

**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 3, 2020**

**REPLIMUNE GROUP, INC.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction  
of incorporation)

**001-38596**  
(Commission  
File Number)

**82-2082553**  
(IRS Employer  
Identification Number)

**500 Unicorn Park  
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 3, 2020, Replimune Group, Inc. (the “Company”) issued a press release announcing new interim data from the Phase 2 part of its Phase 1/2 clinical trial of RP1 in combination with Opdivo. The Company will host a virtual investor event at 8:00 a.m. ET on Wednesday, June 3, 2020 to present the interim data. The webcast and accompanying slides will be available under “Events and Presentations” in the Investors and Media section of the Company’s website at [www.replimune.com](http://www.replimune.com). A copy of the virtual investor event presentation deck and the press release is attached as Exhibits 99.1 and 99.2 to this Current Report on Form 8-K, respectively. The Company undertakes no obligation to update, supplement or amend the materials attached hereto.

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 9.01 Financial Statements and Exhibits.**

<u>Exhibit No.</u>	<u>Description</u>
<a href="#">99.1</a>	<a href="#">Company Presentation dated June 3, 2020.</a>
<a href="#">99.2</a>	<a href="#">Press Release dated June 3, 2020.</a>

---

**SIGNATURES**

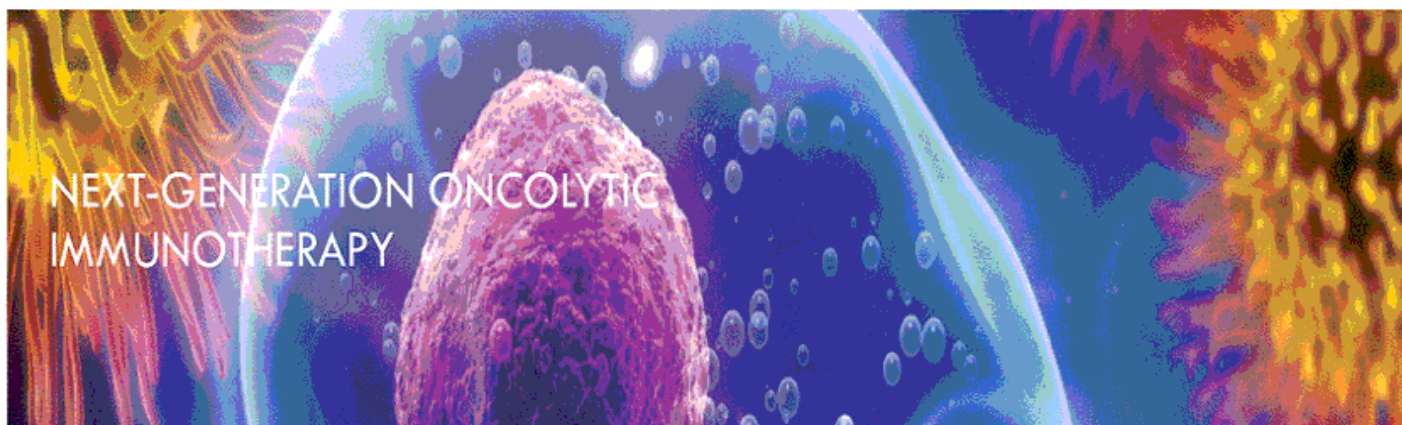
Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**REPLIMUNE GROUP, INC.**

Date: June 3, 2020

By: /s/ Jean Franchi  
Jean Franchi  
Chief Financial Officer

---



Data Update  
June 3<sup>rd</sup> 2020

---



# Safe harbor

Any statements contained herein that are not statements of historical facts may be deemed to be 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 the advancement of our clinical trials, patient enrollments in our existing and planned clinical trials and the timing thereof, the results of our clinical trials, the timing and release of our clinical data, our goals to develop and commercialize our product candidates, our expectations regarding the size of the patient populations for our product candidates if approved for commercial use 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, 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 SARS-COV-2 coronavirus as a global pandemic and related public health issues, and other risks as may be detailed from time to time in our Annual Reports on Form 10-K, 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.

---

# Agenda

3

Introduction

Philip Astley-Sparke / Chief Executive Officer

Summary of Interim Results

Robert Coffin, Ph.D. / Founder & Head of R&D

CSCC Data Update

Kevin Harrington, Ph.D. / The Royal Marsden

Melanoma Data Update

Mark Middleton, Ph.D. / University of Oxford

Pipeline Update

Robert Coffin, Ph.D. / Founder & Head of R&D

Summary Remarks

Philip Astley-Sparke / Chief Executive Officer

## Dr. Kevin Harrington, The Royal Marsden Hospital

4



- Professor of Biological Cancer Therapies at The Institute of Cancer Research, London, and Consultant Clinical Oncologist at The Royal Marsden NHS Foundation Trust
- Leads the Targeted Therapy Team which focuses on two main areas: (i) the use of viruses as anti-cancer agents; and (ii) the development of new drugs that sensitize cancer cells to radiation.
- Specializes in treating patients with head and neck cancer, salivary gland and skin cancers.
- He has published more than 500 articles on cancer treatment and his work has been featured in newspaper and television reports.



## Dr. Mark Middleton, The University of Oxford

5



- Professor of Experimental Cancer Medicine in the Department of Oncology, consultant Medical Oncologist at the Oxford Cancer and Haematology Centre and Head of the Department of Oncology at the University of Oxford.
- Research specializes on the development of new cancer drugs and on the treatment of melanoma and upper gastrointestinal tract cancers.
- Mark has overseen the development of internationally leading melanoma and upper GI clinical research groups and establishment of portfolios of early phase radiotherapy and haematooncology trials in Oxford.



- **Proprietary 'Immulytic' oncolytic immuno-gene therapy platform**
    - Intended to maximally activate the immune system against a patient's cancer
    - Intended to establish Replimune's products as the second cornerstone of immuno-oncology
  - **RP1 – in multiple clinical trials, with current focus on immune-responsive tumors**
    - Lead indication – advanced cutaneous squamous cell carcinoma (CSCC)
      - Strong efficacy signal from single arm data in combination with Opdivo – data updated today
      - Ongoing 240 patient registration directed randomized trial in combination with Libtayo
      - Single agent study in organ transplant recipients contra-indicated for anti-PD1 enrolling
    - Anti-PD1 refractory melanoma
      - 125 patient cohort enrolling
      - Strong signal from current RP1 combined with Opdivo melanoma cohort – data updated today
  - **RP2 & RP3 - intended to treat less immune-responsive tumors**
    - Ongoing Phase 1 clinical trial of RP2 alone & combined with Opdivo
    - Safety & efficacy with single agent RP2 & initial data combined with Opdivo expected by end 2020
    - RP3 intended to enter the clinic in H2 2020
-

# Replimune's platform

7

## 1. A potent underlying virus strain

Replimune believes HSV to be the most potent, versatile & clinically validated virus species for oncolytic use

There is great diversity among clinical HSV strains

29 new clinical strains were tested & the most effective engineered for oncolytic use



Enhanced potency oncolytic immunotherapy backbone



Additionally expresses anti-CTLA-4



Expresses GALV-GP R-, anti-CTLA-4, CD40L & 4-1BBL

## 2. Increased tumor killing & spread

Armed with GM-CSF & a potent fusogenic protein (GALV-GP R-)

