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Preliminary Phase 2 Randomized Data Evaluating GRANITE, a Neoantigen-Directed Personalized Cancer Vaccine, in Patients with Front-line Metastatic MSS-CRC

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Gritstone bio, Inc.

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OVERVIEW: Phase 2 Preliminary Results

Multiple positive signals support driving GRANITE forward toward Phase 3; PFS is viable primary endpoint



Overview

COLORECTAL CANCER OVERVIEW

GRANITE: A PERSONALIZED NEOANTIGEN-DIRECTED IMMUNOTHERAPY

PHASE 1/2 GRANITE DATA IN REFRACTORY COLORECTAL CANCER (CRC)

PHASE 2/3 STUDY DESIGN IN FRONT-LINE METASTATIC MSS-CRC (GO-010)

PATIENT DISPOSITION, BASELINE DEMOGRAPHICS AND DISEASE CHARACTERISTICS

PHASE 2 EFFICACY, BIOMARKER, AND SAFETY DATA TO DATE

NEXT STEPS



GRANITE Aims to Address Lack of Immune Reactivity in Solid Tumors with High Unmet Need

First Indication = MSS-CRC

NC leading cause of cancer-related deaths¹

~153,000+ diagnoses expected in US in 2023¹ ~53,000+ deaths expected in US in 2023¹







Immunotherapy with anti-PD-L1 mAb Does Not Improve Patient Outcomes when Added to 1L Chemotherapy in MSS-CRC

MODUL study: atezolizumab as 1st line maintenance with fluoropyrimidine + bevacizumab after FOLFOX+bev induction chemotherapy



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Gritstone's Approach: Induce CD8+ T cells Against "Cold" Solid Tumors

Antigen selection + prime-boost regimen may be effective in tumors unresponsive to anti-PD(L)-1 therapy



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ctDNA: A Powerful and Versatile Tool in Oncology Drug Development

Circulating tumor DNA (ctDNA) assessment has broad clinical utility across cancer types

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GRANITE: Phase 1/2 Data Showed GRANITE Delivered Against its Original Therapeutic Hypothesis

Vaccine-induced neoantigen-specific cytotoxic T cells kill tumor cells and appeared to prolong OS



GRANITE Generates Neoantigen-Specific T Cells in the Majority of Patients

Results from Phase 1/2 study in late-line solid tumors



Peak Response Post-GRANITE¹

gritstone G5, G19, G23, G26: no samples available; CD8+ T cells as measured by ex vivo ELISpot represent peak responses post-GRANITE treatment

GRANITE Extended Survival in Molecular Responders

Results from Phase 1/2 study in late-line solid tumors; median OS among molecular responders > 22 months



13 MSS-CRC patients treated; 3 patients were not available for analysis of ctDNA changes; 6 of 10 were molecular responders; Molecular responders defined as patients with \geq 30% reduction in ctDNA





Preliminary Efficacy and Safety Data Phase 2 Study of GRANITE in Front-line Treatment of Metastatic MSS-CRC

GRANITE: Registrational Phase 2/3 Study in Front-line MSS-CRC





GRANITE: Registrational Phase 2/3 Study in Front-line MSS-CRC



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69% of GRANITE Recipients Remain on Study vs 50% of Controls



GO-010 Phase 2 Demographics: Vaccine and Control Arms are Well Balanced

Demographics	Statistics	GRANITE ARM (N=51) N (%)	CONTROL ARM (N=53) N (%)
Age at screening (years)	Mean (SD)	58.1 (11.73)	59.7 (11.66)
<65		35 (68.6)	35 (66.0)
>=65 to <75		10 (19.6)	14 (26.4)
>=75 to <85		6 (11.8)	4 (7.5)
Sex at birth			
Male		32 (62.7)	29 (54.7)
Female		19 (37.3)	24 (45.3)
Ethnicity			
Hispanic or Latino		6 (11.8)	6 (11.3)
Not Hispanic or Latino		41 (80.4)	43 (81.1)
Baseline ECOG PS			
0		30 (58.8)	34 (64.2)
1		21 (41.2)	18 (34.0)

