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): **June 6, 2024**

REPLIMUNE GROUP, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-38596**	**82-2082553**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification Number)

500 Unicorn Park Drive
Suite 303
Woburn, MA 01801
(Address of principal executive offices, including Zip Code)

Registrant's telephone number, including area code: **(781) 222-9600**

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 $0.001 per share	REPL	The Nasdaq Stock Market LLC (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 7.01 Regulation FD Disclosure.

On June 6, 2024, Replimune Group, Inc. (the "Company") issued a news release announcing data updates from certain of its RP1 and RP2 programs, and made available a new presentation with respect to such updates. A copy of the press release and the presentation are furnished as Exhibits 99.1 and 99.2 to this Current Report on Form 8-K, respectively and will be available on the Company's website at www.replimune.com under "Investors and Media." The Company undertakes no obligation to update, supplement or amend the materials furnished herewith.

The information contained in this Item 7.01 and in the accompanying Exhibits 99.1 and 99.2 shall not be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing, unless expressly incorporated by specific reference to such filing. The information in this Item 7.01 and the accompanying Exhibits 99.1 and 99.2 shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended.

Item 8.01 Other Events.

On June 6, 2024, the Company announced the topline results from the primary analysis of its IGNYTE clinical trial of RP1 plus nivolumab in anti-PD1 failed melanoma. The results by independent central review show one-third of patients receiving RP1 plus nivolumab responded to treatment, improving upon the investigator-assessed data presented at ASCO 2024, with all responses lasting greater than 6 months from baseline.

The anti-PD1 failed melanoma cohort from the IGNYTE clinical trial includes 140 patients who received RP1 plus nivolumab after confirmed progression while being treated with at least 8 weeks of prior anti-PD1 therapy (+/- anti-CTLA-4). The primary analysis by independent central review was triggered once all patients had been followed for at least 12 months.

The topline results show the overall response rate was 33.6% by modified RECIST 1.1 criteria, the primary endpoint as defined in the protocol, and 32.9% by RECIST 1.1 criteria, an additional analysis requested by the United States Federal Drug Agency (the "FDA"). Responses from baseline were highly durable, with all responses lasting more than 6 months and median duration of response exceeding 35 months. The Company plans to submit the full primary analysis data from the anti-PD1 failed melanoma cohort including key secondary endpoint data and subgroups for presentation at an upcoming medical congress.

RP1 combined with nivolumab continues to be well-tolerated, with mainly Grade 1-2 constitutional-type side effects observed. Treatment-related adverse events associated with RP1 in combination with nivolumab were predominantly Grade 1-2 constitutional type events (> 5% of patients), including fatigue, chills, pyrexia, nausea, influenza-like illness, injection-site pain, diarrhea, vomiting, headache, pruritis, asthenia, arthralgia, myalgia, decreased appetite, and rash, with a low incidence of Grade 3-5 events. Grade 4 events were one each of lipase increased, alanine aminotransferase increased, blood bilirubin increased, cytokine release syndrome, myocarditis, hepatic cytosis and splenic rupture. There were no Grade 5 events.

Item 9.01 Financial Statements and Exhibits.

Exhibit No.	Description
99.1	News Release dated June 6, 2024
99.2	Company Presentation dated June 6, 2024
104	Cover page interactive data file (formatted as Inline XBRL)

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.

REPLIMUNE GROUP, INC.

Date: June 6, 2024

By: /s/ Sushil Patel
Sushil Patel
Chief Executive Officer

Exhibit 99.1

Replimune Announces Positive Topline Primary Analysis Data by Independent Central Review from IGNYTE Clinical Trial of RP1 plus Nivolumab in Anti-PD1 Failed Melanoma

Primary endpoint data shows 12-month overall response rate (ORR) of 33.6%

Biologics license application (BLA) submission intended for 2H 2024; first patient expected to be enrolled in IGNYTE-3 confirmatory trial in Q3 2024

Company to host conference call and webcast today at 8:00 a.m. ET

Woburn, MA, June 6, 2024 – Replimune Group, Inc. (Nasdaq: REPL), a clinical stage biotechnology company pioneering the development of a novel class of oncolytic immunotherapies, today announced the topline results from the primary analysis of the IGNYTE clinical trial of RP1 plus nivolumab in anti-PD1 failed melanoma. The results by independent central review show one-third of patients receiving RP1 plus nivolumab responded to treatment, improving upon the investigator-assessed data presented at ASCO 2024, with all responses lasting greater than 6 months from baseline.

"The overall strength of the IGNYTE data and safety profile further highlights the potential of RP1 in a difficult treatment setting with limited options for patients," said Sushil Patel, Ph.D., CEO of Replimune. "Based on these compelling results and recent FDA interactions, we are increasingly confident in our path forward. We have shared the results with the agency and plan to request a pre-BLA meeting, in advance of our intended BLA submission. With these data in hand, we are preparing for a commercial launch next year."

The anti-PD1 failed melanoma cohort from the IGNYTE clinical trial includes 140 patients who received RP1 plus nivolumab after confirmed progression while being treated with at least 8 weeks of prior anti-PD1 therapy (+/- anti-CTLA-4). The primary analysis by independent central review was triggered once all patients had been followed for at least 12 months.

