr Daniel Catenacci
- **Phase 2 Studies in Advanced Disease** - Dr Andrew Allen
  - GRANITE – advanced CRC & gastric cancer
  - SLATE - post-CPI advanced NSCLC
- **Company Milestones** - Dr Andrew Allen
- **Q&A**
  - Drs Catenacci & Allen, joined by Gritstone Executive Leadership: Dr Rousseau (CMO), Dr Jooss (CSO), Dr Yelensky (CTO) and Mr Bellemin (CFO)

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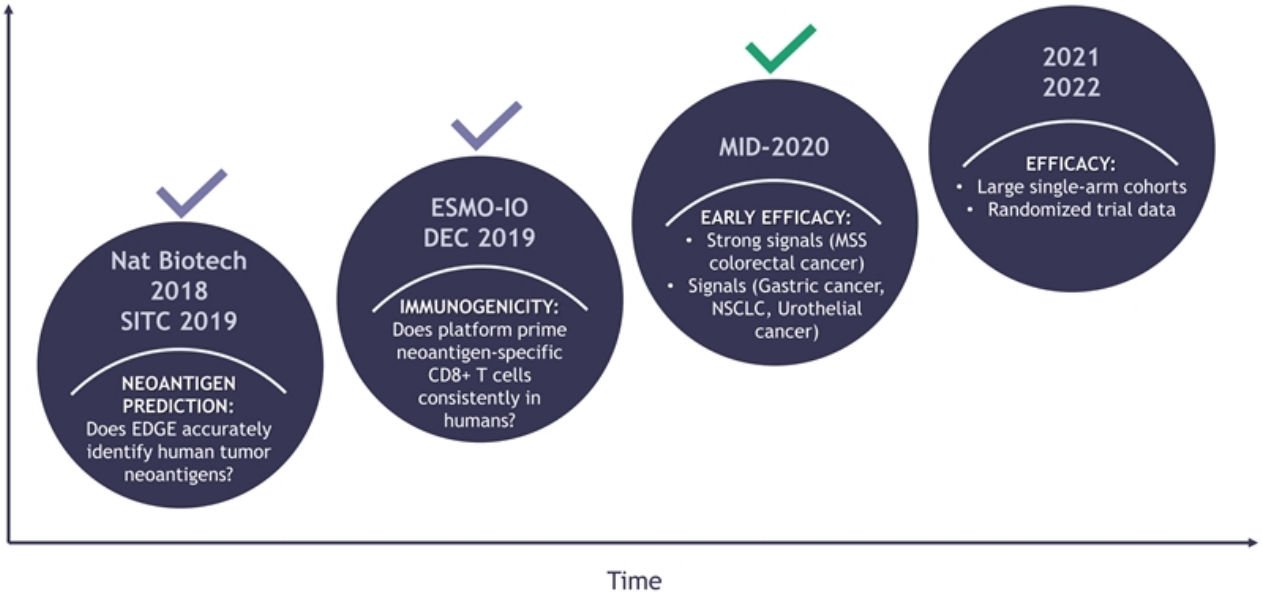
Gritstone Is Steadily Delivering Data to Validate the Platform



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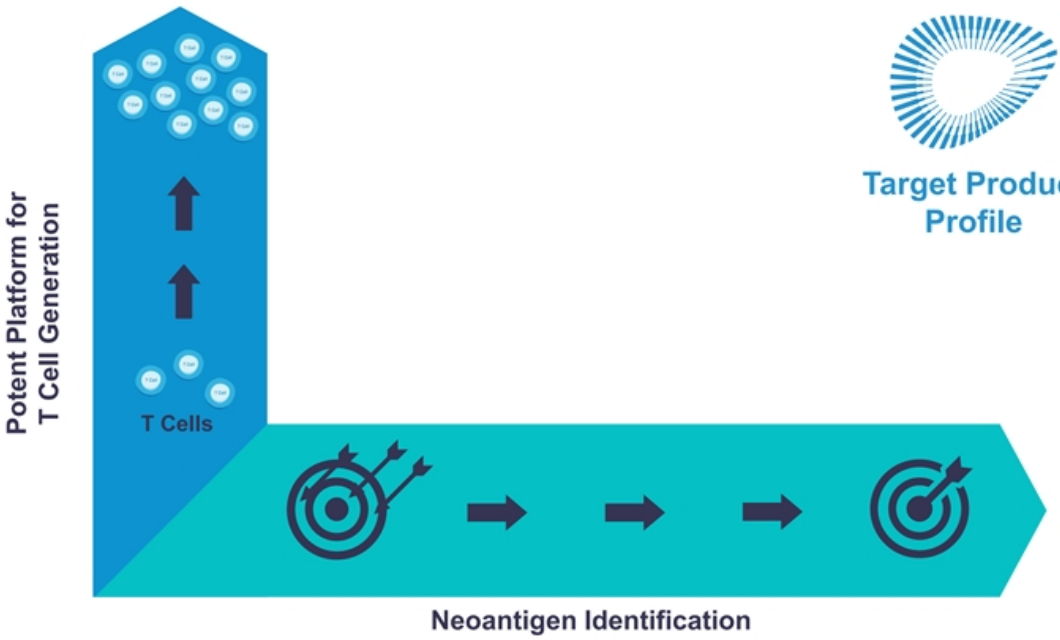
Gritstone's Approach: Next Generation Cancer Immunotherapy Demands Excellence in Two Key Dimensions



Target Product Profile

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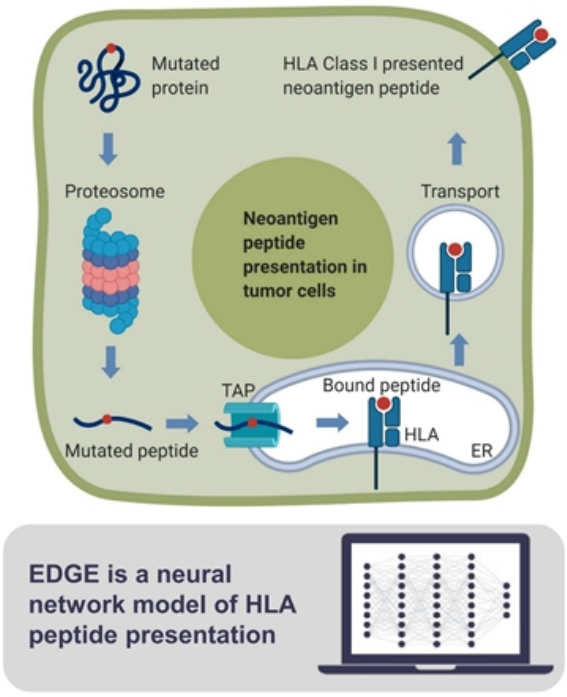
Gritstone's EDGE™ Leads The Field in Neoantigen Identification



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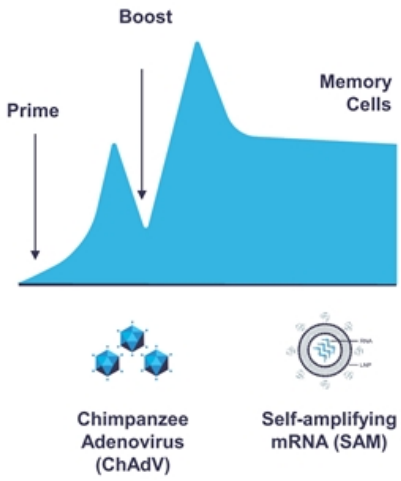
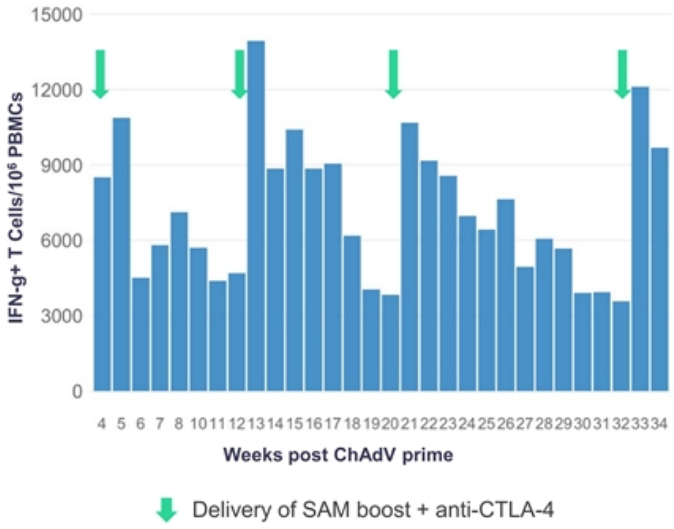
Gritstone Has Developed a Unique, Potent Platform for Delivering Antigens to the Immune System to Drive a Strong T Cell Response