GO-010 Phase 2 Colorectal Cancer Characteristics: Patients are Well Balanced for Multiple Prognostic Features (1 of 2)

Characteristics	Statistics	GRANITE ARM (N=51) N (%)	CONTROL ARM (N=53) N (%)
Sidedness			
Right-side		21 (41.2)	20 (37.7)
Left-side		30 (58.8)	33 (62.3)
KRAS status			
Wild Type		23 (45.1)	31 (58.5)
Mutant		26 (51.0)	20 (37.7)
Time to 1st study treatment from	metastatic disease d	liagnosis date (months)	
	n	39	28
	Mean (SD)	7.6 (3.1)	8.0 (3.4)
Stage at Study Entry			
Stage IVA (1 site of metastasis)		24 (47.1)	24 (45.3)
Stage IVB (2 sites of metastasis	3)	15 (29.4)	15 (28.3)
Stage IVC (peritoneal metastas	is)	12 (23.5)	12 (22.6)

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GO-010 Phase 2 Colorectal Cancer Characteristics: Patients are Well Balanced for Multiple Prognostic Features (2 of 2)

		GRANITE ARM (N=51)	CONTROL ARM (N=53)
Characteristics	Statistics	N (%)	N (%)
Presence of Liver Disease			
Yes		40 (78.4)	39 (73.6)
No		11 (21.6)	14 (26.4)
Number of Metastatic Sites			
1		26 (51.0)	24 (45.3)
2		17 (33.3)	22 (41.5)
≥ 3		7 (14)	7 (14)
Time on Oxaliplatin (weeks)			
	Mean (SD)	22.3 (8.21)	24.9 (11.06)
	Median (Q1, Q3)	22 (17, 25)	24 (18.3, 28.1)
1 st Line Chemotherapy Type			
Doublet		39 (76.5)	38 (71.7)
Triplet		10 (19.6)	10 (18.9)
Tumor Mutation Burden (mutatio	ns/MB)		
	Mean (SD)	2.9 (1.64)	4.2 (5.97)
	Median (Q1, Q3)	2.7 (1.90, 3.30)	3.2 (2.55, 3.95)

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GO-010 Phase 2 Colorectal Cancer Characteristics: Patients who Received Study Treatment are Well Balanced for Multiple Prognostic Features

Characteristics	Statistics	GRANITE ARM (N=39) N (%)	CONTROL ARM (N=28) N (%)
Sidedness			·
Right-side		14 (35.9)	13 (46.4)
Left-side		25 (64.1)	15 (53.6)
KRAS Status			
Wild Type		18 (46.2)	15 (53.6)
Mutant		19 (48.7)	12 (42.9)
Missing		2 (5.1)	1 (3.6)
Presence of Liver Disease			
Yes		32 (82.1)	20 (71.4)
No		7 (17.9)	8 (28.6)
Stage at Study Entry			
Stage IVA (1 site of metastasis)		19 (48.7)	13 (46.4)
Stage IVB (2 sites of metastasis)		11 (28.2)	8 (28.6)
Stage IVC (peritoneal metastasis)		9 (23.1)	7 (25.0)



GO-010 Phase 2: Gritstone Successfully Manufactured Vaccine for All Patients



100% Vaccine Manufacturing Success

Gritstone completed manufacturing for 100% of patients who advanced to study treatment stage (GRANITE Arm)







Median PFS in 1st line Metastatic CRC is ~10mo



Median follow up for PFS in this study is ~6 months, well short of the expected median PFS

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Early PFS Trend in All Patients Favors GRANITE Recipients



Progression Free Survival in All Patients Who Received Study Treatment

gritstone *#* calculated using piecewise Cox-PH model for the following periods: 0 <= t <=6 months and t > 6 months post-randomization