The topline results show the overall response rate was 33.6% by modified RECIST 1.1 criteria, the primary endpoint as defined in the protocol, and 32.9% by RECIST 1.1 criteria, an additional analysis requested by the FDA. Responses from baseline were highly durable, with all responses lasting more than 6 months and median duration of response exceeding 35 months. The Company plans to submit the full primary analysis data from the anti-PD1 failed melanoma cohort including key secondary endpoint data and subgroups for presentation at an upcoming medical congress.

RP1 combined with nivolumab continues to be well-tolerated, with mainly Grade 1-2 constitutional-type side effects, observed. Treatment-related adverse events associated with RP1 in combination with nivolumab were predominantly Grade 1-2 constitutional type events (> 5% of patients), including fatigue, chills, pyrexia, nausea, influenza-like illness, injection-site pain, diarrhea, vomiting, headache, pruritis, asthenia, arthralgia, myalgia, decreased appetite, and rash, with a low incidence of Grade 3-5 events. Grade 4 events were one each of lipase increased, alanine aminotransferase increased, blood bilirubin increased, cytokine release syndrome, myocarditis, hepatic cytosis and splenic rupture. There were no Grade 5 events.

Conference Call Details

Replimune will host a conference call and webcast today at 8:00 a.m. ET. Listeners can register for the conference call via this link. Analysts wishing to participate in the question-and-answer session should use this link. The webcast and slides of the presentation can be accessed in the Investors section of the Company's website at www.replimune.com. A replay of the webcast will be available on the Company's investor website approximately two hours after the call's conclusion. Those who plan on participating are advised to join 15 minutes prior to the start time.

About RP1

RP1 is Replimune's lead product candidate and is based on a proprietary strain of herpes simplex virus engineered and genetically armed with a fusogenic protein (GALV-GP R-) and GM-CSF intended to maximize tumor killing potency, the immunogenicity of tumor cell death, and the activation of a systemic anti-tumor immune response.

About Replimune

Replimune Group, Inc., headquartered in Woburn, MA, was founded in 2015 with the mission to transform cancer treatment by pioneering the development of a novel portfolio of oncolytic immunotherapies. Replimune's proprietary RPx platform is based on a potent HSV-1 backbone intended to maximize immunogenic cell death and the induction of a systemic anti-tumor immune response. The RPx platform is designed to have a unique dual local and systemic activity consisting of direct selective virus-mediated killing of the tumor resulting in the release of tumor derived antigens and altering of the tumor microenvironment to ignite a strong and durable systemic response. The RPx product candidates are expected to be synergistic with most established and experimental cancer treatment modalities, leading to the versatility to be developed alone or combined with a variety of other treatment options. For more information, please visit www.replimune.com.

Forward Looking Statements

This press release contains forward looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding our expectations about our cash runway, the design and advancement of our clinical trials, the timing and sufficiency of our clinical trial outcomes to support potential approval of any of our product candidates, our goals to develop and commercialize our product candidates, patient enrollments in our existing and planned clinical trials and the timing thereof, and other statements identified by words such as "could," "expects," "intends," "may," "plans," "potential," "should," "will," "would," or similar expressions and the negatives of those terms. Forward-looking statements are not promises or guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in such forward-looking statements. These factors include risks related to our limited operating history, our ability to generate positive clinical trial results for our product candidates, the costs and timing of operating our in-house manufacturing facility, the timing and scope of regulatory approvals, the availability of combination therapies needed to conduct our clinical trials, changes in laws and regulations to which we are subject, competitive pressures, our ability to identify additional product candidates, political and global macro factors including the impact of the coronavirus as a global pandemic and related public health issues and the Russian-Ukrainian and Israel-Hamas political and military conflicts, and other risks as may be detailed from time to time in our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q and other reports we file with the Securities and Exchange Commission. Our actual results could differ materially from the results described in or implied by such forward-looking statements. Forward-looking statements speak only as of the date hereof, and, except as required by law, we undertake no obligation to update or revise these forward-looking statements.

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Primary Analysis of the IGNYTE Registrational Cohort in Anti-PD1 Failed Melanoma

June 6, 2024

Safe Harbor

Replimu

Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements within t meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amend including statements regarding the advancement, timing and sufficiency of our clinical trials, patient enrollments in our existing a planned clinical trials and the timing thereof, the results of our clinical trials, the timing and release of our clinical data, stateme regarding our expectations about our cash runway, our goals to develop and commercialize our product candidates, our expectatic regarding the size of the patient populations for our product candidates if approved for commercial use and other statements identif by words such as "could," "expects," "intends," "may," "plans," "potential," "should," "will," "would," or similar expressions and t negatives of those terms. Forward-looking statements are not promises or guarantees of future performance, and are subject t variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially fr those contemplated in such forward-looking statements. These factors include risks related to our limited operating history, our abi to generate positive clinical trial results for our product candidates, the costs and timing of operating our in-house manufactur facility, the timing and scope of regulatory approvals, changes in laws and regulations to which we are subject, competitive pressur our ability to identify additional product candidates, political and global macro factors including the impact of global pandemics a related public health issues, the ongoing military conflicts between Russia-Ukraine and Israel-Hamas and the impact on the glo economy and related governmental imposed sanctions, and other risks as may be detailed from time to time in our Annual Reports Form 10-K, Quarterly Reports on Form 10-Q, and other reports we file with the Securities and Exchange Commission. Our actual resu could differ materially from the results described in or implied by such forward-looking statements. Forward-looking statements spe only as of the date hereof, and, except as required by law, we undertake no obligation to update or revise these forward-look statements.