Heterologous Prime/Boost



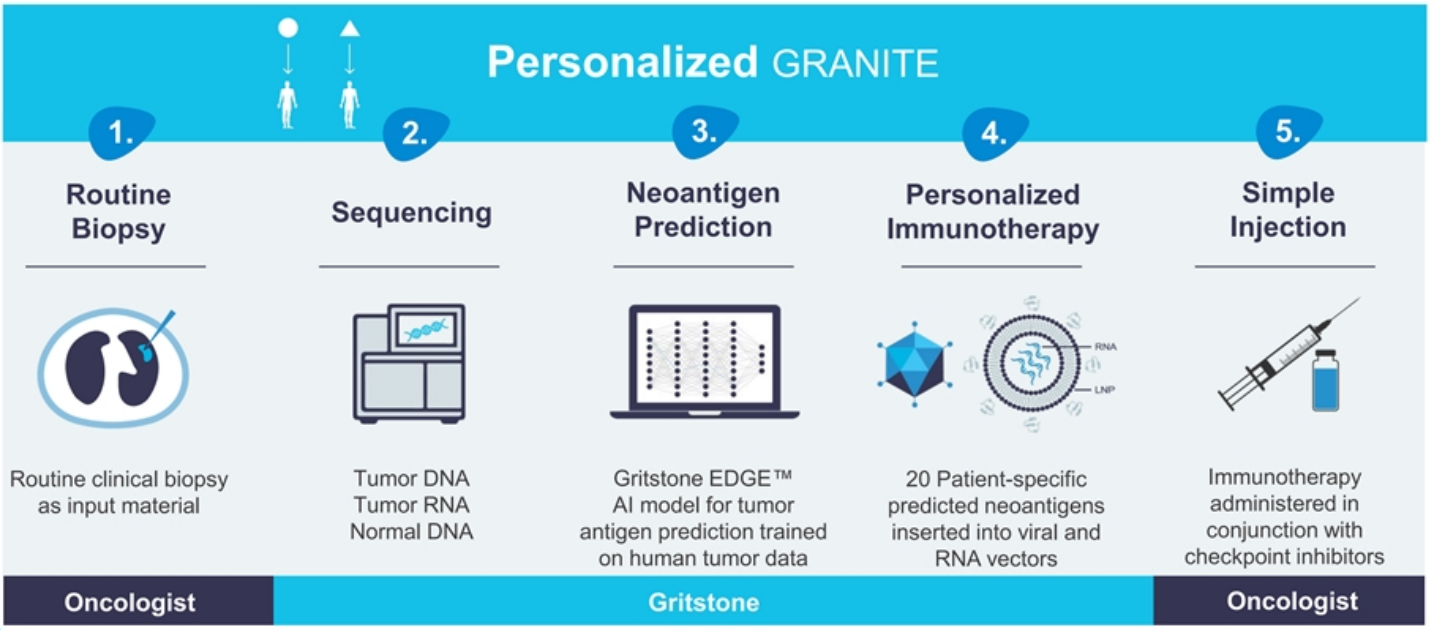
Non-Human Primate Experiment: 6 SIV antigens
ChAdV + SAM + anti-CTLA-4



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)

Many Solid Tumor Patients Will Have Their Own Unique Neoantigens Enabling Personalized Immunotherapy - GRANITE



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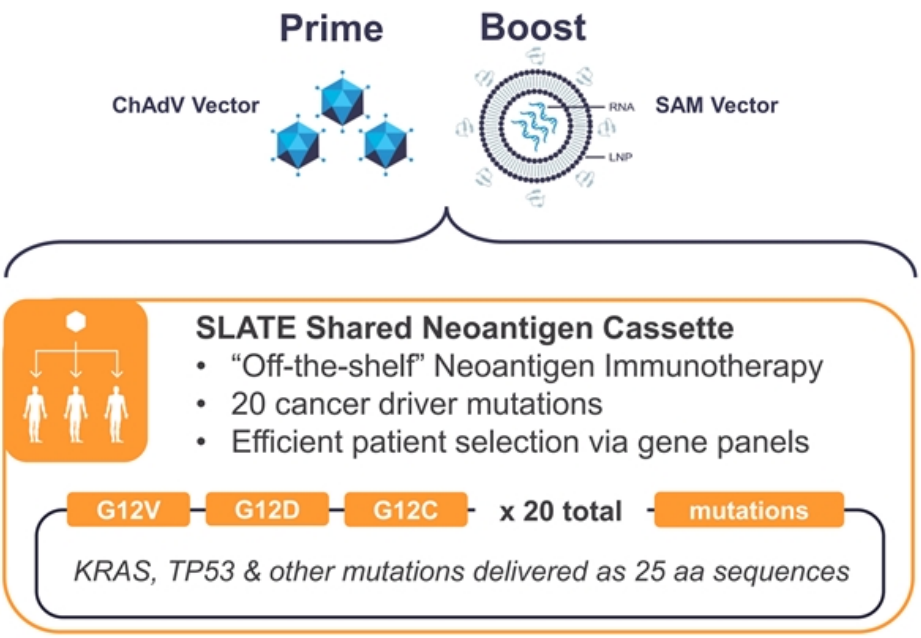
SLATE Delivers Shared Neoantigens To Selected Patients Using Gritstone's Prime/Boost Platform - Off-the-Shelf Therapy



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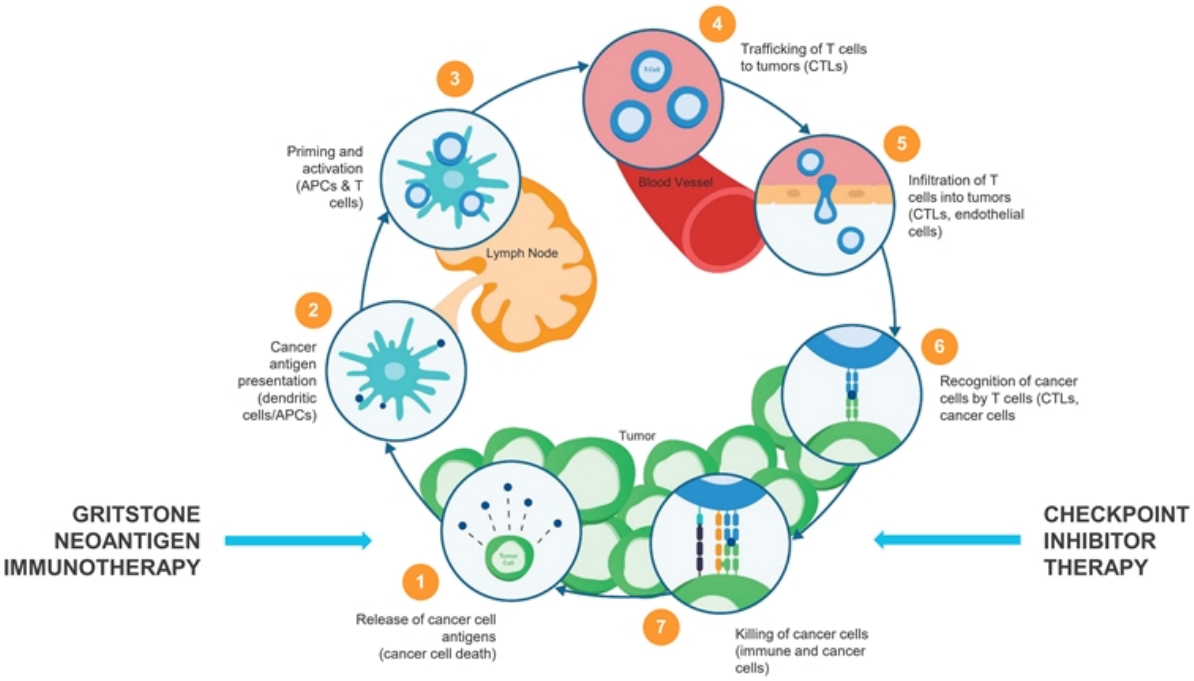
Efficacy of Neoantigen Immunotherapy: How Will it Manifest?

Form of response to neoantigen immunotherapy likely different vs CPI alone where intra-tumoral T cells already present



Chen & Mellman Immunity (2013)

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PHASE ONE CLINICAL TRIAL DATA

Dr Dan Catenacci

Director GI Oncology Program
Assistant Director of Translational Research
Comprehensive Cancer Center
University of Chicago

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GRANITE and SLATE Phase One Studies Are Very Similar

GRANITE
personalized

Lung

Gastric

Colorectal (MSS)

Bladder

SLATE
off-the-shelf

High Frequency KRAS Mutation

Lung

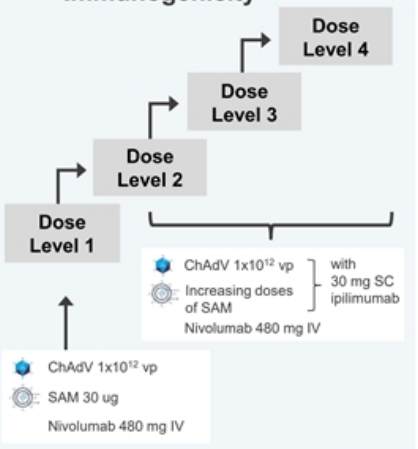
Pancreatic

Colorectal (MSS)

Mutation Positive Tumors

PHASE 1

Objectives:
- Safety and RP2D
- Immunogenicity



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GRANITE and SLATE: Treatment of Previously Treated Metastatic Patients

	GRANITE (n=10)	SLATE (n=19)
Age (mean, range)	59 (38-76)	58 (33-83)
Gender (Female/Male)	4/6	12/7
# of doses		
ChAdV	11	19
SAM	44	39
Nivolumab (IV)	61	58
Ipilimumab (SC)	14	47
Tumor Types		
NSCLC	1	6
Microsatellite stable (MSS)-CRC	5	6
Gastroesophageal adenocarcinoma (GEA)	4	0
Pancreatic Ductal Adenocarcinoma	N/A	5
Ovarian adenocarcinoma	N/A	1
Ampullary adenocarcinoma	N/A	1
Prior anti-PD(L)1 therapy	1	6

Data cut-off 6/30/2020

GRANITE Therapy is Well Tolerated with TRAEs Indicative of an Immune Response to the Vaccine

No DLTs; TRAEs all Grade 1/2 with exception of Grade 3 Hyperthyroidism in 1 patient and self-limiting, asymptomatic Grade 3 CK elevation in 1 patient

Treatment-related adverse events (TRAEs) after ChAdV or SAM

Safety	n = 10 (all patients treated with concurrent nivolumab)						
	ChAdV ($1x10^{12}$ vp)			SAM			
	No SC IPI (n=5)	With SC IPI (n=5)		30 ug (n=3)	100 ug[a] (n=2)	100 ug + SC IPI (n=2)	300 ug + SC IPI (n=2)
Treatment-related adverse events							
Fever	4	3		1	-	1	-
Injection-site reactions	1	4		1	1	-	-
Fatigue	1	1		1	-	1	-
Skin rash	1	-		1	-	1	-
Anorexia	-	1		-	-	1	-
Chills	-	-		-	-	1	-
CK Elevation	-	-		1	-	-	-
Congestion	-	1		-	-	-	-
Diarrhea	-	-		1	-	1	-
Hot flashes	-	1		-	-	-	-
Hyperthyroidism	-	-		-	-	1	-
Hypotension	-	-		1	-	-	-
Infusion-related reaction	-	-		-	1	-	-
Myalgia	-	1		-	1	-	-
Pruritus	-	-		1	-	-	-
Vomiting	-	-		-	-	1	-