Baseline ctDNA is Prognostic and Enables Identification of High-Risk Group (mean VAF>2%^{1,2}) in Which Progression Events Occur Faster

Progression Free Survival in All Patients (independent of therapy) who Received Study Treatment and Have Baseline ctDNA Data From Time of Randomization



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calculated using Piecewise Cox- PH model for the following periods: 0 <= t <= 6 month and t > 6 months post-randomization 1. Yi et al. Signal Transduction and Targeted Therapy 2021; 2. Reichert et al. Annals of Oncology 2023; VAF = variant allele frequency

Data cut: 08 Mar 2024

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The 2% VAF Threshold Evenly Separates Trial Patients into High and Low Groups



VAF at time of randomization

	GRANITE	Control
ctDNA High (25)	16	9
ctDNA Low (19)	10	9

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1. Yi et al. Signal Transduction and Targeted Therapy 2021; 2. Reichert et al. Annals of Oncology 2023; VAF = variant allele frequency

Data cut: 12 Mar 2024

GO-010 Phase 2: Patients in ctDNA High Group are Well Balanced for Multiple Prognostic Features

Demographics/Characteristics	Statistics	GRANITE ARM (N=16) N (%)	CONTROL ARM (N=9) N (%)
Age at screening (years)	Mean (SD)	55.8 (11.55)	56.1 (10.26)
Baseline ECOG PS			
0		10 (62.5)	6 (66.7)
1		6 (37.5)	3 (33.3)
Sidedness			
Right-side		4 (25.0)	3 (33.3)
Left-side		12 (75.0)	6 (66.7)
1 st Line Chemotherapy Type			
Doublet		13 (81)	8 (89)
Triplet		3 (19)	1 (11)
KRAS Status			
Wild Type		9 (56.3)	4 (44.4)
Mutant		7 (43.8)	4 (44.4)
Presence of Liver Disease			
Yes		14 (87.5)	9 (100)
No		2 (12.5)	0

gritstone The number of patients may not equal the total due to missing data

GRANITE Extends PFS in High-Risk Group^{*} With Median PFS 12 vs 7mo and Hazard Ratio[#]=0.52



* High-risk group is ctDNA evaluable patients (ctDNA samples before and after study treatment) with mean VAF >2% at time of randomization; All pts had liver mets except 2 in vaccine arm (1 of which had PD)

gritstone # HR calculated using Piecewise Cox- PH model for the following periods: 0 <= t <= 6 month and t > 6 months post-randomization Note: Patients without baseline ctDNA data at study enrollment are excluded

Data cut: 08 Mar 2024

Very Few Events in Low-Risk Group* - PFS Not Currently Evaluable



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*Low risk group ctDNA evaluable patients (ctDNA samples before and after study treatment) with mean VAF $\leq 2\%$ at time of randomization Note: Patients with no baseline ctDNA data at study enrollment are excluded

Published Data from Moderna Show Emergence of Neoantigen Vaccine Benefit Quickly in ctDNA^{hi} Patients and More Slowly in ctDNA^{lo} Patients

Moderna's personalized cancer vaccine studied in high-risk resected melanoma patients



RFS in patients with high-risk melanoma by baseline ctDNA status

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CONSORT Diagram for ctDNA Evaluable Patients



¹ctDNA evaluable analysis set = patients who received at least 1 study treatment and have mean VAF data from study treatment start (STS) and at least one post-STS datapoint ² ctDNA > 0.001% (limit of blank of the assay) is positive; ctDNA <= 0.001% is negative

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Molecular Response Rate, Defined Per Protocol, Similar in Both Arms

ctDNA Positive Patients at Study Treatment Start (STS)			
	Vaccine Arm	Control Arm	
Number of patients	20	12	
Median STS ctDNA: VAF (Q1, Q3)	0.5 (0.3, 1.9)	2.1 (0.5, 8.7)	
Patients with molecular response ¹ , n	6	5	
Molecular response rate (%)	30.0	41.7	
Patients with any reduction in ctDNA 9 7			