Today's Speakers/Q&A Panel

SUSHIL PATEL
CEO
Replimune

KOSTAS XYNOS
Chief Medical Officer
Replimune

ROBERT COFFIN
Founder and Chief Scientist
Replimune

MICHAEL WONG
Professor
Melanoma Medical Oncology, University of Texas MD Anderson Cancer Center

CAROLINE ROBERT
Professor
Head of Dermatology Unit, Institute Gustave Roussy and Co-Director Melanoma Research Unit INSERM, Paris-Sud University.

Today's Agenda

- Data Summary
- ASCO 2024 Recap: IGNYTE 12-month Investigator-assessed Data
- Topline IGNYTE Primary Analysis by Independent Central Review
- Progress to BLA
- Q&A

Data Summary

- Strong primary analysis data: ORR of 33.6% (mRECIST 1.1) and 32.9% (RECIST 1.1) by independent central review
  - Improvement versus investigator-assessed ORR of 32.1% (mRECIST 1.1)
- Median DOR >35 months; 100% of responses last >6 months (from baseline)
  - DOR by independent central review consistent with investigator assessment
- Phase 3 confirmatory study (IGNYTE-3) with first patient expected to be enrolled in Q3 2024; BLA submission planned for 2H 2024

*N=140

ASCO Recap: Anti-PD1 Failed Melanoma Patients from the IGNYTE Clinical Trial

Options are Limited in Melanoma Following Progression on Anti-PD1 Therapy

- Further single agent anti-PD1 for patients having confirmed PD on prior anti-PD1 gives a response rate of 6-7%[1,2]
- Nivolumab + ipilimumab is a potential option[3,] but toxicity is high[4-5]
- Anti-LAG3 plus anti–PD1 has not demonstrated meaningful efficacy in the anti–PD1 failed setting[6]
- For BRAF mutant tumors, BRAF-targeted therapy responses are generally transient[7]
- T-VEC + pembrolizumab has limited activity outside of the adjuvant setting, with no responses seen in patients with visceral disease[8-9]
- TIL therapy for select patients gives response rates of ~30%, but comes with toxicity (nearly all patients have grade 4 toxicity)[10]

CTLA-4, cytotoxic T-lymphocyte antigen 4; LAG3, lymphocyte-activation gene 3; PD-1, programmed cell death protein 1; TIL, tumor infiltrating lymphocyte

1. Mooradian MJ, et al. Oncology. 2019;33(4):141-8. 2. Beaver JA, et al. Lancet Oncol. 2018;19(2):229-39. 3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Melanoma: Cutaneous. Version 2.2024. 4. Pires da Silva I, et al. Lancet Oncol. 2021;22(6):83
VanderWalde AM, et al. Presented at the American Association of Cancer Research Annual Meeting 2022. New Orleans. 6. Ascierto PA, et al. J Clin Oncol. 2023;41(15)2724-35. 7. Dixon-Douglas JR, et al. Curr Oncol Rep. 2022;24(8):1071-9. 8. Gastman B, et al. J Clin Oncol. 2022;40(16_suppl):9518. 9. Hu-Lieskov
al. Cancer Res. 2023;83(7_suppl):3275. 10. US Food and Drug Administration. BLA clinical review and evaluation - AMTAGVI. BLA 125773. Updated February 6, 2024. Accessed May 31, 2024].https://www.fda.gov/media/176951/download.

IGNYTE Study Design
Anti-PD1 Failed Melanoma Cohort

Replimu

Anti–PD1 failed melanoma cohort

(140 pts; 16 pts treated in prior cohorts: Total=156)

Primary objectives
- Safety and tolerability
- Efficacy as assessed by ORR using modified RECIST 1.1 criteria

Secondary objective
DOR, CR rate, DCR, PFS, by central & investigator review, ORR by investigator review, and 1-year and 2-year OS

Key eligibility criteria

Confirmed progression while on prior anti-PD1 therapy[c]

At least 8 weeks of prior anti–PD1, confirmed progression while on anti–PD1; anti–PD1 must be the last therapy before clinical trial. Patients on prior adjuvant therapy must have progressed while on prior adjuvant treatment.

Primary analysis to be conducted when all patients have ≥ 12 months follow up

[a]Dosing with nivolumab begins at dose 2 of RP1 (C2D15). [b]Option to reinitiate RP1 for 8 cycles if criteria are met. c. Non-neurological solid tumors CR, complete response; CT, computed tomography; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; LD, longest diameter; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PFS, progression-free survival; pfu, plaque-forming unit; Q4W, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

Baseline Clinical Characteristics

A 'real world' anti-PD1 failed melanoma population was enrolled

- Good representation of each of the sub-groups of patients who progress on prior anti-PD1 therapy

Patients, n (%)	All patients (N = 156)
Age (median [range])	62 (21-91)
Sex	
Female	52 (33.3)
Male	104 (66.7)
Stage	
IIIb/IIIc/IVM1a	75 (48.1)
IVM1b/c/d	81 (51.9)
Prior therapy	
Anti–PD1 only as adjuvant therapy	39 (25.0)
Anti–PD1 not as adjuvant therapy	117 (75.0)
Anti–PD1 & anti–CTLA-4	74 (47.4)
Received BRAF-directed therapy	17 (10.9)