Increases direct & immunogenic tumor killing\*

*Intended for immune responsive tumor types*

## 3. Delivery of potent immune stimulatory proteins

Focus on *clinically validated* pathways which function at the time & place of immune response initiation, but where systemic engagement is sub-optimal

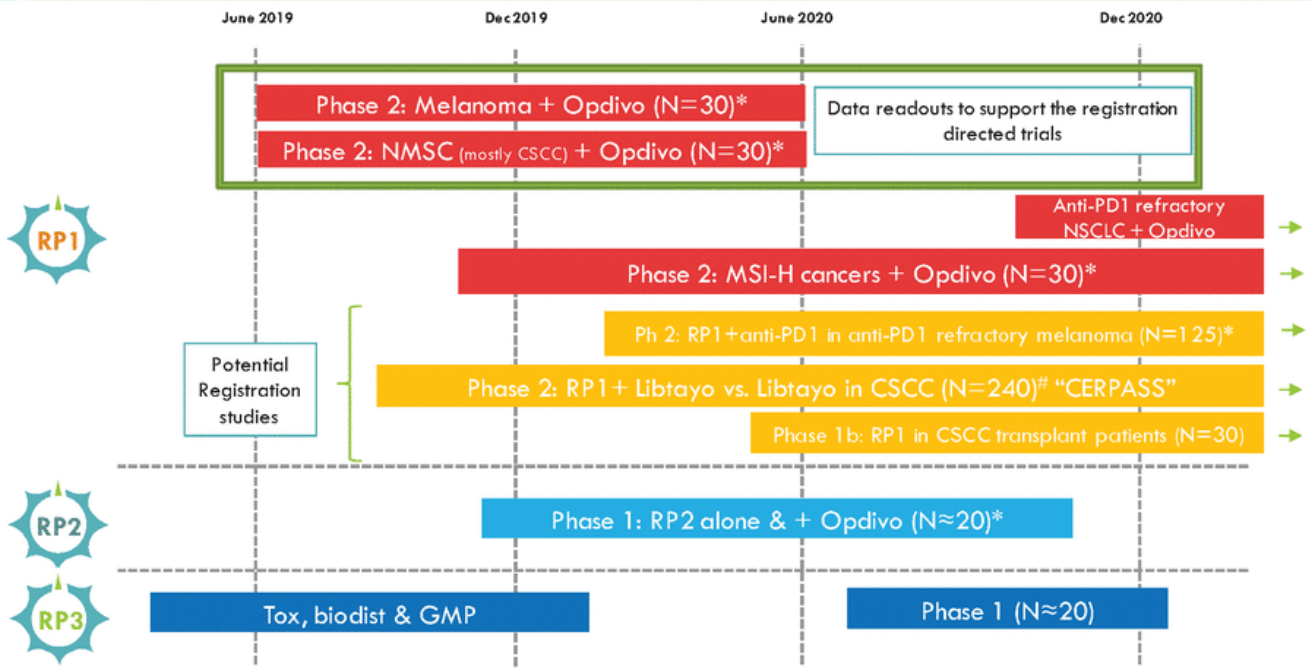
- Anti-CTLA-4
- Immune-costimulatory pathway activators
- Aims to *increase efficacy while reducing toxicity*

*Intended for less & non-immune responsive tumor types*

\* Replimune pre-clinical data published in Thomas et al JITC 2019

# Replimune's development plan

8



\* Under clinical trial collaboration & supply agreement with BMS for the supply of Opdivo – full commercial rights retained by Replimune

# Under clinical trial collaboration agreement with Regeneron; 50:50 sharing of clinical trial costs – full commercial rights retained by Replimune



# Summary of today's data



9

## Cutaneous squamous cell carcinoma data update

- Six of seven patients with follow up treated with RP1+Opdivo have ongoing PRs or CRs
- Four patients with ongoing CRs (including of uninjected distant tumors): *Clear differentiation from anti-PD1 monotherapy*
- Data continues to highlight RP1 is well tolerated, demonstrates immune activation & continues to drive durable and deep responses in patients with CSCC

## Anti-PD1 refractory cutaneous melanoma data update

- 16 patients treated with RP1 in combination with Opdivo
  - 5 patients in response - 2 further patients remain on treatment with the opportunity for response
  - These responses (which include patients with extensive visceral disease) wouldn't be expected with a second line of anti-PD1; 4/5 had failed prior combined Yervoy/Opdivo
- Activity also shown in anti-PD1 refractory uveal and mucosal melanoma patients

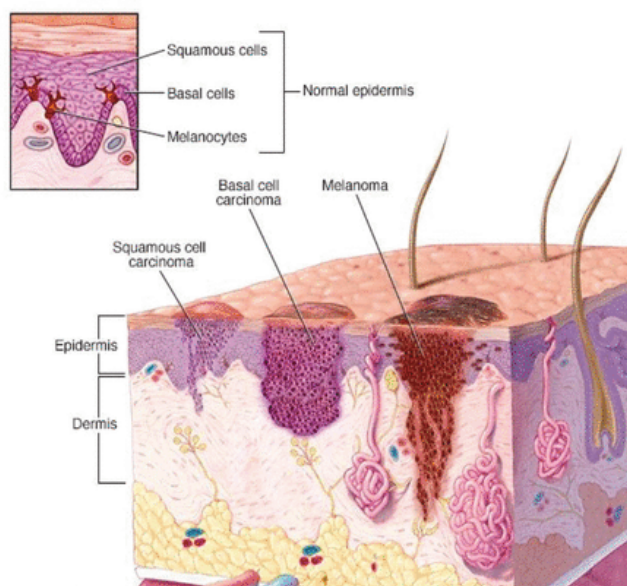
**Data presented today continues to support the current registration-directed clinical trials**



## CSCC opportunity overview

# Lead indication overview: CSCC

- The second most common skin cancer with ≈700,000 patients annually in the U.S.<sup>1</sup>
- Occurs when DNA damage from exposure to ultraviolet radiation or other agents triggers abnormal changes to squamous cells
- 10% have 'high risk' disease (recurs following initial surgery)
- Approximately 7,000-15,000 US deaths annually<sup>1-3</sup>
  - Most conservative addressable population
  - 80% of patients die from locoregional progression, not metastatic disease<sup>4,5</sup>
- Potential US market estimated at 7,000-28,000 patients annually<sup>1-4</sup>
- Only approved anti-PD-1 therapy: Libtayo (Regeneron)



© MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH. ALL RIGHTS RESERVED.