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Some Control Patients Exhibit Unexpectedly Persistent ctDNA Drop Beyond Induction Chemotherapy, Confounding Molecular Response Analysis

Longitudinal ctDNA measured by mean VAF in all control patients that are ctDNA positive at STS



MR = molecular response (>30% reduction in mean VAF from study treatment start); VAF = variant allele frequency



Several Patterns of ctDNA Response Over Time Observed with GRANITE

Longitudinal ctDNA measured by mean VAF in GRANITE patients that are ctDNA positive at STS



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Majority of GRANITE Recipients With High Baseline ctDNA Have Seen Levels Drop and Remain Progression Free, Unlike Controls

VAF threshold of 2% at baseline; change in VAF from baseline to last timepoint (schema below)

Baseline	ctDNA <u><</u> 2% at Last Timepoint		Patients with PD		
(at time of randomization) ¹	GRANITE	Control	GRANITE	Control	
High ctDNA	9 / 16 (56%)	2 / 9 (22%)	7 / 16 (44%)	7 / 9 (78%)	
Low ctDNA	9 / 10 (90%)	8 / 9 (89%)	2 / 10 (20%) ²	2 / 9 (22%) ³	
1:1 Randomization		STUDY TREATMEN	Last Tin (Last availabl	nepoint e timepoint)	

Clinical data cut: 08 Mar 2024 ctDNA data cut: 12 Mar 2024

gritstone ¹Baseline ctDNA taken at time of randomization; ²one of the two GRANITE patients with low ctDNA at baseline had clinical progression that was not confirmed radiologically; ³one of the two Control patients with low ctDNA at baseline had clinical progression that was not confirmed radiologically.

Long-term ctDNA Trends Correspond with PFS and Favor GRANITE



Sustained ctDNA Negativity in 67% of GRANITE Treated Patients (1/9 with PD) Compared to 38% of Control Patients (3/8 with PD)

ctDNA over time in ctDNA negative patients at study treatment start

GRANITE ARM





CONTROL ARM



G10-0008 surgery prior to study treatment start G10-0003 surgery ~12-16 wks after study treatment start G10-0033 surgery ~8-12 wks after study treatment start

GRANITE Exhibits Favorable Tolerability Profile

GRANITE ARM CONTROL ARM Fatigue Pyrexia Diarrhoea Peripheral sensory neuropathy Palmar-plantar erythrody saesthesia syndrome Nausea Vomiting Decreased appetite Stom atitis Chills Headache My algia Pain in extremity Influenza like illness Urinary tract infection COVID-19 Backpain Cough Hypertension Constipation Rash pustular Blood alkaline phosphatase increased Oedema peripheral Dry mouth Injection site pain Aspartate aminotransferase increased Dry skin Epistaxis Pruritus Abdom inal pain 50 40 30 20 10 10 20 30 40 50 n Percentage Grade 1-2 (Vaccine Arm) Grade 1-2 (Control Arm) Grade 3-4 (Vaccine Arm) Grade 3-4 (Control Arm)

Treatment-Emergent Adverse Events

- No pts discontinued study treatment due to an AE
- One treatment-related SAEfatigue (upon recovery, pt continued vaccinations without recurrence)
- Common adverse events are the mild systemic and local effects associated with any potent vaccine, i.e. transient flu-like illness

gritstone Treatment-emergent adverse events captured from initiation of study treatment

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Preliminary Conclusions

EARLY PFS TRENDS FAVOR GRANITE

- Overall progression free survival (PFS) data demonstrate trend of extended PFS in GRANITE recipients; data immature (62% censoring)
 - 69% of GRANITE recipients remain on treatment vs 50% of controls
 - Arms begin separating 1-2 months after initiation of GRANITE, consistent with expected kinetics
- ctDNA assessment at time of randomization allows for population separation into high- and low-risk groups (>2% and \leq 2% variant allele frequency respectively) and progression events are frequent/early in the high-risk group
- In high-risk patients, PFS prolongation is seen in GRANITE recipients (median PFS 12 vs 7 mo; HR=0.52)