Patients, n (%)	All patients (N = 156)
Other disease characteristics	
Primary resistance to prior anti–PD1[a]	105 (67.3)
Secondary resistance to prior anti–PD1[b,c]	51 (32.7)
BRAF wt	103 (66.0)
BRAF mutant	53 (34.0)
LDH ≤ULN	105 (67.3)
LDH >ULN	50 (32.1)
LDH unknown	1 (0.6)

Median follow up is 15.4 months (range 0.5-55.5)

Data cutoff: March 8th 2024. [a]Primary resistance: Progressed within 6 months of starting the immediate prior course of anti–PD-1 therapy; [b]Secondary resistance: Progressed after 6 months of treatment on the immediate prior course of anti-PD-1 therapy; [c]Includes 2 pt unknown resistance status. CTLA-4, cytotoxic T-lymphocyte antigen 4; LDH, lactate dehydrogenase; PD-1, programmed cell death protein 1; ULN, upper limit of normal; wt, wild-type.

Efficacy

Investigator assessed data with all patients having at least 12 months follow up

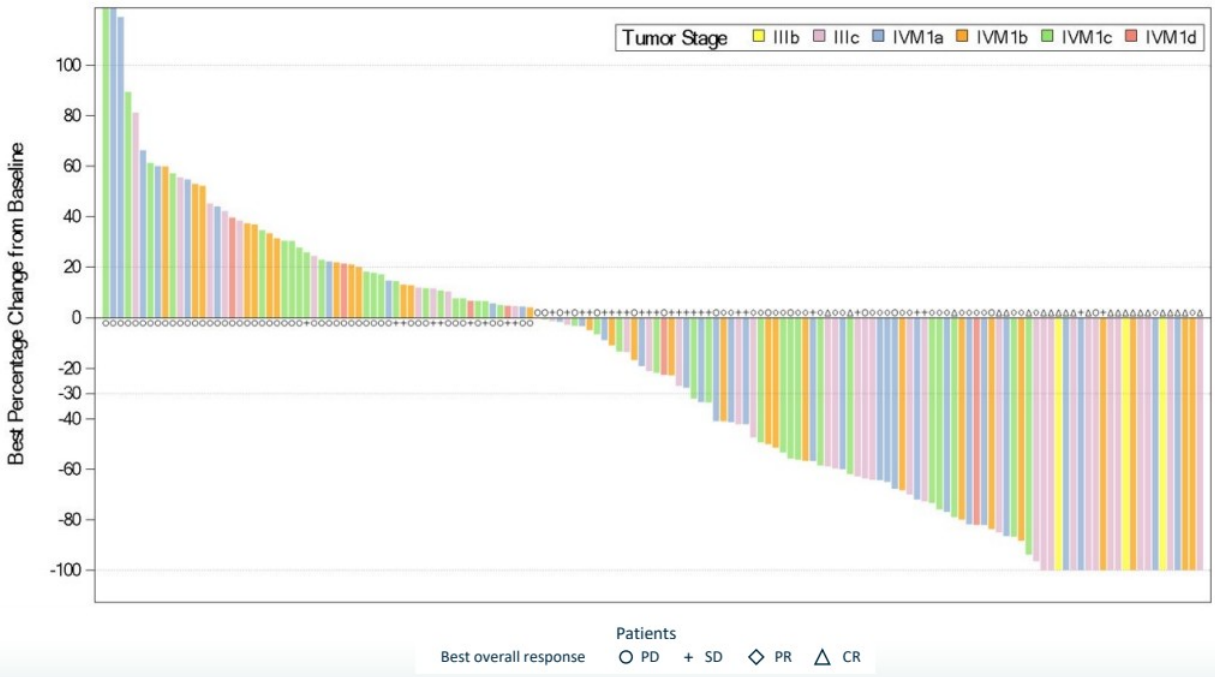
	All patients enrolled in IGNYTE						
BOR n (%)	All patients (n = 156)	Prior single-agent anti–PD1 (n = 82)	Prior anti–PD1/CTLA-4 (n = 74)[a]	Stage IIIb-IVM1a (n = 75)	Stage IVM1b-d (n = 81)	1° resistance to anti–PD1 (n = 105)	2° resistance to anti–PD1 (n = 51)[b]
CR	23 (14.7)	18 (22.0)	5 (6.8)	18 (24.0)	5 (6.2)	18 (17.1)	5 (9.8)
PR	28 (17.9)	13 (15.9)	15 (20.3)	13 (17.3)	15 (18.5)	18 (17.1)	10 (19.6)
SD	34 (21.8)	18 (22.0)	16 (21.6)	19 (25.3)	15 (18.5)	17 (16.2)	17 (33.3)
PD	63 (40.4)	31 (37.8)	32 (43.2)	24 (32.0)	39 (48.1)	47 (44.8)	16 (31.4)
ORR	**51 (32.7[c])**	**31 (37.8)**	**20 (27.0)**	**31 (41.3)**	**20 (24.7)**	**36 (34.3)**	**15 (29.4)**

[a]Eight patients were treated with sequential anti-CTLA-4 and anti-PD1 (ORR for prior combined anti-CTLA-4/anti-PD1 was 25.8%). [b]Includes one patient with unknown resistance status. [c]ORR for the 140-patient registration intended cohort was 32.1%

- 1 in 3 patients achieved an objective response (32.7%)
- Consistent ORR across subgroups, including:
  - 27% ORR in patients who had prior anti–PD1 & anti–CTLA-4
  - 34% ORR in patients who are primary resistant to their prior anti-PD1 therapy

Data cutoff: March 8th 2024. BOR, best overall response; CR, complete response; CTLA-4, cytotoxic T-lymphocyte antigen 4; PD-1, programmed cell death protein 1; PD, progressive disease; PR, partial response; ORR, objective response rate; SD, stable disease.