<sup>1</sup>Rogers et al JAMA Dermatol 10 2015

<sup>2</sup>Clayman et al JCO 23 2005

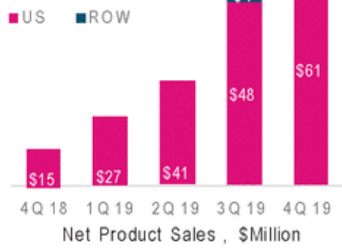
<sup>3</sup>Mansouri et al J Am Acad Dermatol 153 2017

<sup>4</sup>Schmults et al JAMA Dermatol 149 2013

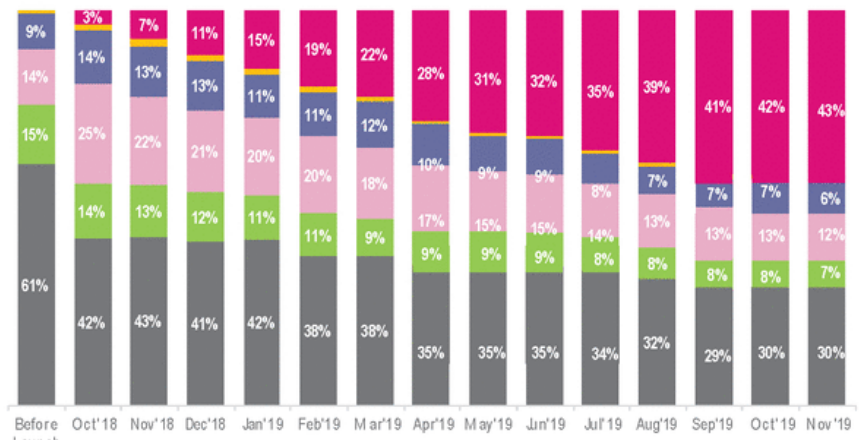
<sup>5</sup>Motaparthy et al Adv Anat Pathol 24 2017

# Regeneron has paved the way in CSCC

Libtayo generated ~\$200M in 1<sup>st</sup> year sales



Libtayo captured market share of systemic therapies



Advanced CSCC - Total U.S. Patient Share by Products†

CSCC - Cutaneous Squamous Cell Carcinoma  
 † Source: Regeneron Q1 2020 Corporate Presentation  
 Updated IQVIA - Claims through Nov'19



## Single agent anti-PD1 data in advanced CSCC

13

	Libtayo				Keytruda	Opdivo
<b>Patient population</b>	Locally advanced		metastatic		47 locally advanced + 58 metastatic	4 locally advanced, 16 locoregional, 4 metastatic
<b>Number of patients</b>	37 (per label, 2018)	33 (ASCO 2020)	75 (per label, 2018)	59 (ASCO 2020)	105 (ESMO 2019)	24 (ASCO 2020)
<b>ORR</b>	48.5%	45%	46.7%	51%	34.3%	54.5%
<b>CR</b>	0%	13%	5.3%	20%	3.8%	0%





- Registration-directed randomized controlled trial in collaboration with Regeneron
    - 240 patients
    - Randomized 2:1 (RP1+ Libtayo vs. Libtayo alone)
    - Primary endpoint ORR
    - Secondary endpoints include CR rate, duration of response, PFS, OS
  - Aim to show 15% delta improvement in ORR
    - Control arm ORR expectation based on anti-PD1 single agent data 34-51%
    - Control arm CR expectation based on anti-PD1 single agent data <10% at data cut off
  - Aim to also improve durability and show multi-fold (2-3x) improvement in CR rate
-



- 30 patient clinical trial of single agent RP1 open for enrollment in solid organ transplant recipients (liver & kidney)
  - Organ transplant recipients are at increased risk of malignancy, with CSCC most prevalent
  - 70% of patients develop CSCC within 20 years<sup>1</sup>
  - Anti-PD1 therapy contra-indicated due to the risk of organ rejection in around 40% of patients
  - Clinical data indicates that RP1 has single agent activity in CSCC
- Intend expansion of the CSCC program to also include neoadjuvant use

<sup>1</sup>Fisher et al J Am Acad Dermatol 82 2020

---

## Current CSCC data

# RP1 + Opdivo data summary in advanced CSCC

17

So far, nine patients have been treated with RP1 + Opdivo:

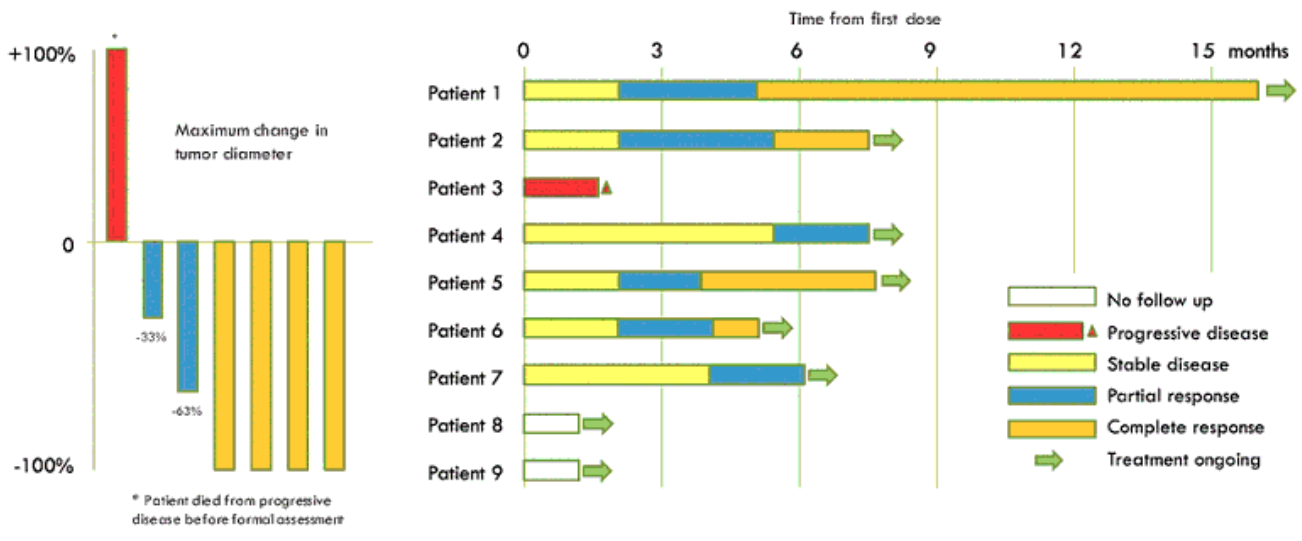
- 4 locally advanced, 5 metastatic, 56% had prior systemic therapy
- 6/7 patients with follow up in ongoing response
  - Patient 1: Ongoing CR
  - Patient 2: Ongoing CR (previously PR)
  - Patient 3: PD
  - Patient 4: Ongoing PR
  - Patient 5: Ongoing CR
  - Patient 6: Ongoing CR (new)
  - Patient 7: Ongoing PR (new)
  - Patient 8: Initiated dosing 24<sup>th</sup> April 2020 (no follow up)
  - Patient 9: Initiated dosing 28<sup>th</sup> April 2020 (no follow up)

Other NMSC patients enrolled:

- BCC: N=2 (PD, no follow up yet)
- Merkel cell carcinoma: N=1 (PD)
- Angiosarcoma: N=2 (PR, no follow up yet)