[a] One patient did not receive SAM boosts

Data cut-off 6/30/2020

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Fever is the Only SAE Associated with GRANITE Neoantigen Vaccination

All serious adverse events (SAEs) after ChAdV or SAM

Safety	n = 10 (all patients treated with concurrent nivolumab)					
	ChAdV ($1x10^{12}$ vp)		SAM			
	No SC IPI (n=5)	With SC IPI (n=5)	30 ug (n=3)	100 ug[a] (n=2)	100 ug + SC IPI (n=2)	300 ug + SC IPI (n=2)
SAEs						
Abdominal pain	1[e]	-	-	-	-	-
Fever	1[b]	-	1[b]	-	-	-
Bradycardia	-	-	1[c,e]	-	-	-
Heart Failure	-	-	1[c,e]	-	-	-
Hyperthyroidism	-	-	-	-	1[d]	-
Respiratory Failure	-	-	-	-	1[d,e]	-

Grade 5 respiratory failure resulted from patient's altered mental status (checkpoint inhibitor-induced acute thyrotoxicosis), with associated aspiration pneumonia, respiratory failure leading to patient death and is not related to vaccine treatment

[a] One patient did not receive SAM boosts
[b] Occurring in the same patient
[c] Occurring in the same patient
[d] Occurring in the same patient
[e] Not treatment-related

Data cut-off 6/30/2020

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SLATE Therapy is Well Tolerated with TRAEs Indicative of an Immune Response to the Vaccine

Treatment-related adverse events (TRAEs) after ChAdV or SAM

Safety	n = 19 (all patients treated with concurrent nivolumab)						
	ChAdV ($1x10^{12}$ vp)			SAM			
	No SC IPI (n=2)	With SC IPI (n=17)		30 ug (n=2)	30 ug + SC IPI (n=4)	100 ug + SC IPI (n=6)	300 ug + SC IPI (n=6[a])
Treatment-related adverse events							
Fever	-	7		-	1	2	5
Fatigue	-	6		-	-	1	2
Diarrhea	-	2		-	-	1	1
Nausea	-	2		-	-	1	1
Pruritus	1	1		-	1	1	-
Chills	-	2		-	-	-	1
Vomiting	-	2		-	-	-	1
ALT increased	-	1		-	-	-	1
AST increased	-	1		-	-	-	1
Myalgia	-	2		-	-	-	-
Neutropenia	-	1		-	-	-	1
Rash	-	-		1	-	1	-
Anorexia	-	-		-	1	-	-
Arthralgia	-	1		-	-	-	-
Dizziness	-	-		1	-	-	-
Dry skin	-	-		1	-	-	-
Gait disturbance	-	-		1	-	-	-
Generalized weakness	-	-		1	-	-	-
Headache	-	1		-	-	-	-
Injection site reaction	-	1		-	-	-	-
Insomnia	-	1		-	-	-	-
Myositis	-	1		-	-	-	-
Night Sweats	-	1		-	-	-	-
Rhabdomyolysis	-	1		-	-	-	-
Thrombocytopenia	-	-		-	-	-	1

- All grade 1/2 with exception of:
  - one patient with grade 3 fever after 300 μg SAM + SC IPI; resolved with acetaminophen
  - one patient with reversible grade 3 ALT and grade 4 AST elevation attributed to nivolumab (DLT
  - one patient with grade 3 neutropenia and thrombocytopenia
  - one patient with grade 3 rhabdomyolysis
- Two DLTs after ChAdV in combination with nivolumab and ipilimumab (1 each of CPI-induced autoimmune hepatitis and myositis)

[a] 1 patient discontinued after ChAdV due to autoimmune myositis

Data cut-off 6/30/2020

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SLATE SAEs: Mostly attributable to CPI, no other clear pattern

All serious adverse events (SAEs) after ChAdV or SAM

Safety	n = 19 (all patients treated with concurrent nivolumab)						
	ChAdV ($1x10^{12}$ vp)			SAM			
	No SC ipi (n=2)	With SC ipi (n=17)		30 ug (n=2)	30 ug + SC IPI (n=4)	100 ug + SC IPI (n=6)	300 ug + SC IPI (n=6[f])
SAEs							
Abdominal pain	-	-		-	-	-	1[a]
Acute kidney failure	-	1[a,b]		-	-	-	-
Anemia	-	-		-	1[a, f]	-	-
ALT elevation	-	1[c]		-	-	-	-
AST elevation	-	1[c]		-	-	-	-
Cervical fracture	-	-		1[a]	-	-	-
Fever	-	1[c]		-	-	-	1[c, g]
Hypotension	-	-		-	1[a, f]	-	-
Myositis	-	1[e]		-	-	-	-
Nausea	-	-		-	1[a,b]	1[a,d]	-
Neutropenia	-	-		-	-	-	1[c, g]
Right Frontal Brain Metastasis	-	1[a]		-	-	-	-
Rhabdomyolysis	-	1[e]		-	-	-	-
Small bowel obstruction	-	-		-	1[a,b]	-	-
Vomiting	-	-		-	-	1[a,d]	-

[a] Not treatment-related
[b] Occurring in the same patient
[c] Occurring in the same patient
[d] Occurring in the same patient
[e] Occurring in the same patient
[f] Occurring in the same patient
[g] One patient not treated with nivolumab or ipilimumab in combination with SAM

Data cut-off 6/30/2020

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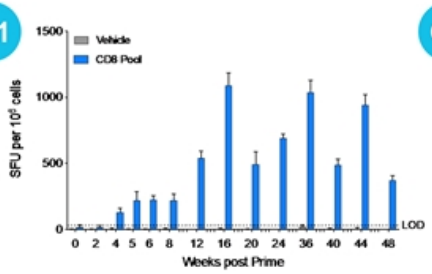
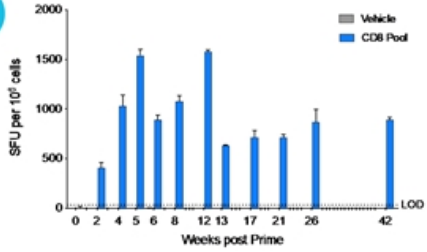
GRANITE

Strong Neoantigen-specific CD8+ T Cell Responses Consistently Induced Across All Patients (Ex Vivo ELISpot Assay with Short Peptides)

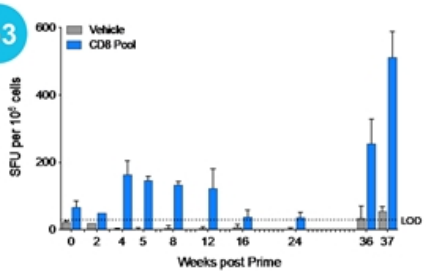
G1



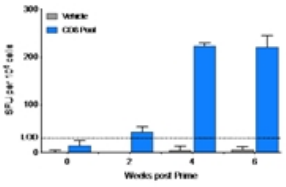
G2



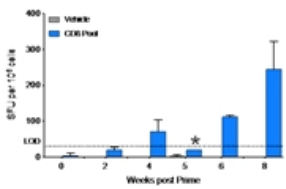
G3



G4

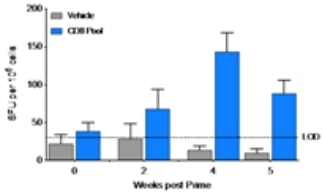


G6

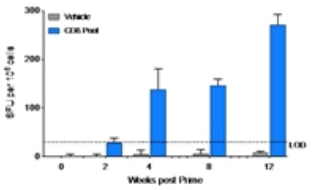


* Poor cellular recovery

G7



G8

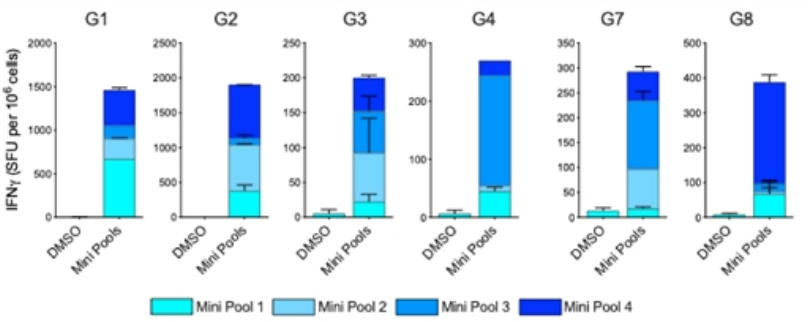


G5: Data not available due to lack of samples

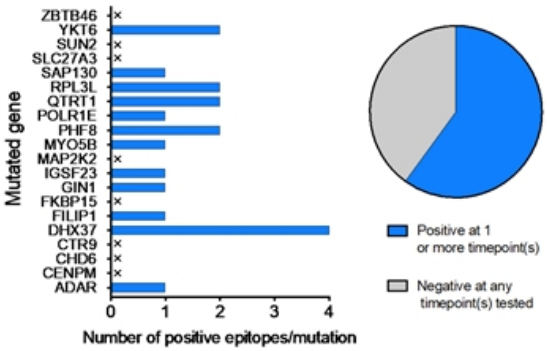
LOD = limit of detection

Each Patient Has CD8+ T Cell Responses To Multiple Neoantigens

Mini-pools of multiple short neoantigenic peptides (a mini-pool is a subset of the 20 in the vaccine) studied in each patient with sufficient PBMCs