Depth of Response

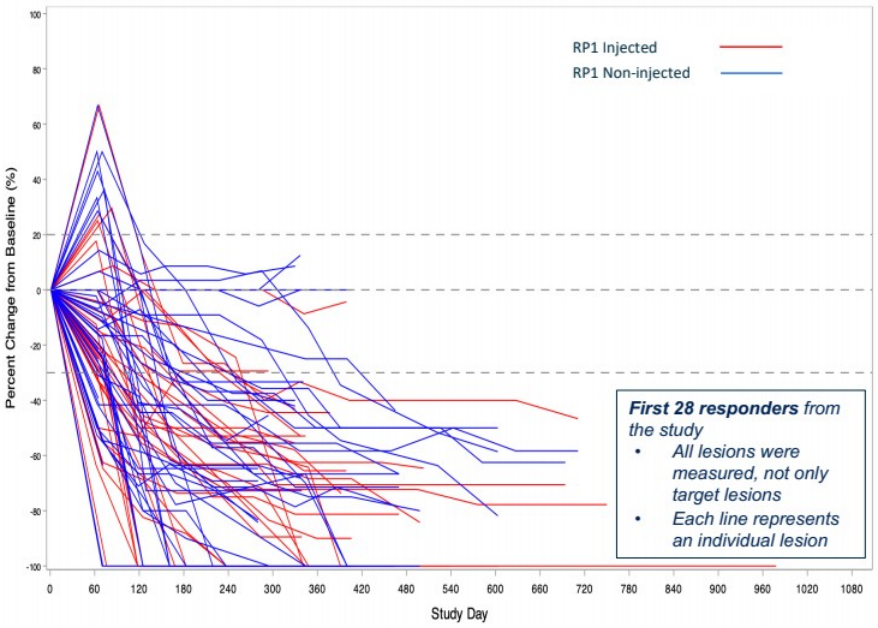


- Target lesions wer reduced in >50% o patients
- Responses were s across disease sta including CRs in patients with **stag IVM1b/c disease**

Data cutoff: March 8th 2024. The target lesion response is shown for patients with at least one post-baseline assessment. CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

Responses are Systemic

Change in size of individual injected and non-injected lesions

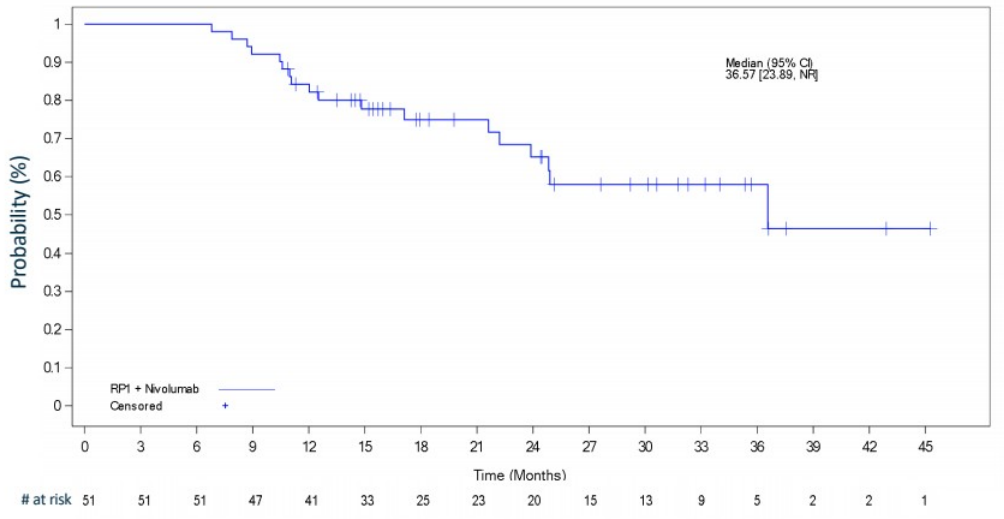


- 70.4% of responding patients had non-injected lesions
- Injected and non-injected lesions responded wi similar duration and kinetics
- Depth of response independent of injection stat

Responses in non-injected lesions demonstrate systemic benefit

Includes both target and non-target lesions for RECIST assessment, measured from CT/MRI scans for radiologically assessable lesions (responders from the first 75 patients enrolled into the registration intended cohort). 58/75 patients had at ≥ 1 non-injected lesion, of whom 15 achieved a response based on those lesions only (excludes possible response in injected lesions); ORR of 25.9% on the basis of non-injected lesions only. First presented at ASCO 2023.

Duration of Response
From baseline



>6 months	>12 months	>18 months	>24 months
100%	84.2%	74.9%	65.2%

The median follow up for responders is 27.9 months (range 10.5-55.5)

- Responses are durable, with **median DOR** of **36.6 months**

Data cutoff: March 8th 2024. Duration of response defined as time from baseline to end of response for responders. DOR, duration of response.