# Responses are deep & all are ongoing to date



## Example CSCC patients

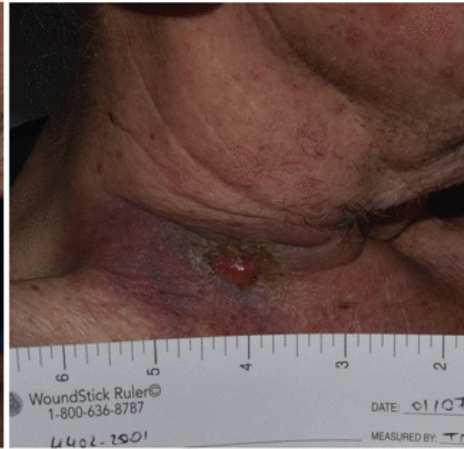
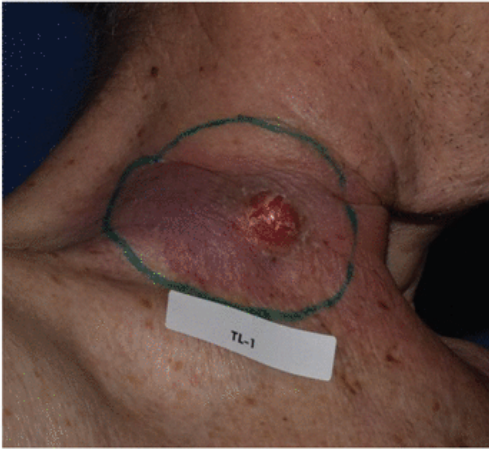
## Patient 2 (4402-2001): Ongoing CR

20

16<sup>th</sup> June 2019  
(baseline)

1<sup>st</sup> July 2019  
(post one dose of RP1, no  
Opdivo)

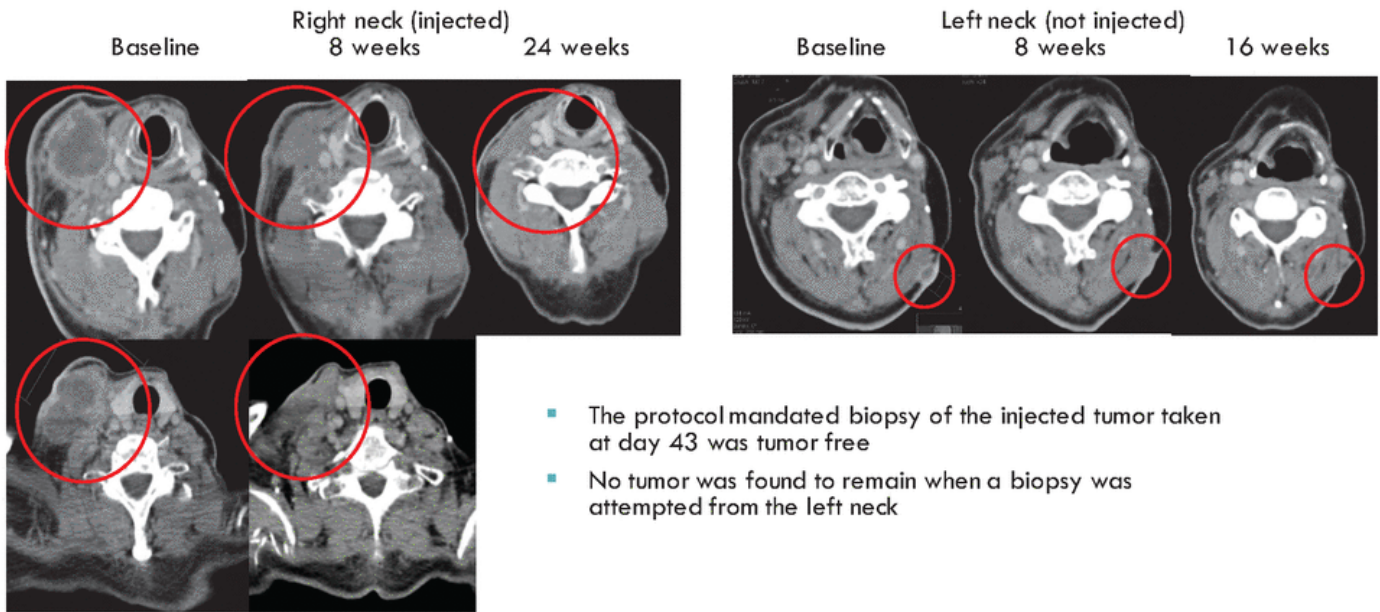
16<sup>th</sup> July 2019  
(post 2 doses of RP1 & 1 dose  
of Opdivo)



- Patient with recurrent CSCC of the neck (bilateral, right injected), retroperitoneal nodes & bone metastases (not injected)
- Previously treated with cisplatin-based chemoradiation & carboplatin/5-FU
- Both the large injected tumor & the smaller contralateral tumor in the neck reduced considerably before the first Opdivo dose, i.e. after the first dose of RP1, followed by resolution of all disease

# Patient 2 (4402-2001): Ongoing CR

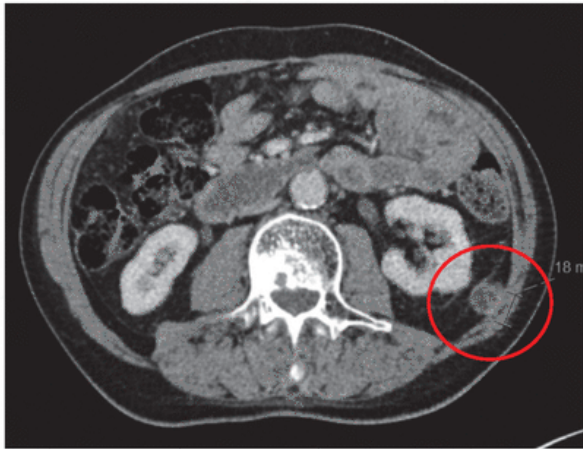
21



## Patient 2 (4402-2001): Ongoing CR

22

Baseline



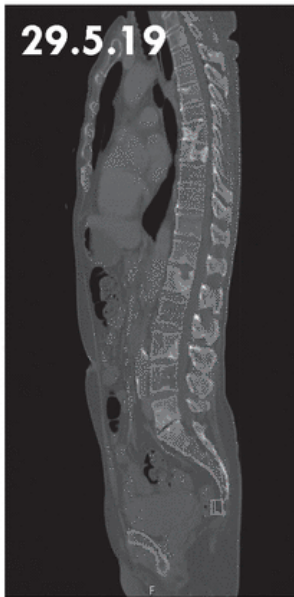
16 weeks



- The patient also had baseline retroperitoneal tumors which have completely resolved

## Patient 2 (4402-2001): Ongoing CR

23

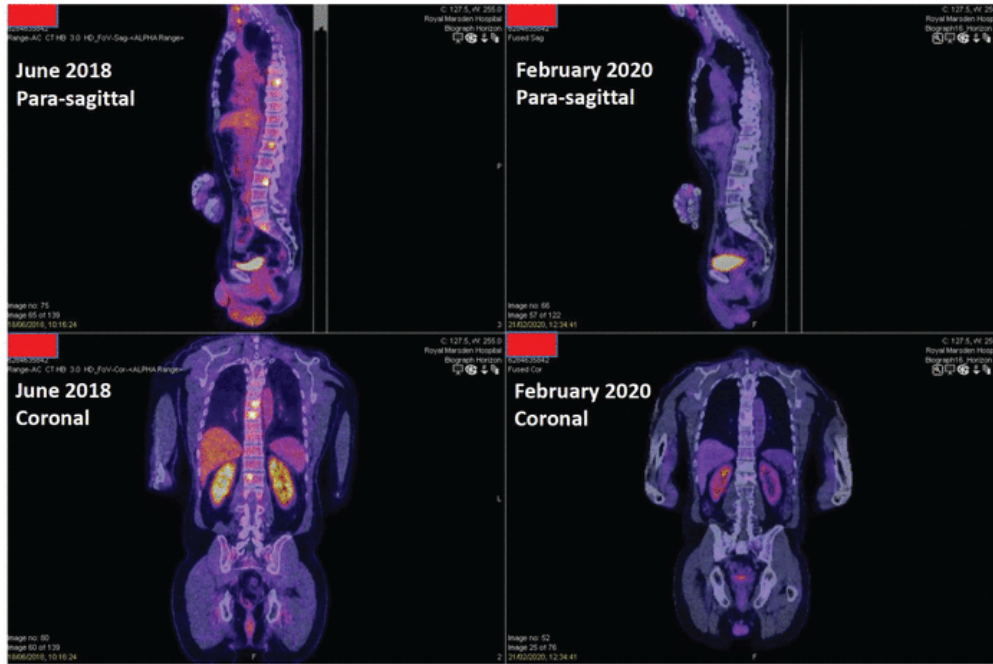


Complete sclerosis of all bone lesions with no areas of active disease. Declared radiological CR. Confirmed by PET scan (next slide)