Patient G2 (leukapheresis): 12 of 20 neoantigens elicit CD8⁺ T-cell responses



G6: Data not available due to lack of sample

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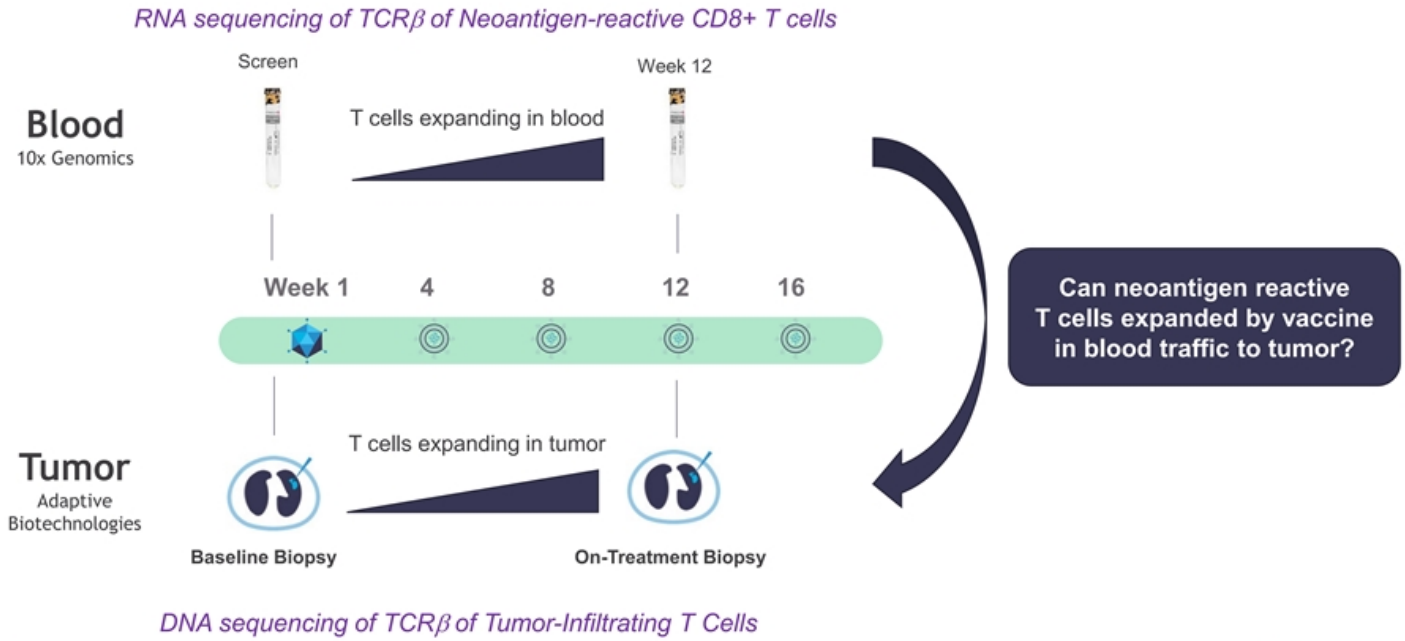
Do Therapy-Induced Neoantigen-Specific T Cells Traffic to the Tumor? T Cell Receptor (TCR) Sequence Analysis Can Address This



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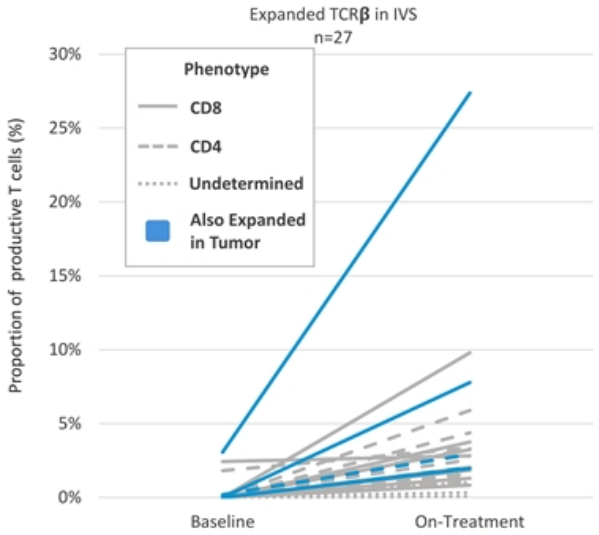
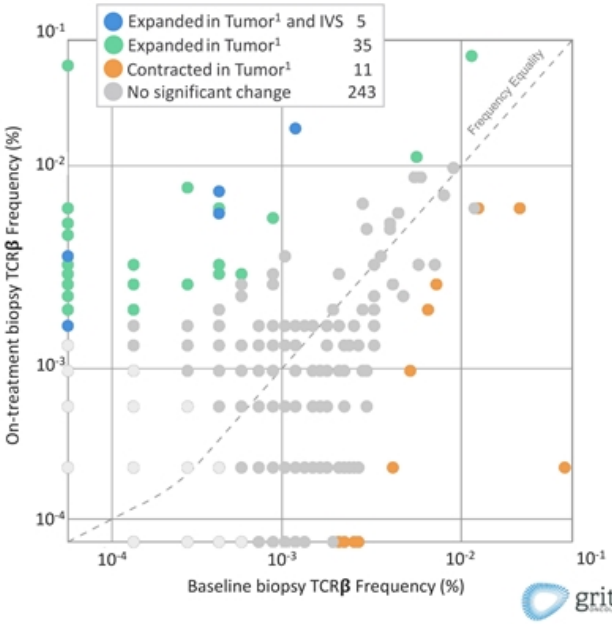
G3: Joint Expansion of Neoantigen Reactive CD8 T cells in the Blood and Tumor On Treatment Indicates Vaccine Driven Tumor T cell Infiltration

27 TCRβs were expanded on-treatment in neoantigen-peptide-stimulated PBMCs, 5 of which infiltrated the tumor



40 TCRβs significantly expanded in the on-treatment tumor biopsy, 5 of which also expanded in PBMCs



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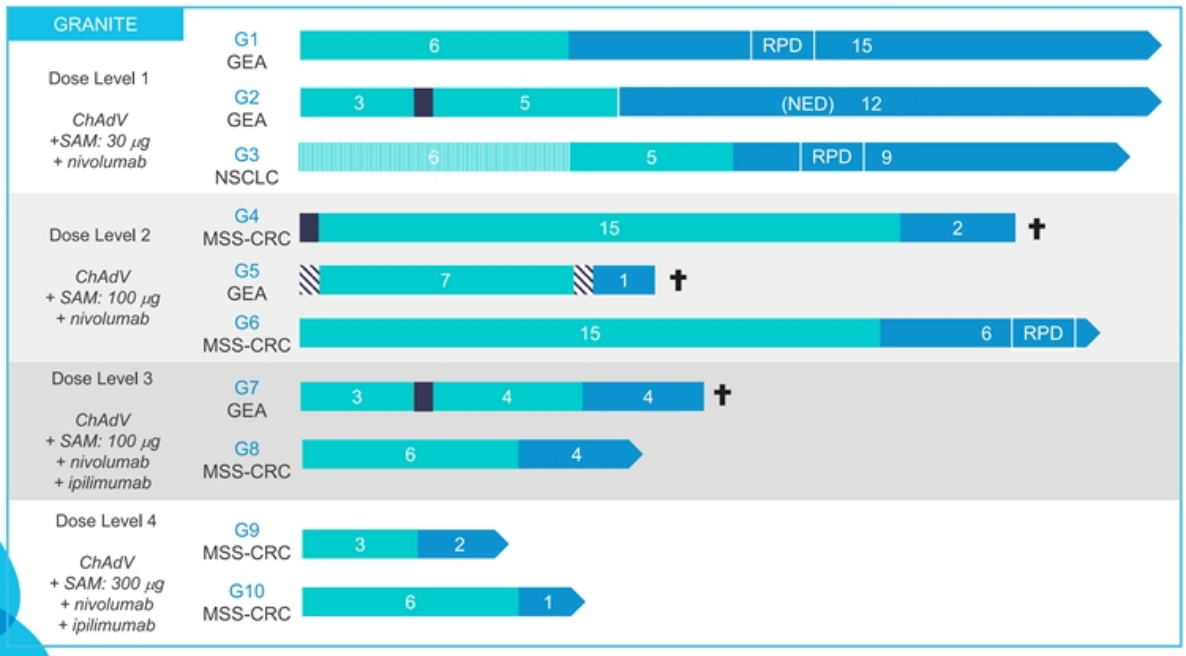
GRANITE: No DLTs and frequent treatment beyond apparent radiologic progression



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G2 (DL1): Prolonged disease-free period on therapy after surgery

59-year old male with metastatic gastric cancer

Prior Therapy

FOLFOXIRI (2 months) → Surgery → FOLFOXIRI (2 months)

Study Treatment

Every 4 weeks over first 6 months, then every 3 months x 2

Weeks: 0 4 8 12 16 20 24 36 52

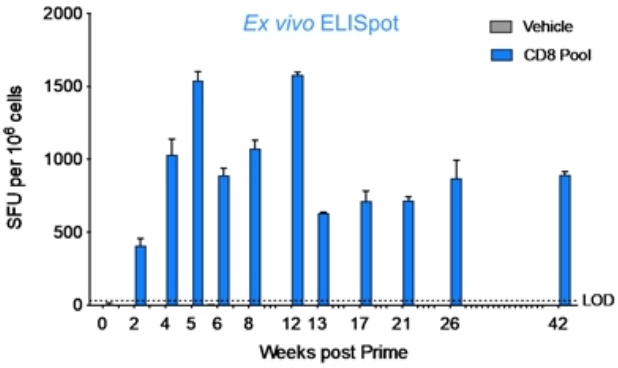
Nivolumab

Clinical status
- 365+ days on study, back to work, discontinued study treatment per patient request, continuing to monitor

Tumor response
- no evidence of disease at any timepoint on study (post-surgery)

T-cell response
- CD8 T-cell expansion with 12 neoantigen-specific CD8 T-cell clones

ctDNA kinetics
- No mutations detected above the lowest call threshold for the patient's mutations



No ctDNA detected at any point from week 0-52

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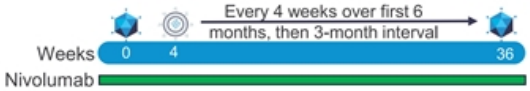
G3 (DL1): NSCLC Patient with Progression on Prior CPI - Evidence of Tumor Control (Clinical Benefit, ctDNA Control) Until T Cell Decline

72-year old female with squamous NSCLC

Prior Therapy

chemoradiation + durvalumab (9 months) → PD → carboplatin + gemcitabine (~4 months) → SD

Study Treatment



Clinical status

- 180+ days on study, symptomatically improving since study entry without any complaint compared to prior lines of treatment, treated beyond radiologic progression

Tumor response

- Best overall response: PD at week 8 (+ 34% from baseline), at week 16 (+3% relative to week 8) and confirmed at week 24 (+16% relative to week 16), with apparent lesion cavitation