Safety: Treatment-related AEs (N = 156)

Preferred term, n (%)	TRAEs occurring in >5% of patients				
	Grade 1–2	Grade 3	Grade 4	Grade 5	Total (N = 156)
Chills	53 (34.0)	1 (0.7)	0	0	53 (34.0)
Fatigue	51 (32.7)	2 (1.3)	0	0	52 (33.3)
Pyrexia	49 (31.4)	0	0	0	49 (31.4)
Nausea	35 (22.4)	0	0	0	35 (22.4)
Influenza-like illness	30 (19.2)	0	0	0	30 (19.2)
Injection-site pain	23 (14.7)	0	0	0	23 (14.7)
Diarrhea	21 (13.5)	1 (0.6)	0	0	21 (13.5)
Vomiting	21 (13.5)	0	0	0	21 (13.5)
Headache	20 (12.8)	0	0	0	20 (12.8)
Pruritus	20 (12.8)	0	0	0	20 (12.8)
Asthenia	13 (8.3)	1 (0.6)	0	0	14 (9.0)
Arthralgia	11 (7.1)	1 (0.7)	0	0	11 (7.1)
Myalgia	11 (7.1)	0	0	0	11 (7.1)
Decreased appetite	9 (5.8)	1 (0.6)	0	0	10 (6.4)
Rash	9 (5.8)	1 (0.6)	0	0	10 (6.4)

RP1 combined with nivolumab continue
be a generally well tolerated regimen

- Predominantly grade 1 and 2 constitutional-type side effects
- Low incidence of grade 3 and 4 ev
- No grade 5 events

Additional grade 3 and 4 events <5%
Grade 3: Two each of rash maculo-papular and hypophysitis; 1 each of tumor p infusion-related reaction, muscular weakness, abdominal pain, amylase increas dermatitis bullous, eczema, immune-mediated enterocolitis, immune-mediated h paresthesia, acute left ventricular failure, arthritis, cancer pain, enterocolitis, extr marginal zone B-cell lymphoma (MALT type), hyponatremia, injection site necro ventricular dysfunction, memory impairment, meningitis aseptic, edema, palmar- erythrodysesthesia syndrome, peripheral sensory neuropathy, radiculitis brachia arrhythmia, tricuspid valve incompetence, and type 1 diabetes mellitus

Grade 4: One each of lipase increased, alanine aminotransferase increased, blo bilirubin increased, cytokine release syndrome, myocarditis, and hepatic cytolysi splenic rupture

Data cutoff: March 8th 2024. MALT, mucosa-associated lymphoid tissue; TRAE, treatment-related adverse event.

Conclusions

- RP1 combined with nivolumab in melanoma patients who had confirmed progression on prior anti-PD1 continues to show:
  - Deep and durable, systemic responses
  - A favorable safety profile, with generally 'on target' and transient grade 1–2 side effects indicative of systemic immune activation
- 1 in 3 patients experienced a response (ORR: 32.7%)
  - 27% ORR in patients had prior anti–PD1/anti–CTLA-4
  - 34% ORR in patients who had primary resistance to their immediate prior anti-PD1 therapy
  - Clinically meaningful activity was seen across all enrolled subgroups
  - 55% of patients experienced clinical benefit (CR + PR + SD)
- Responses were highly durable
  - All patients followed for at least 12 months
  - All responses lasted at least 6 months, with median DOR >36 months

Topline Data for the IGNYTE Registrational Cohort in Anti-PD1 Failed Melanoma Assessed by Independent Central Review

Strong IGNYTE Primary Analysis Data by Independent Central Review

Overall Response Rate (registration-intended cohort: n=140) (%)		
Investigator Assessment	**Independent Central Review[1]**	
Modified* RECIST 1.1 **32.1%**	**Primary Endpoint** **Modified* RECIST 1.1** **33.6%**	**RECIST 1.1**** **32.9%**

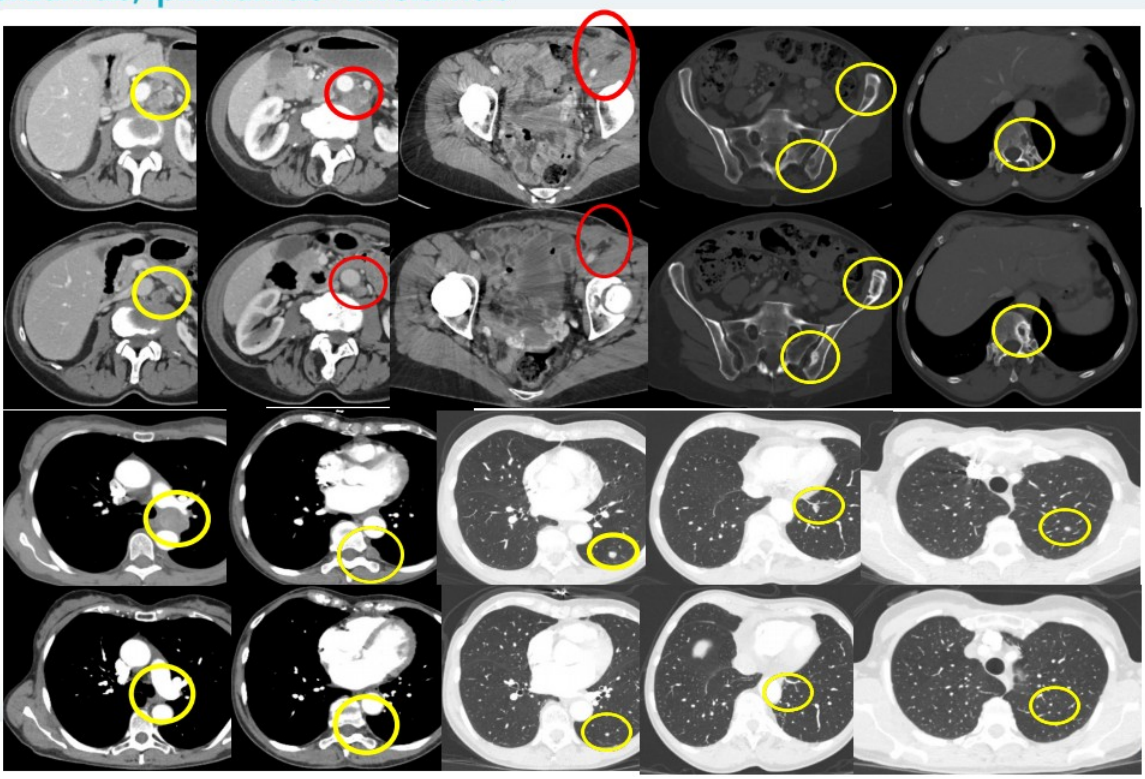
* Confirmation of PD requires further tumor increase from the first observation of PD; responses can be captured at any time up until next anti-cancer therapy[2]
** Requested by FDA, with confirmation of PD required; responses not included in ORR after the first confirmed PD
All patients with at least 12 months follow up