→ Indicates area of increased bony sclerosis, indicative of healing response of lytic metastases



# Patient 2 (4402-2001): Ongoing CR

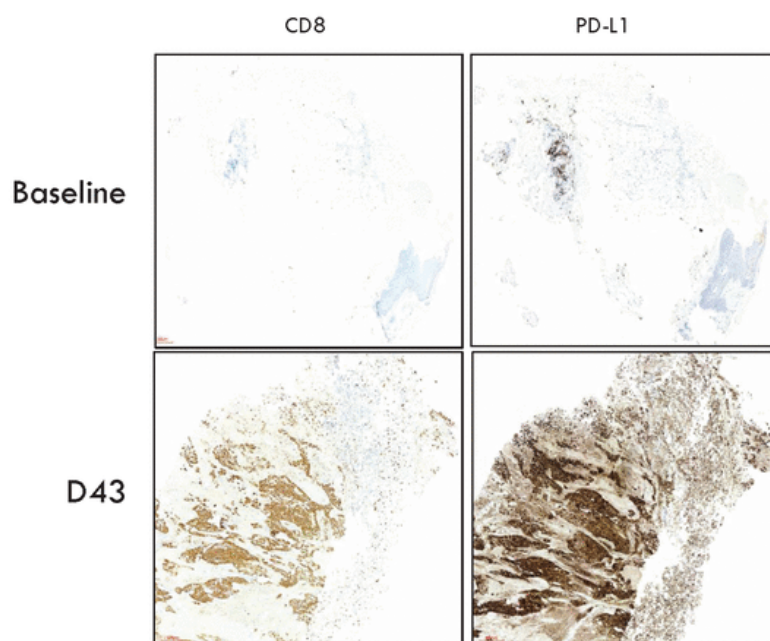


Bone metastases had substantially increased by CT between the prior PET scan (June 2018) and initiating the trial (June 2019), but no PET scan was performed at screening.

The PET scan to confirm CR of bone mets performed Feb 2020 showed no active disease

# Patient 2 (4402-2001): CD8 T cell & PD-L1 staining

25





# Patient 4 (4402-2004): Ongoing PR

26

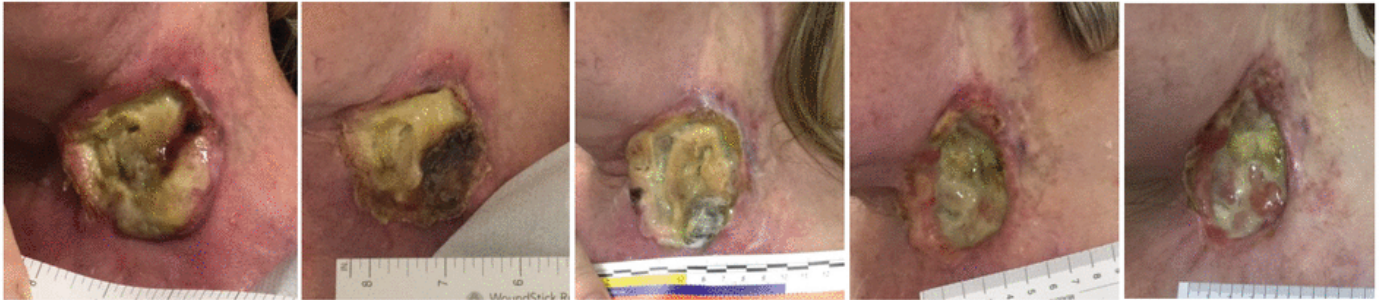
2<sup>nd</sup> Sept 2019  
(pre-dosing)

16<sup>th</sup> Sept  
(post single RP1 dose, no Opdivo)

15<sup>th</sup> Oct

2<sup>nd</sup> Dec

13<sup>th</sup> Jan



Baseline scan



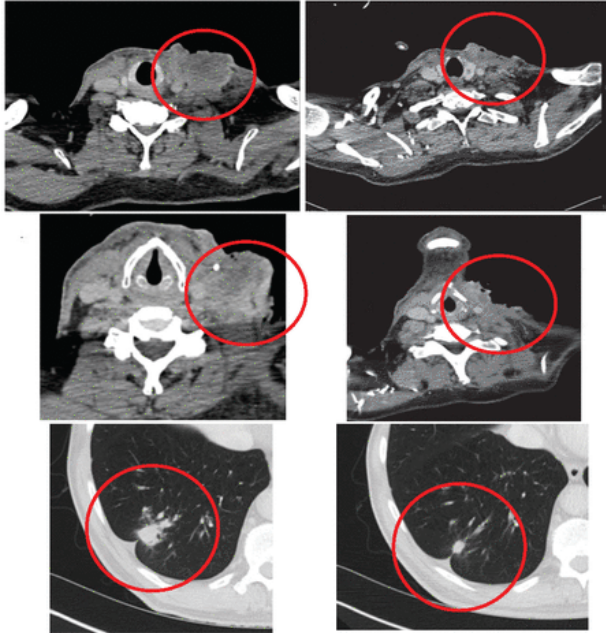
- Recurrent CSCC of the neck (injected) and lung metastases (not injected)
- Previously treated with radiotherapy with immediate relapse
- The large injected tumor in the neck flattened considerably after the first dose of RP1 (i.e. before the first Opdivo dose), & continued to reduce thereafter

## Patient 4 (4402-2004): Ongoing PR

27

28th August 2019

25<sup>th</sup> October 2019



- The only other sites of disease were lesions in the lung, which have also significantly reduced

# Patient 5 (4402-2005): Ongoing CR

28

25<sup>th</sup> Sep 2019  
(Baseline)

9<sup>th</sup> Oct 2019  
(post single RP1 dose, no  
Opdivo)