T cell response

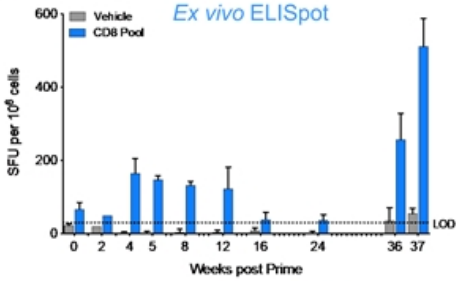
- CD8 T cell expansion following ChAdV prime, expansion of pre-existing responses

ctDNA kinetics

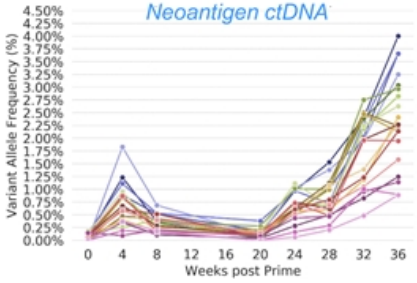
- Trending down following an initial increase at week 4 (20 of 20 variants detected)

Avg VAF 0.69%	Max reduction 6x	Avg VAF 0.12%
Week 4		Week 20

Ex vivo ELISpot



Neoantigen ctDNA



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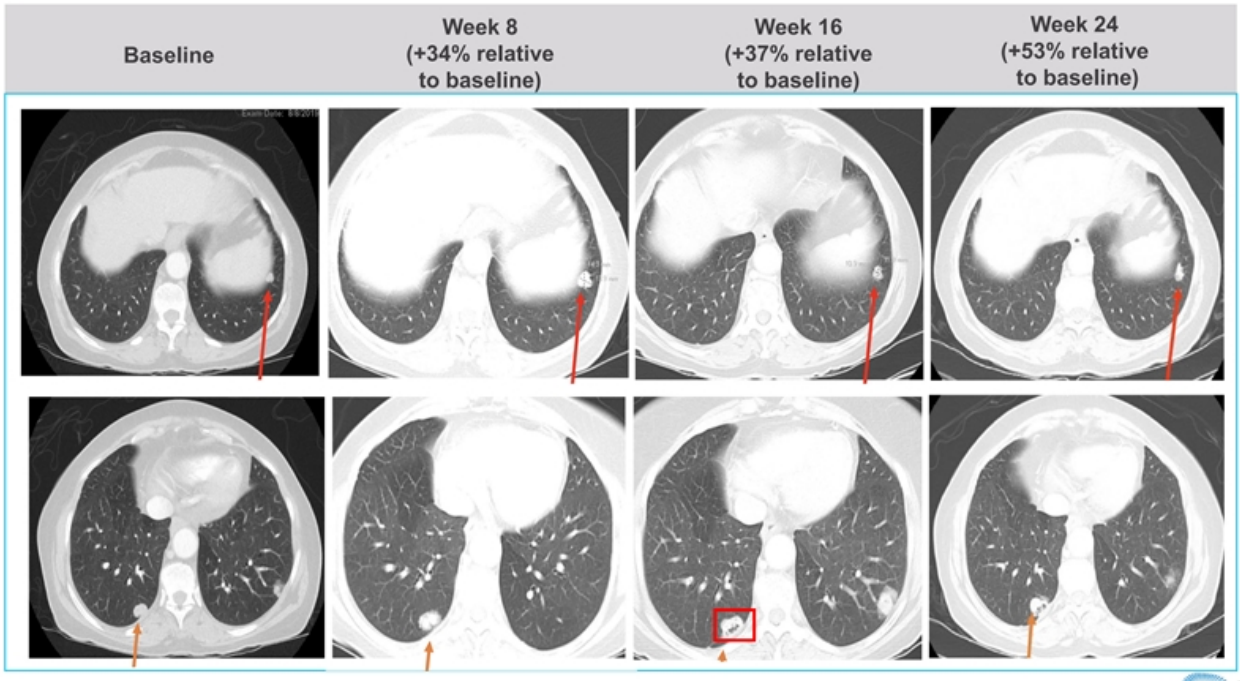
G3 (DL1): Slow Expansion of Lung Nodules on CT Imaging with Cavitation and No New Lesions

G3



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ctDNA May Help Understand Tumor Biology when CT Scans Uninformative

Advanced melanoma patients treated with CPI can show pseudoprogression - ctDNA changes may identify these patients

1 29 Patients with metastatic melanoma treated with anti-PD1 who progressed on first scan

2 9 of 29 (31%) has pseudo progression on subsequent scan

3 All 9 had a favorable ctDNA profile, defined as:

- ctDNA undectable at baseline or on therapy
- ctDNA with >10x reduction over time

In patients with progression on first scan, a favorable ctDNA profile identified 100% of pseudoprogression events

Lee et al JAMA Oncology (2018)

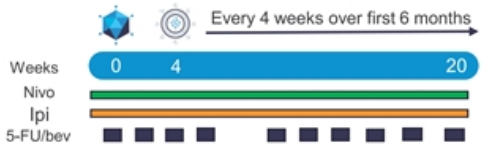
G8 (DL3): Clear Evidence of Clinical Benefit in MSS-CRC Patient

50-year old female with MSS-CRC

Prior Therapy

FOLFOX/bev (15 months) → PD → FOLFIRI/bev (6 months) →

Study Treatment



Clinical status

- 112+ days on study, clinically feeling well

Tumor response

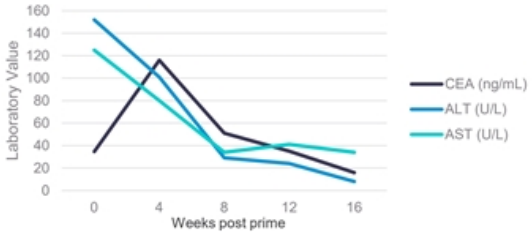
- Best overall response: SD at week 16 (one liver lesion stable, all other lesions shrinking)
- TMB = 7 mutations/MB

T-cell response

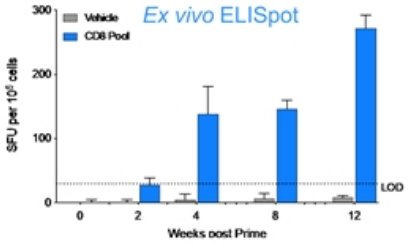
- T cells induced with prime and further increased with boost

ctDNA kinetics

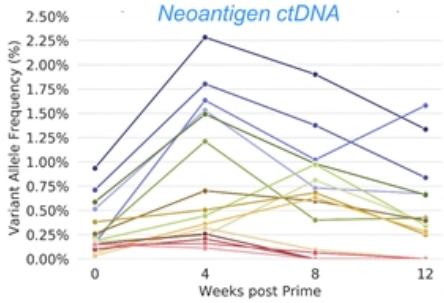
- Increase in ctDNA levels at 1 month correlating with CEA spike followed by decrease with loss of some variants (16 of 20 total variants detected)



Ex vivo ELISpot



Neoantigen ctDNA



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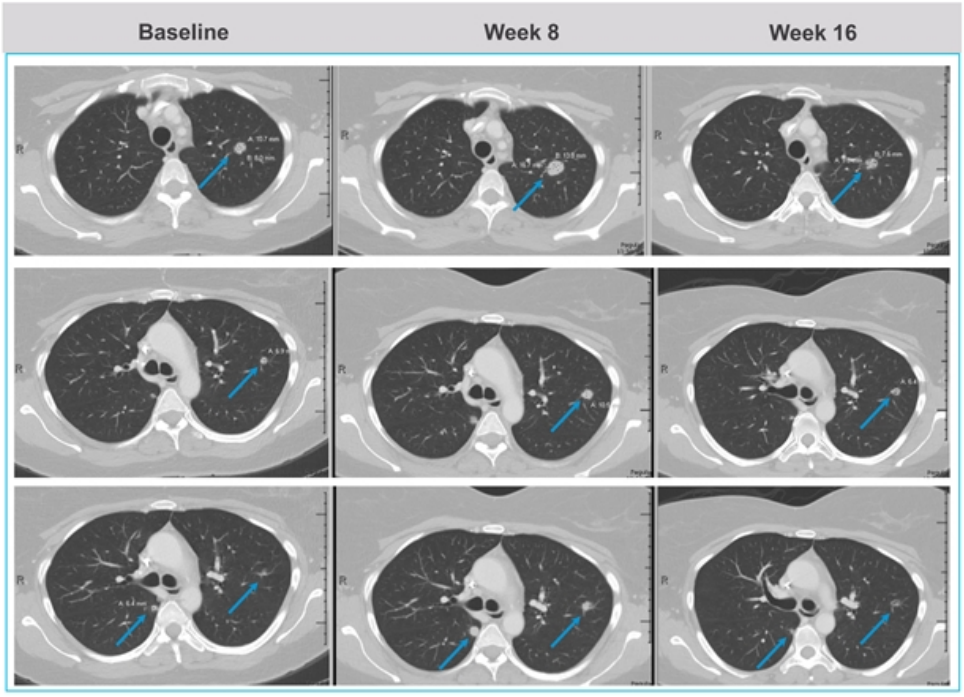
G8 (DL3): Lung CT Shows Transient Lesion Expansion at Week 8 (T Cell Infiltration?) then Contraction (Slide 1 of 2)