LONG-TERM CTDNA TRENDS ASSOCIATE WITH PFS, FAVOR GRANITE

- Longer-term ctDNA responses align with PFS trends and favor GRANITE vs. control patients
 - High-risk group: ctDNA shifted from high (>2% VAF) to low (<2% VAF) in 56% (9/16) GRANITE patients vs 22% (2/9) control patients; PD observed in 44% (7/16) vs 78% (7/9), respectively
 - Low risk group (ctDNA negative): Sustained ctDNA negativity was observed in 67% (6/9) GRANITE recipients vs 38% (3/8) control patients. PD observed in 11% (1/9) and 38% (3/8) of these patients, respectively
- Short-term molecular response as defined by protocol (\geq 30% decrease in ctDNA) is uninformative;
 - ctDNA response as defined (≥30% reduction at any one time point in this setting) approximately equal in both arms:
 30% (6/20) in vaccine arm; 42% (5/12) in control arm

FOLLOW UP

- Mature PFS data in total population expected in 3Q24
- Mature OS data in total population expected 1H25

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Colorectal Cancer Patient Funnel



Sources: SEER, Global Data, and Gritstone estimates



1 Estimate of 37k includes roughly 9k patients recurring from Stage I-II, 13k from Stage III resectable, and 15k from Stage III unresectable 2 65% is Gritstone's current, conservative cutoff for eligibility based on patients' mutational burden

3 Estimate of 58k includes roughly 14k patients recurring from Stage I-II, 20k from Stage III resectable, and 24k from Stage III unresectable

Competitive Landscape: Gritstone is Taking a "Leapfrog" Approach

Unlike Moderna and BioNTech, we have selected a cold tumor for randomized POC based on prior signals

	gritstone '	BIONTECH	moderna
POC Tumor Type	MSS-CRC (1L) Cold	Melanoma (1L) <i>Hot</i>	Melanoma (Adj) <i>Hot</i>
Neoantigen Prediction	Proprietary	Proprietary	Proprietary
Regimen/Vector	ChAd prime + samRNA boosts (heterologous, intramuscular)	mRNA ² prime + boosts (homologous, intravenous)	mRNA ² prime + boosts (homologous, intramuscular)
CD8+ T cell Priming ³	♣ ♣ ⁴	+	+
Data	 ✓ Prelim randomized Phase 2 data (a Phase 2/3 study) 	Randomized Phase 2 data expected in 2024	 ✓ Recurrence-free survival benefit (HR=0.56)

¹GRTS vaccine candidates have not been studied head-to-head with those listed. ²BioNtech uses optimized Uridine mRNA. Moderna uses Modified Uridine mRNA.

³Semi-quantitative assessment of strength and breadth of human T cell immune response to neoantigen vaccine based on cross-study comparisons of published data

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⁴CD8 T cell priming: Miao et al., Molecular Cancer 20, 41 (2021)

Potential Phase 2/3 Success in MSS-CRC Unlocks Greenfield GRANITE Opportunity Spanning Solid Tumor Spectrum



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GRANITE Next Steps

CONTINUE TO COLLECT PHASE 2 DATA

PFS data to maturity (3Q24)
 Add'l ctDNA data (3Q24)
 OS data (Expected 1H25)

DISCUSS PHASE 3 ENDPOINT WITH FDA (& OTHER REGULATORS) ONCE PFS DATA MATURE

LAUNCH (GLOBAL) PHASE 3 PIVOTAL TRIAL IN 1L MSS-CRC IN 2025

CONTINUE TO REFINE BIOMANUFACTURING PROCESS FOR SCALE AND EFFICIENCY

DISCUSS GRANITE PROGRAM EXPANSION WITH PROSPECTIVE PARTNERS



THANK YOU