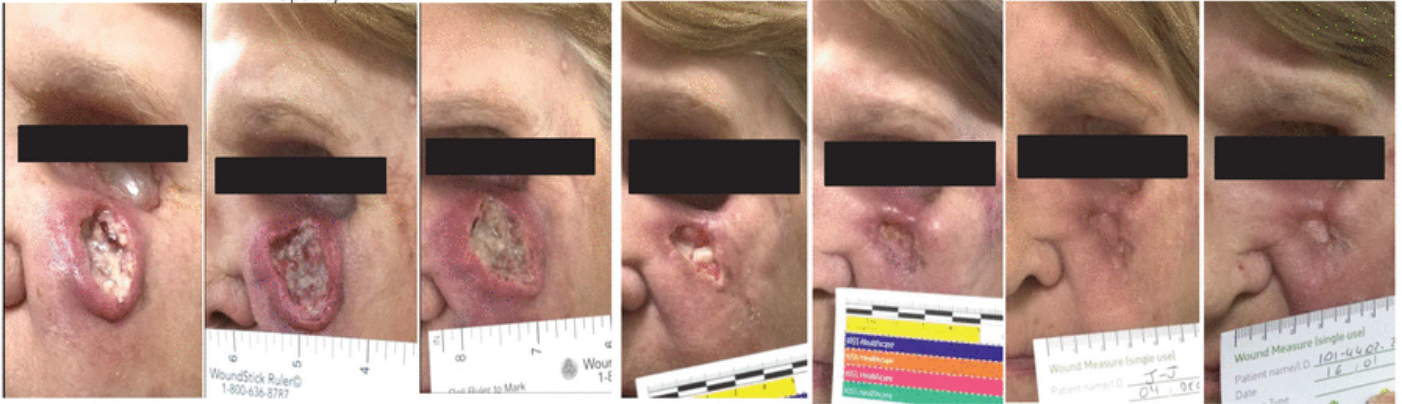
23<sup>rd</sup> Oct 2019

6<sup>th</sup> Nov 2019

20<sup>th</sup> Nov 2019

4<sup>th</sup> Dec 2019

16<sup>th</sup> Jan 2020



- Recurrent, rapidly progressing CSCC of the left cheek with bone invasion through the maxillary region, previously treated with surgery & radiation before trial entry
- The lesion flattened considerably after the first dose of RP1, and continued to reduce after the first dose of Opdivo
- CR confirmed by biopsy in December

# Patient 6 (4402-2006): Ongoing CR

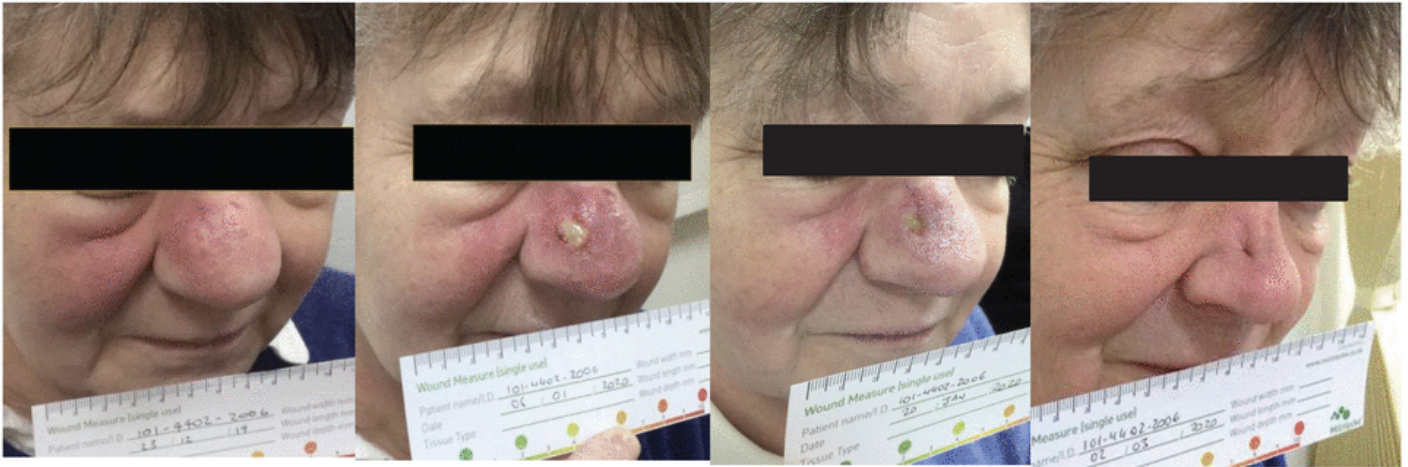
29

23rd December 2019  
(Baseline)

6th January 2020  
(post single RP1 dose, no Opdivo)

20th January 2020

2nd March 2020



- Recurrent, rapidly progressing CSCC of the nasal region (3.5cm tumor), previously treated with carboplatin & radiation before trial entry





# Patient 6 (4402-2006): Ongoing CR

Baseline



Day 57



# Patient 6 (4402-2006): Ongoing CR

31

18<sup>th</sup> Dec 2019  
(Screening)



2<sup>nd</sup> Feb 2020



14<sup>th</sup> April 2020\*

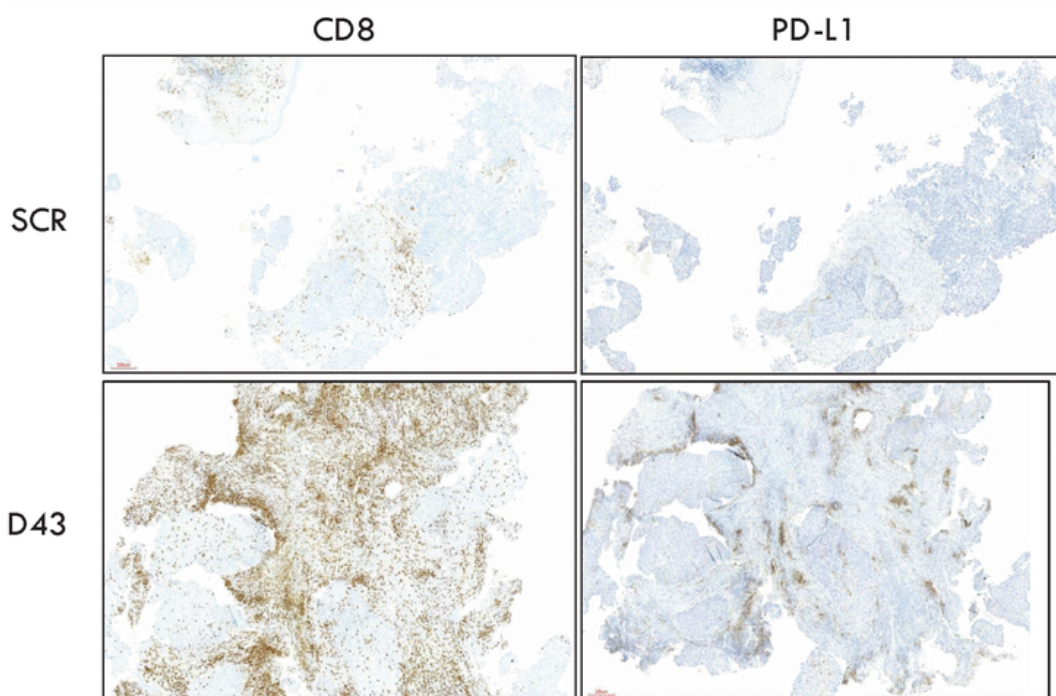


- The alternative to study treatment was rhinectomy

\* CT done in a different plane to prior scans to maximally capture the affected area