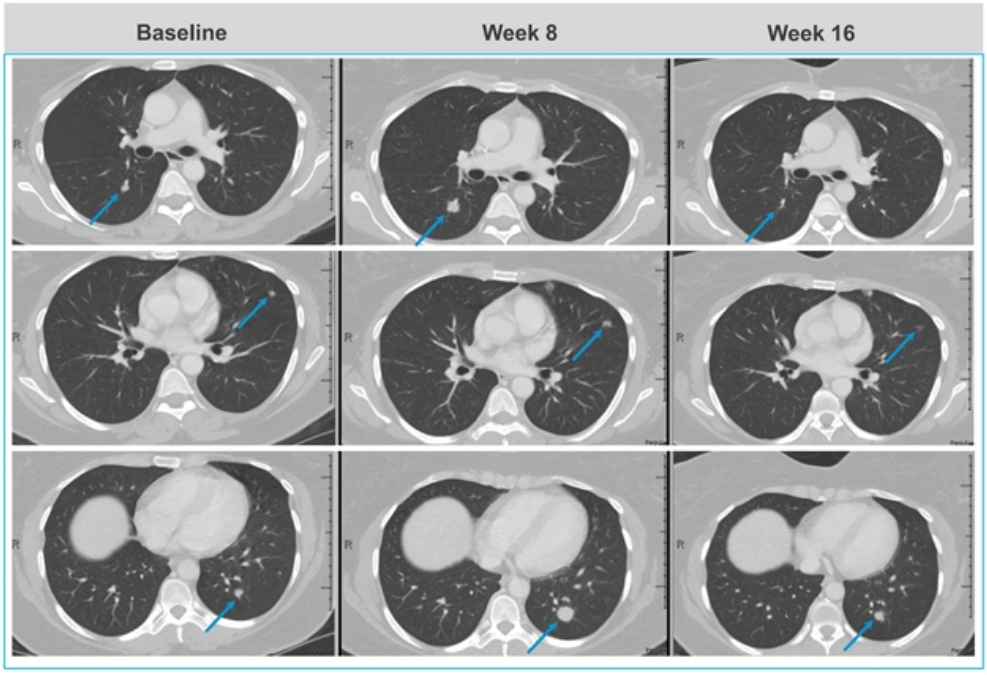
Multiple lung lesions increasing in size at 8 weeks and shrinking at 16 weeks below baseline



gritstone

G8 (DL3): Lung CT Shows Transient Lesion Expansion at Week 8 (T Cell Infiltration?) then Contraction (Slide 2 of 2)

Multiple lung lesions increasing in size at 8 weeks and shrinking at 16 weeks below baseline



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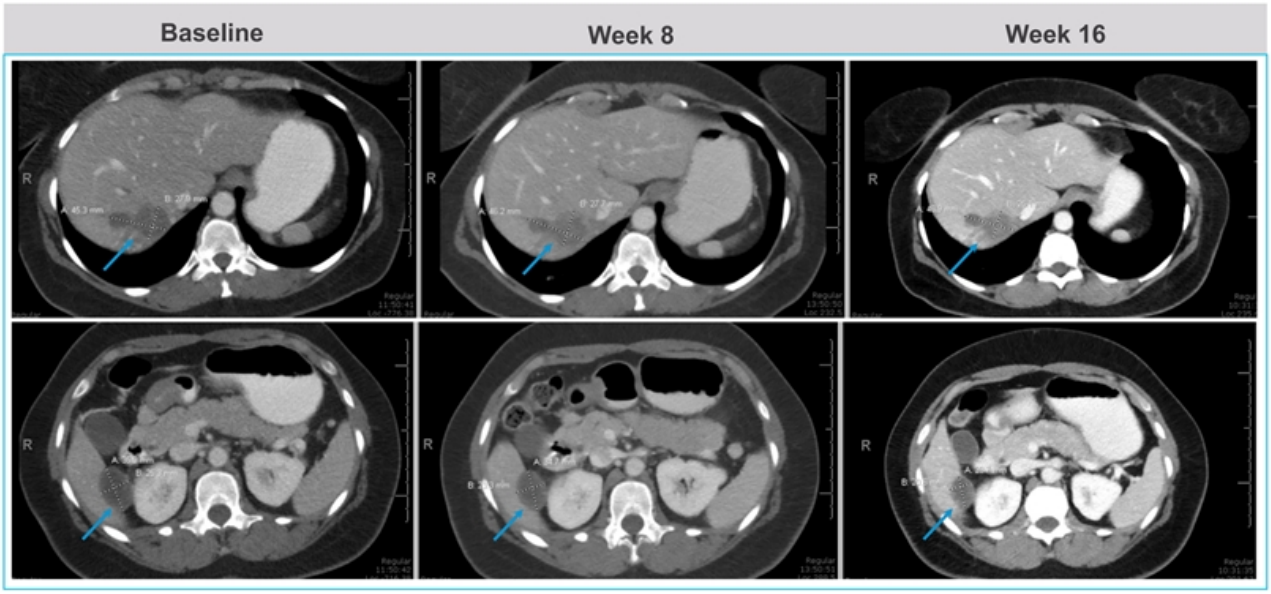
G8 (DL3): Large Liver Lesion Unchanged in Size (but LFTs Normalized)

Mixed response of two target liver lesions with one stable and one decreasing in size



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GRANITE Conclusions to Date

- Data to dose level 3 show good tolerability
  - Vaccine elicits transient fever and injection site reaction as expected
  - Customary CPI-induced immune-related adverse events
- Strong, consistent induction of killer CD8+ T cells, specific to multiple neoantigens, which have now been shown to accumulate in tumor (in 2/2 patients studied to date)
- Dose/intensity level 1 efficacy data suggest induction of disease control, perhaps more durable in the adjuvant-like context
  - Early tumor lesion expansion observed –consistent with T cell infiltration and proliferation in tumor
- Dose/intensity level 2 data suggest that since development of T cell response (and thus, presumably, any consequent benefit) takes multiple weeks, patients about to progress and die within a few weeks are unlikely to benefit from this form of immunotherapy
- Dose/intensity level 3 data very encouraging – no disease progression observed – clear clinical benefit ongoing in metastatic colorectal cancer patient (MSS genotype)
- More MSS-CRC patients under study at dose/intensity level 4

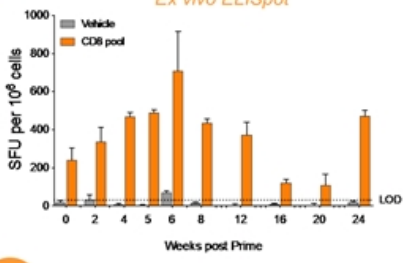

SLATE

SLATE: 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

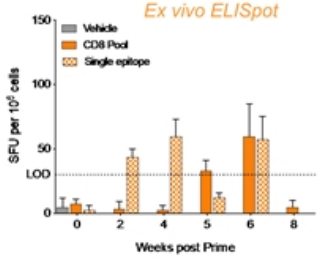
S2 *KRAS G12C*

Ex vivo ELISpot

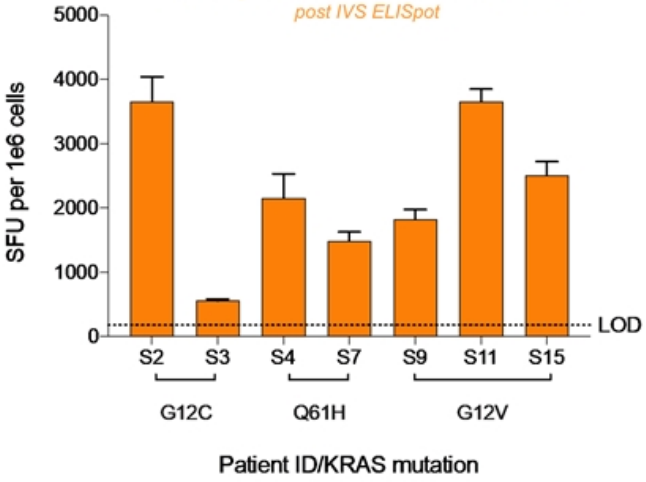


S4 *KRAS Q61H*

Ex vivo ELISpot



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



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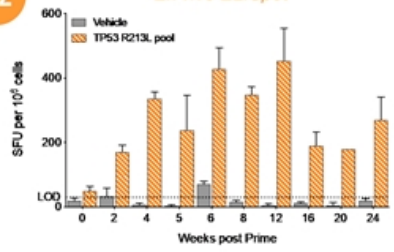
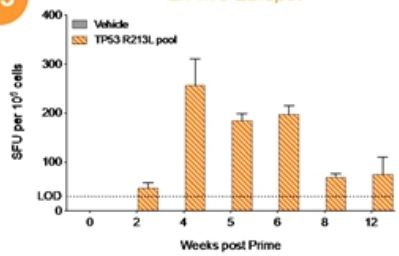
SLATE: TP53^{mut} Neoantigens Seem Immunodominant – Although Rarer than KRAS^{mut} Neoantigens, they Drive Strong CD8+ T Cell Responses

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

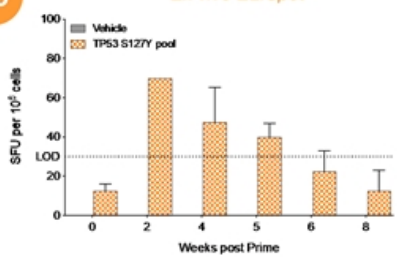
S2



S3



S9



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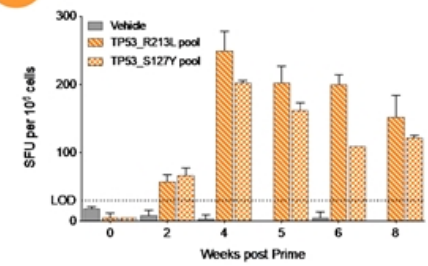
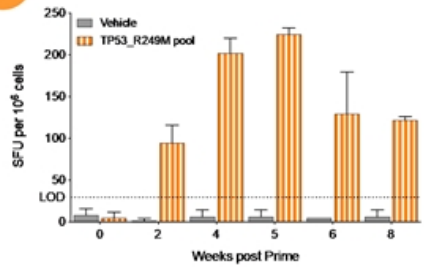