Data cutoff: March 8th 2024. Median follow up for the 140 patients in the registration intended cohort is 15.8 months (range 0.5-47.6); [1]Each central reviewer selects their own target lesions without knowledge of RP1 injection status. [2]This was to allow for the potential for prolonged pseudo-progression (>1 scan interval) before response; however, in practice the pseudo-progression seen was transient (generally <1 scan interval)

Patient Example

Prior atezolizumab+cobimetinib, ipilimumab, SX682 (CXCR-inhibitor)+ atezolizumab, ipilimumab+nivolumab

Replimu



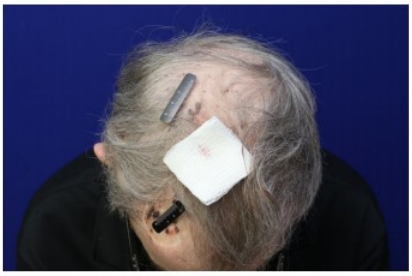
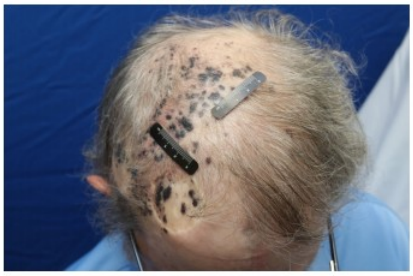
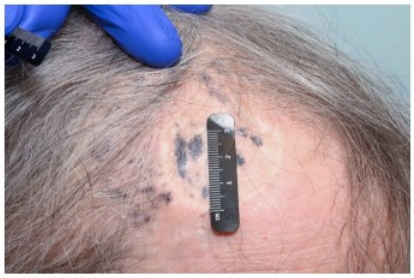
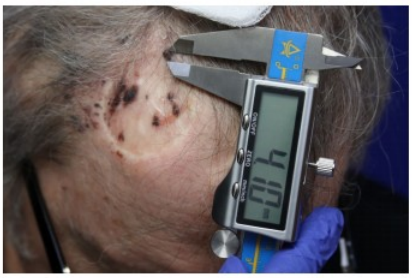
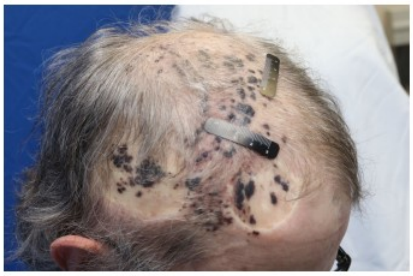
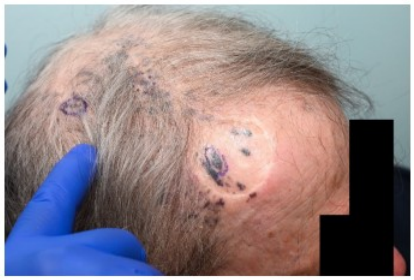
Responses in uninjected distan and visceral tum including healing lytic bone lesions (increasing sclerosis & new internal bone formation seen)

RP1 injected
Non-injected

Patient Example

Prior pembrolizumab (1L), encorafenib+binimetinib (2L), and nivolumab+relatlimab (3L)

Replimu

Baseline	4 months	15 months
		
		

IGNYTE Data Shows Clinically Meaningful Benefit

- One third of patients respond (ORR: 33.6%)
- Responses are durable
  - 100% last >6 months, median DOR >35 months (from baseline)
- RP1 combined with nivolumab continues to be a generally well tolerated regimen
  - Predominantly grade 1/2 constitutional-type side effects
  - Low incidence of grade 3 and 4 events; no grade 5 events
- Full data to be submitted for presentation at an upcoming medical congress

Progress to BLA

IGNYTE Data and Phase 3 Confirmatory Trial Incorporates FDA Feedback

Replimu

Type B meeting in 2021

A real-world population, representative of the IO progressed landscape should be enrolled