# Patient 6 (4402-2006): Ongoing CR

32



## **Anti-PD-1 refractory melanoma opportunity overview**







- Approximately half of advanced melanoma patients still die of their disease, despite multiple approved therapies now being available
  - Anti-PD1, anti-CTLA-4, combined anti-CTLA-4/anti-PD1, BRAF targeted agents
- Approximately 7,230 US deaths annually from metastatic melanoma<sup>1</sup>
- Approximately 62,000 deaths annually world-wide
  
- High unmet medical need for patients with baseline resistance to checkpoint therapy
- 40-65% of all metastatic melanoma are primary refractory to initial anti-PD1 therapy<sup>2</sup>
- The expected response rate to retreatment with anti-PD1 therapy following progression on single agent anti-PD1 is 6-7%<sup>3</sup>
- The expected response rate to Yervoy having failed initial single agent anti-PD1 is 13%<sup>4</sup>

<sup>1</sup> <https://seer.cancer.gov> (2019 data)

<sup>2</sup> Gide et al Clin. Cancer Res **24** 2018

<sup>3</sup> Ribas et al Lancet Oncology **19** 2018; Hodi et al JCO **34** 2016

<sup>4</sup> Pires de Sliva et al ASCO 2020



- Enrollment of a 1 25 patient potentially registrational cohort underway
  - RP1 combined with Opdivo
  - Hurdle for success intended to be discussed with FDA late 2020
  - ORR to a second line of anti-PD1 is estimated at **6-7%**<sup>1</sup>
- Targeting patients with primary/acquired resistance to anti-PD1 therapy
  - Treated with anti-PD1 or anti-PD1/anti-CTLA-4 for at least 12 weeks with progression confirmed on successive scans
  - Includes patients failing anti-PD1 adjuvant therapy
  - Very unlikely to respond to further treatment with single agent anti-PD1
  - High un-met medical need

<sup>1</sup>Ribas et al Lancet Oncology **19** 2018; Hodi et al JCO **34** 2016

## Current melanoma data

# Melanoma data summary

37

- 36 melanoma patients have been enrolled & treated with RP1 combined with Opdivo, with the last patient enrolled on Jan 7th 2020\*
- As of May 2<sup>nd</sup> 2020 (data cut off), the status of the patients in this immature data set was:
  - Anti-PD1 refractory cutaneous melanoma (N=16 [8 having had prior anti-CTLA-4 and anti-PD1]): Nine patients showed initial clinical benefit\*\*, seven ongoing, with five so far having met the formal definition of response\*\*\*
  - Anti-PD1 naive cutaneous melanoma (N=8): Eight patients showed initial clinical benefit\*\*, six ongoing, with four so far having met the formal definition of response
  - Mucosal melanoma (N=6): 3 patients showed initial clinical benefit\*\*, two ongoing (one anti-PD1 naive, one having had prior anti-PD1), with both having met the formal definition of response\*\*\*
  - Uveal melanoma (N=6): Five patients showed initial clinical benefit\*\* (all anti-PD1 refractory), two ongoing, one having a 27.3% reduction by RECIST (uni-dimensional measurement)/61% reduction by WHO (bi-dimensional measurement)

\*Phase 1 expansion cohort & phase 2 melanoma cohort combined      \*\*SD or better with evidence of anti-tumor activity

\*\*\*RECIST other than PD requires confirmation on successive scans

## Melanoma patients treated with RP1 + Opdivo

38

	All	Cutaneous melanoma	Mucosal melanoma	Uveal melanoma
Number	36	24	6	6
Age: Range	28-95	28-95	40-78	44-85
Prior anti-PD1	25	16*	5	4
Prior single agent anti-PD1	9	7	1	1
Prior anti-PD1/anti-CTLA-4	16	9	4	3
Prior anti-PD1 %	69%	67%	83%	67%
Stage IIIc	2	2	0	0
Stage IV M1a	7	3	4	0
Stage IV M1b	11	10	1	0
Stage IV M1c	16	9	1	6
Stage IV M1b/c %	75%	79%	33%	100%

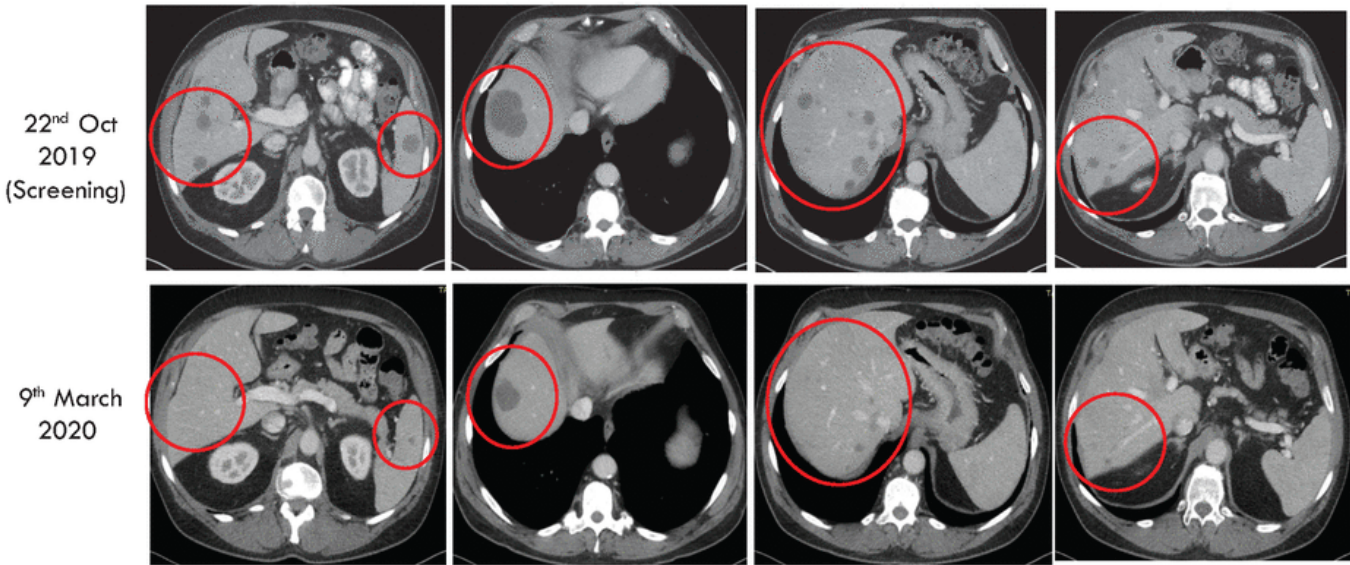
\* 87.5% with Stage IV M1b/c (visceral) disease