S13



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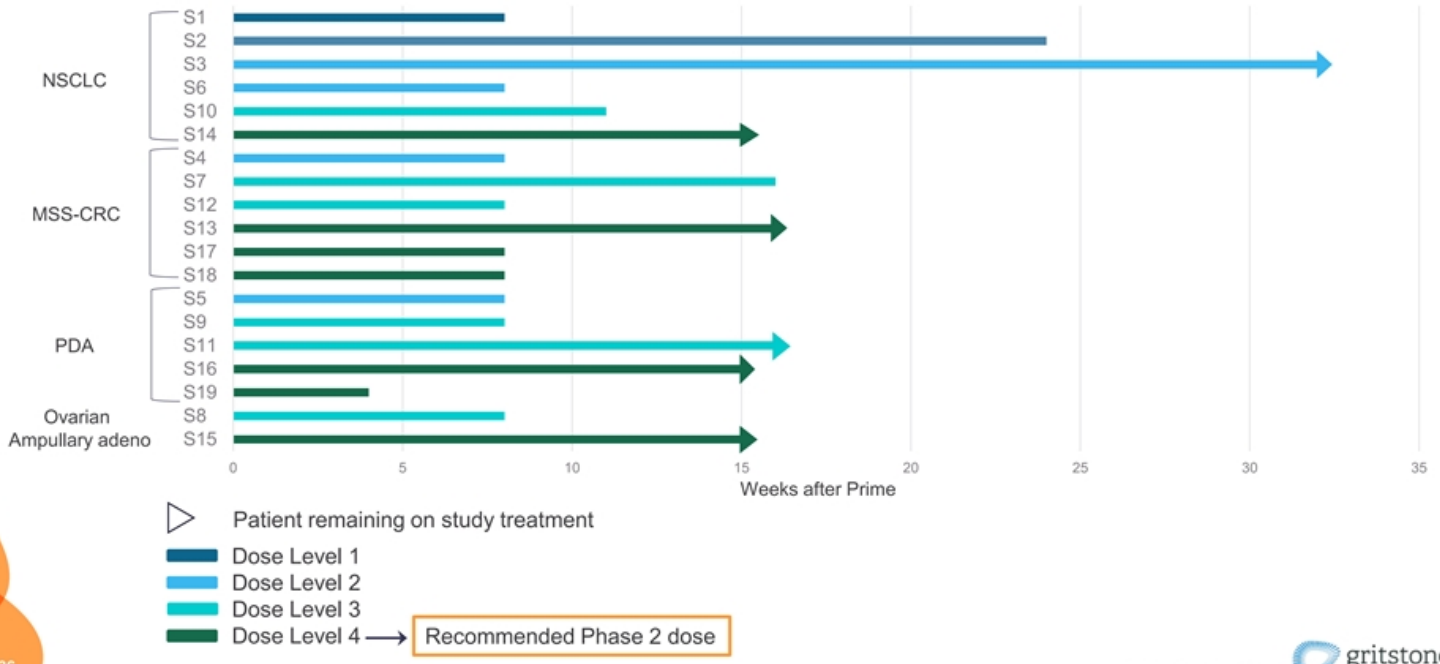
SLATE: Patients with NSCLC (All of Whom Progressed on Prior IO) Have Largest Degree of Clinical Benefit



Data cut-off 06/30/20

S2 (DL1): Good Clinical Response to Therapy with ctDNA Reduction and Minor Tumor Shrinkage on CT Scan

S2

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

Prior Therapy

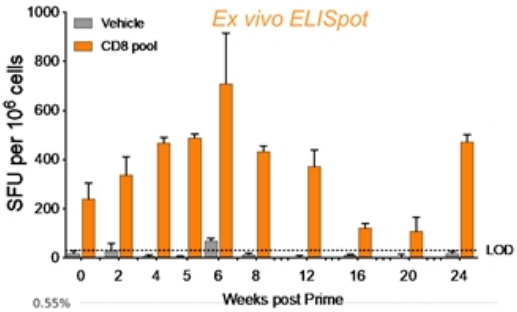
Pembrolizumab (4 months, BOR = PD) → PD → Anti-TIGIT (10 months, BOR = SD) → Carboplatin/pemetrexed/ SBRT (2 months)

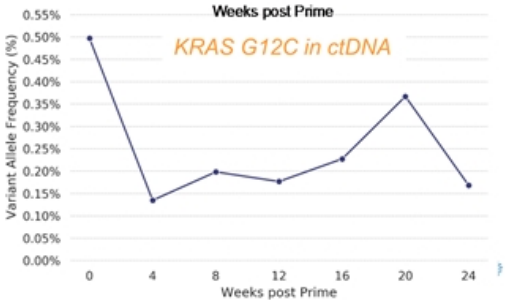
Clinical status
- 168 days on study, then declined further treatment due to fatigue

Tumor response
- Best overall response: stable disease with a 20% reduction from baseline

T-cell response
- Expansion of pre-existing CD8 T-cell against *KRAS* G12C

ctDNA kinetics
- Drop in ctDNA correlates with 20% tumor reduction at week 8 by CT scan





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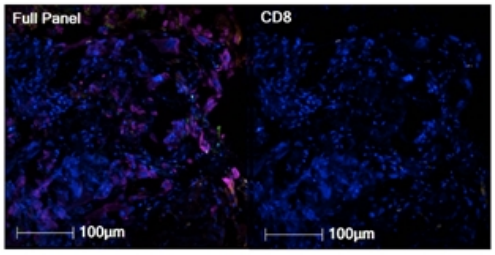
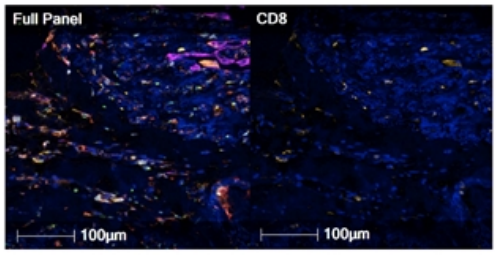
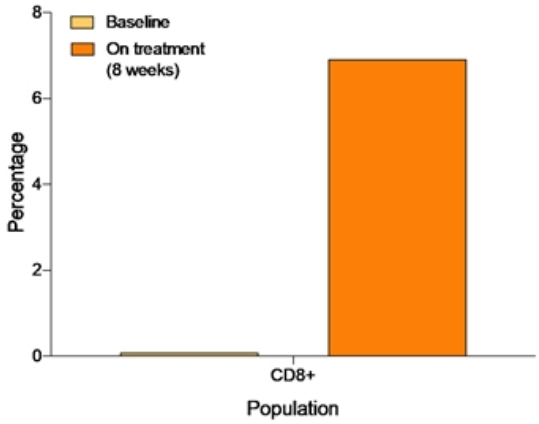
S2 (DL1): Increased Immune Infiltration, Including CD8+ T Cells, Observed in Post Treatment Biopsy

Baseline



On treatment





Full panel analysis	
CD4	PD-L1
CD8a	CD68
CD45RO	Pan-Cytokeratin
Granzyme B	DAPI
FoxP3	

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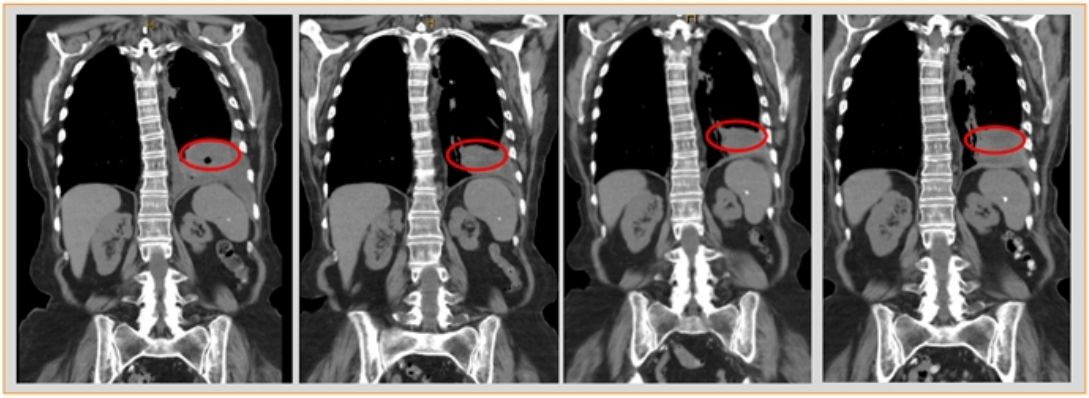
S2 (DL1): Good Clinical Response to Therapy with ctDNA Reduction and Minor Tumor Shrinkage on CT Scan

S2

Baseline	Week 8	Week 16	Week 24
95 mm*	77 mm* (-19% relative to baseline)	75 mm* (-21% relative to baseline)	89 mm* (-6% relative to baseline)



*Sum of longest diameters of two target lesions

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S3 (DL2): Sustained Clinical Benefit in Patient after Progression on Front-Line Pembrolizumab-Chemotherapy

55-year old male with NSCLC; *KRAS* G12C

Prior Therapy

Pembrolizumab + Carboplatin/pemetrexed (8 months, BOR = PD)

PD

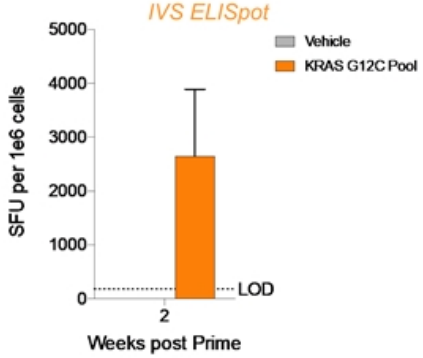
Clinical status
- 196+ days on study, clinically doing well

Tumor response
- Best overall response: stable disease with a 15% reduction from baseline at week 24 and 32

T-cell response
- Detection of CD8 T-cell against *KRAS* G12C following in vitro stimulation

ctDNA kinetics
- *KRAS* G12C mutation not detected at any timepoint

IVS ELISpot



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SLATE Conclusions to Date

- Data to dose level 4 show good SLATE tolerability with expected CPI-induced immune-related adverse events
- RP2D at highest evaluated dose in Phase 1 (dose level 4)
- Strong, consistent induction of CD8+ T cells to some neoantigens (TP53 mutations) which display features of immunodominance
- Less consistent induction of CD8+ T cells to KRAS neoantigens which are less immunodominant
- Evidence of clinical benefit and minor but sustained tumor shrinkage in multiple NSCLC patients with KRAS G12C mutations who had progressed on prior CPI therapy; no patients with TP53 mutations treated yet

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PHASE TWO STUDIES IN ADVANCED DISEASE