Patients should have confirmed progression while **on** anti-PD1 therapy, with minimum 8 weeks exposure

Responses should be durable

Clinically meaningful activity should be seen across all melanoma sub-groups enrolled

Responses should be demonstrably systemic, i.e. of both injected and uninjected lesions

Type C meeting in Sept 2023

FDA acknowledged that the IGNYTE population represents one of unmet need

Contribution of components demonstrated by reference to the literature*

Centrally reviewed data by RECIST 1.1 and mRECIST 1.1

All patients followed for at least 12 months (protocol primary analysis timepoint)

All responding patients followed for at least 6 months from response initiation

Phase 3 confirmatory study will be underway by BLA submission

*The response rate for further single agent anti-PD1 for patients having confirmed PD on prior anti-PD1 is expected to be 6-7%; Ribas et al Lancet Oncology 2018 (19), Hodi et al JCO 2016 (34)

IGNYTE-3: Confirmatory Phase 3 Trial Design*

RP1 and Nivolumab in Ipi-Nivo Pretreated Patients

Advanced cutaneous melanoma

Progressed on anti-PD1 AND anti-CTLA-4 OR not candidates for anti-CTLA-4

Up to 2 prior lines of systemic therapy for advanced disease

BRAF mutant patients must have been treated with BRAF/MEK-directed therapy[1]

N=~400

Randomized 1:1

RP1 + Nivolumab

Treatment of Physician's Choice (TPC)

- *Nivolumab-Relatlimab (Opdualag)*
- *Chemotherapy (DTIC, TMZ, paclitaxel/nab-paclitaxel)*
- *Rechallenge with anti-PD1 monotherapy (nivolumab or pembrolizumab)*

Primary Endpoint
Overall Survival

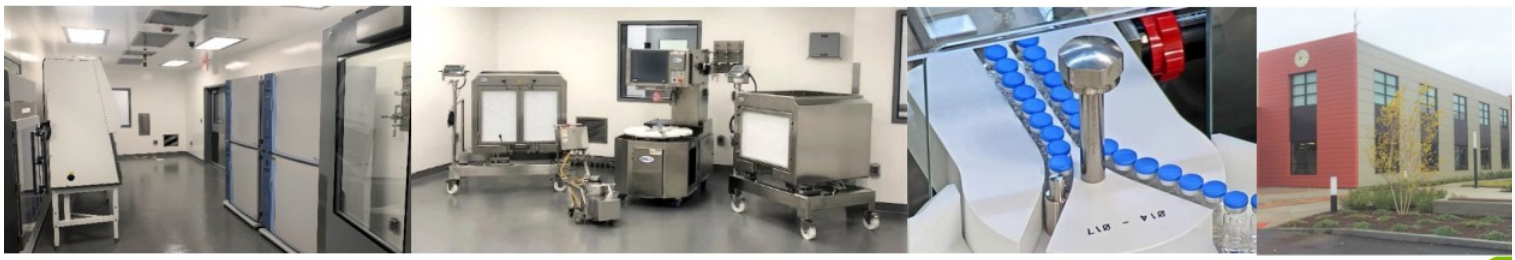
Key Secondary Endpoints
Progression Free Survival and Objectiv Response Rate

[1] For BRAF mutant patients prior BRAF/MEK-directed therapy is required unless deemed not clinically indicated at investigator's discretion due to documented concurrent medical condition or prior toxicity; *ClinicalTrials.gov ID: NCT6264180

Manufacturing on Track to Support RP1 BLA and Commercialization

Commercial scale in-house manufacturing established

- Type C meeting with FDA confirmed alignment on Chemistry, Manufacturing and Controls (CMC) plans to support RP1 BLA submission
- 63,000 square foot state-of-the-art facility for GMP manufacturing in Framingham, MA
  - RP1 BLA consistency lot runs complete
  - Commercial inventory build underway
- Scale expected to be sufficient to cover global commercialization of RP1 and RP2
- Commercially attractive cost of goods & 'off the shelf' product practicality



U.S. Melanoma RP1 Patient Opportunity

Compelling potential option for a broad range of anti-PD1 failed patients

Anti-PD1 failed melanoma

~13K patients[1]

1L prior adjuvant

2L+ BRAF WT

2L+ BRAF MT

Addresses a high unmet need in anti-PD1 failed settings

RP1+nivolumab is well positioned to be the **first option for patients who progress on a PD1-based regimen** (in adjuvant or 1L setting), given:

1. Deep & durable responses
2. Safety profile
3. Ease of administration

Source: [1]Melanoma US treated patient population for 2030 based on CancerMPact® Patient Metrics, Cerner Enviza (available from www.cancermpact.com Accessed 15 Oct 2023), with adjustments to future 2L+ treatment rates based on primary market research.

RP1 Well Positioned for BLA Submission and Commercialization

- Strong IGNYTE primary endpoint ORR data by independent central review of 33.6% (mRECIST 1.1)
- Durable responses: 100% last >6 months, median DOR >35 months (from baseline)
- Manufacturing on track to support RP1 BLA & global commercialization
  - Type C meeting with FDA confirmed alignment on CMC plans
- First patient expected to be enrolled in the phase 3 confirmatory study (IGNYTE-3) in Q3 2024, with BLA submission planned for 2H 2024
- Attractive commercial RP1 opportunity in anti-PD1 failed melanoma
  - Significant patient population and unmet need
  - Compelling risk:benefit profile


Thank You