Dr Andrew Allen

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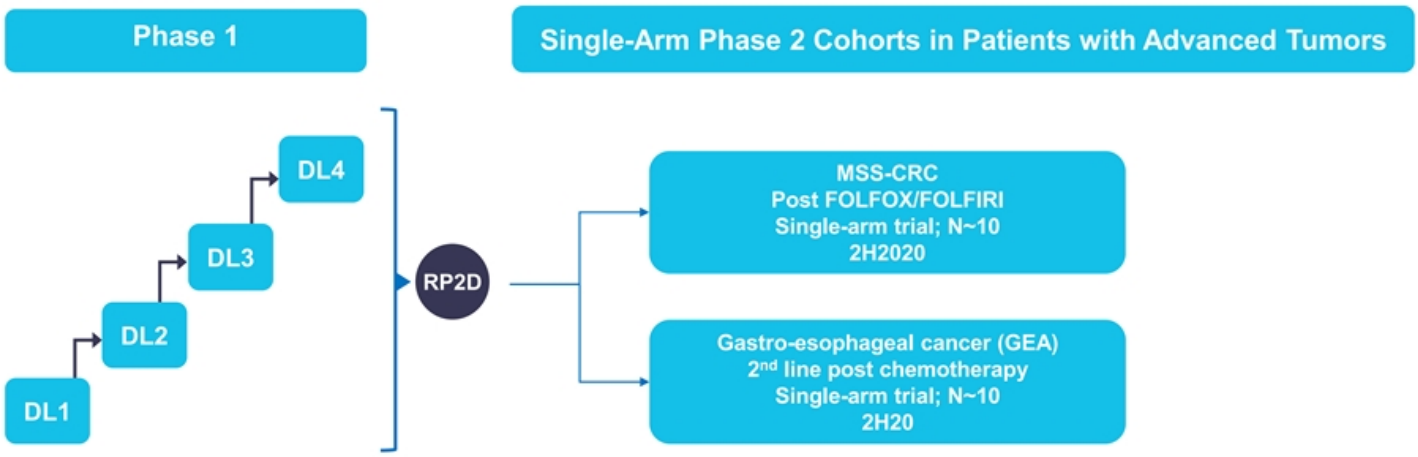
GRANITE Phase 2 Begins 2H20: Pursue Colorectal Cancer Signal & Continue to Study Gastric Cancer

Strong Efficacy Signal with Single-Arm Trial if Multiple Responses Observed in MSS-CRC



DL = dose level

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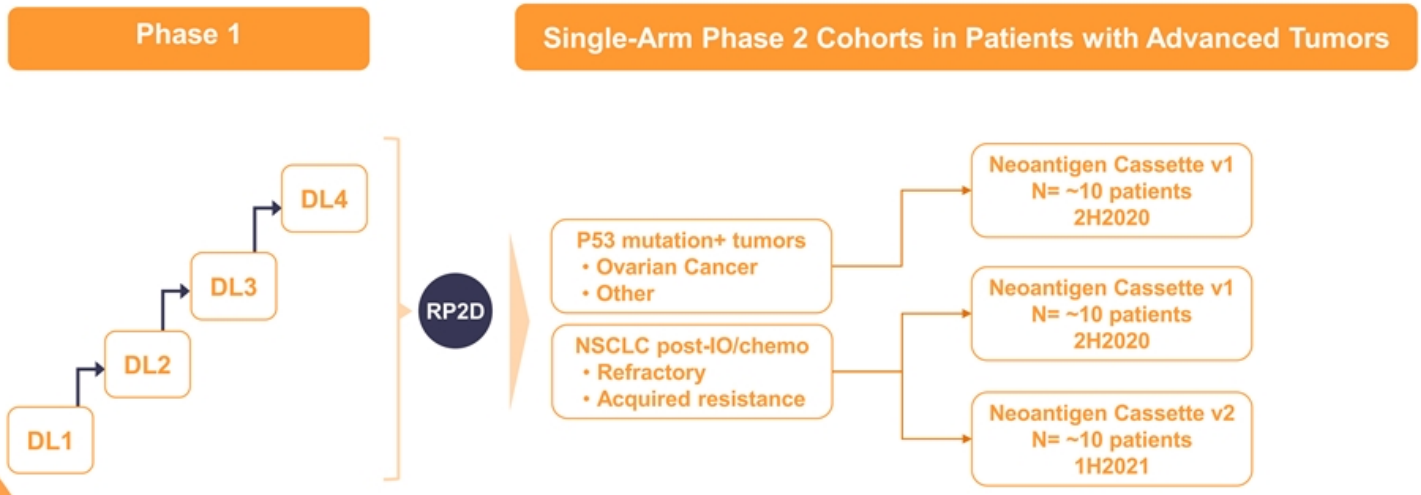
SLATE Phase 2 Begins 2H20 With Focus on Post-IO NSCLC

Pursue signals observed in dose escalation (KRAS^{mut} & TP53^{mut}) and optimize epitope cassette



DL = dose level

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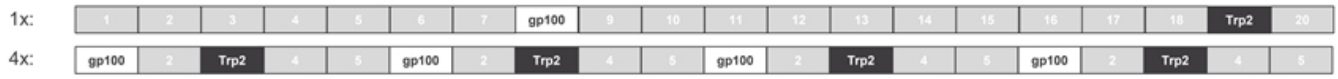
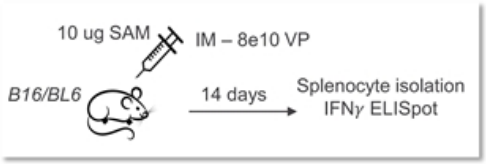
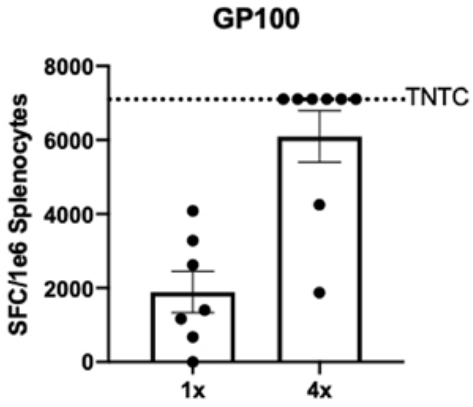
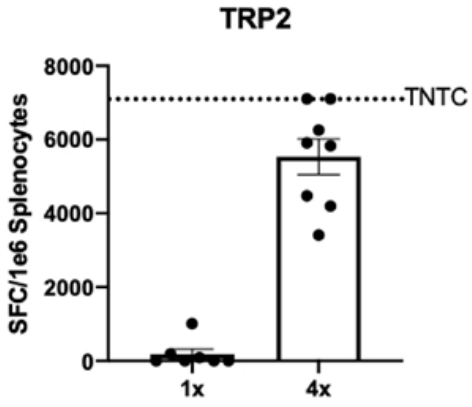
SLATE Optimization: Repeating Epitopes Within the Vaccine Antigen Cassette Strongly Increases Antigen-Specific T-cell Response

Key issues are epitope competition and epitope immunodominance









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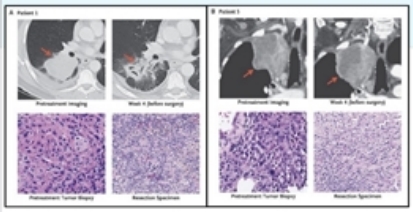
Future Step: Assess Adjuvant Immunotherapy in Stage II/III NSCLC

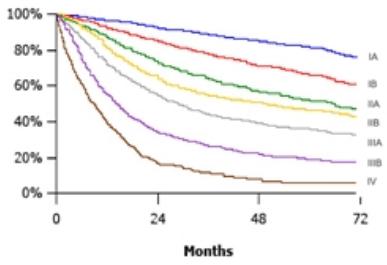
Neoadjuvant*



Neoadjuvant nivolumab linked to 45% major pathologic response rate in 20 NSCLC patients with untreated resectable disease

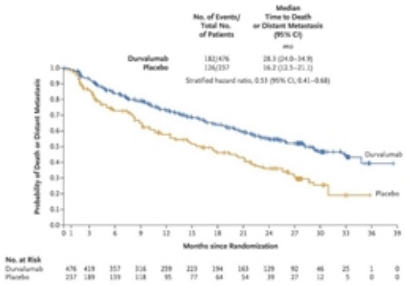
Adjuvant**

Overall survival in NSCLC patients by disease stage at diagnosis



Stage III***

PACIFIC trial of durvalumab maintenance after chemoradiation for unresectable Stage III NSCLC



*Forde et al (2018) NEJM; **Goldstraw et al (2016) JTO; ***Antonia et al (2018) NEJM

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CONCLUSIONS & COMPANY MILESTONES

Dr Andrew Allen

GRANITE & SLATE IMMUNOTHERAPY

Demonstrating clear signals of efficacy – now driving into phase 2 trials to establish path to registration

- Phase 1 trials with intensive translational medicine elements generating substantial insights – series of “N of 1” clinical trials informing program development
- GRANITE is demonstrating clear signals of efficacy
  - At intensity/dose level 1, consistent & strong CD8+ T cell induction with evidence of disease control
  - At intensity/dose level 3, no disease progression in treated patients to date and clear clinical benefit emerging in patient with metastatic MSS-CRC
  - Intensity/dose level 4 patients (including MSS-CRC) underway now
- GRANITE will advance rapidly into phase 2 single-arm cohorts in advanced MSS-CRC and gastric cancer (where CPI have low utility)
- SLATE neoantigens sorting into immunodominant versus non-dominant classes – the former driving strong, consistent CD8+ T cell responses; the latter less consistently so
  - TP53 mutations (immunodominant, common in ovarian cancer) to be studied immediately using current SLATE neoantigen cassette in current clinical trial
  - KRAS mutations (non-dominant) to be studied in post-CPI NSCLC patients, using both current neoantigen cassette (building on clinical signals) and an optimized version 2 neoantigen cassette that increases T cell response to KRAS mutations in pre-clinical models

GRTS: Sequential Data Readouts Over Next 18 Months

Anticipated Milestones

	2H20	1H21	2H21	1H22
GRANITE Phase 1 Dose Level 4 Data	◯			
Bispecific Antibody DC Nomination	◯			
SLATE Phase 2 $TP53^{mut}$ & $KRAS^{mut}$ Cassette 1 Data		◯		
GRANITE Phase 2 MSS-CRC Data			◯	
GRANITE Phase 2 Gastric Cancer Data			◯	
SLATE Phase 2 Post-IO NSCLC Cassette 2 Data			◯	

Acknowledgements

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

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Thank You

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