## Example melanoma patients

## **Anti-PD1 refractory cutaneous melanoma patients**

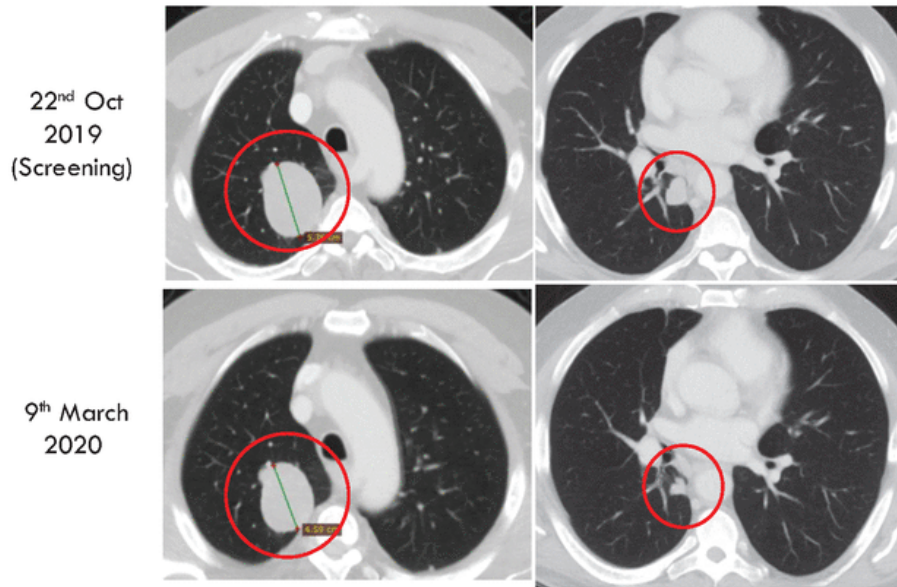






D43 liver biopsy tumor free

Reduction of injected & uninjected liver lesions

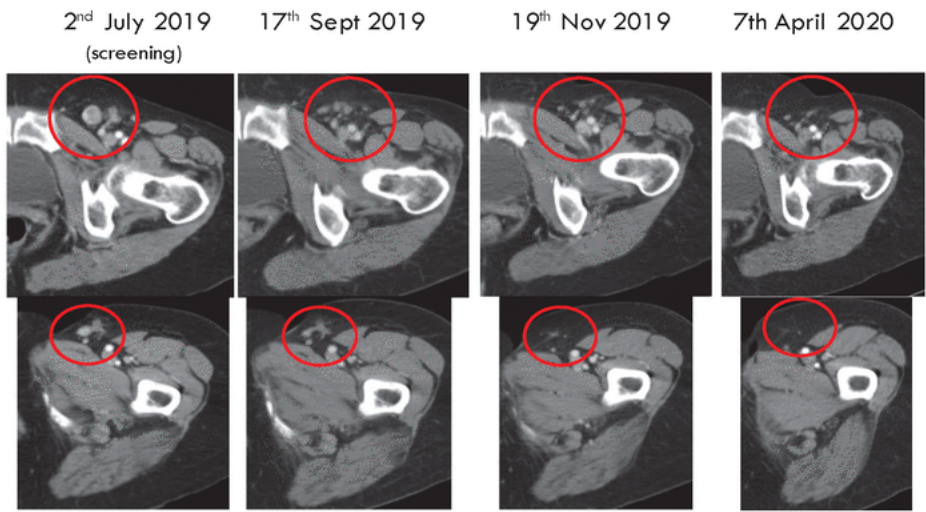


Reduction of uninjected lung lesions



Biopsy  
awaited to  
confirm CR

- Disease in the foot, leg & nodes in the groin
- Initial progression in the leg/foot followed by response





Patient #: 4403-1003 (Yervoy/Opdivo refractory melanoma) – Ongoing PR

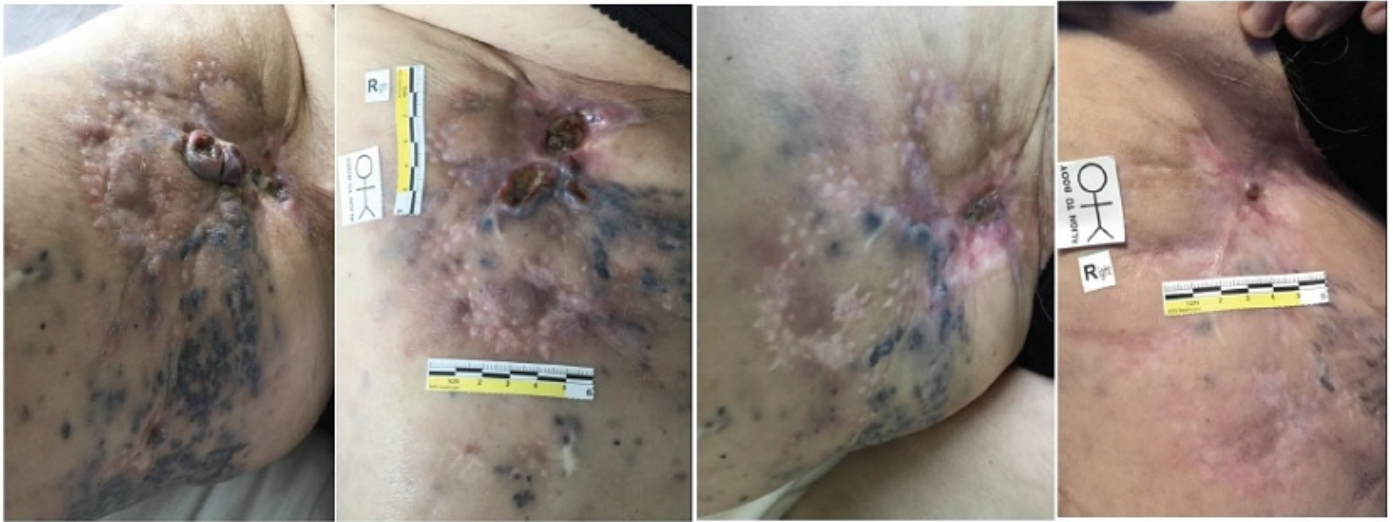
45

10<sup>th</sup> June 2019

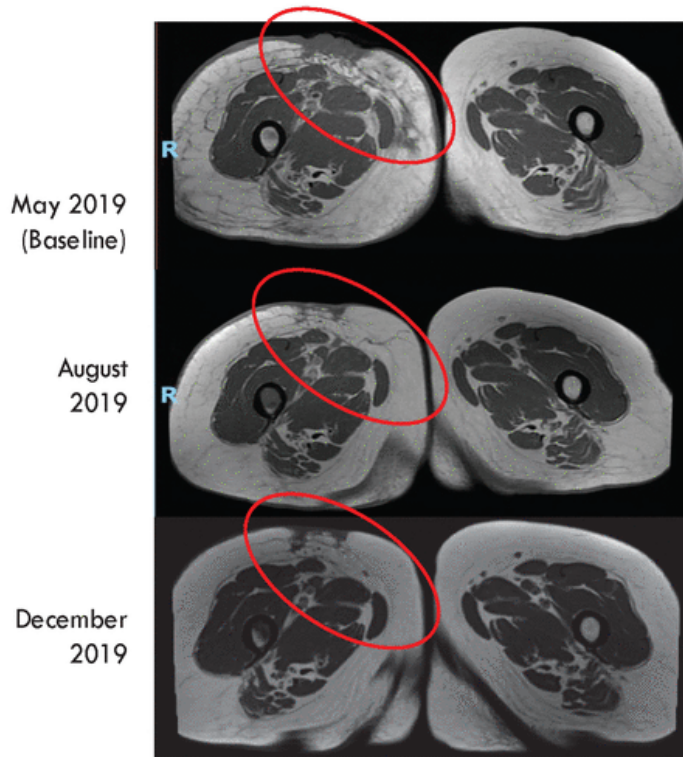
24<sup>th</sup> June 2019 (pre Opdivo)

2<sup>nd</sup> September 2019

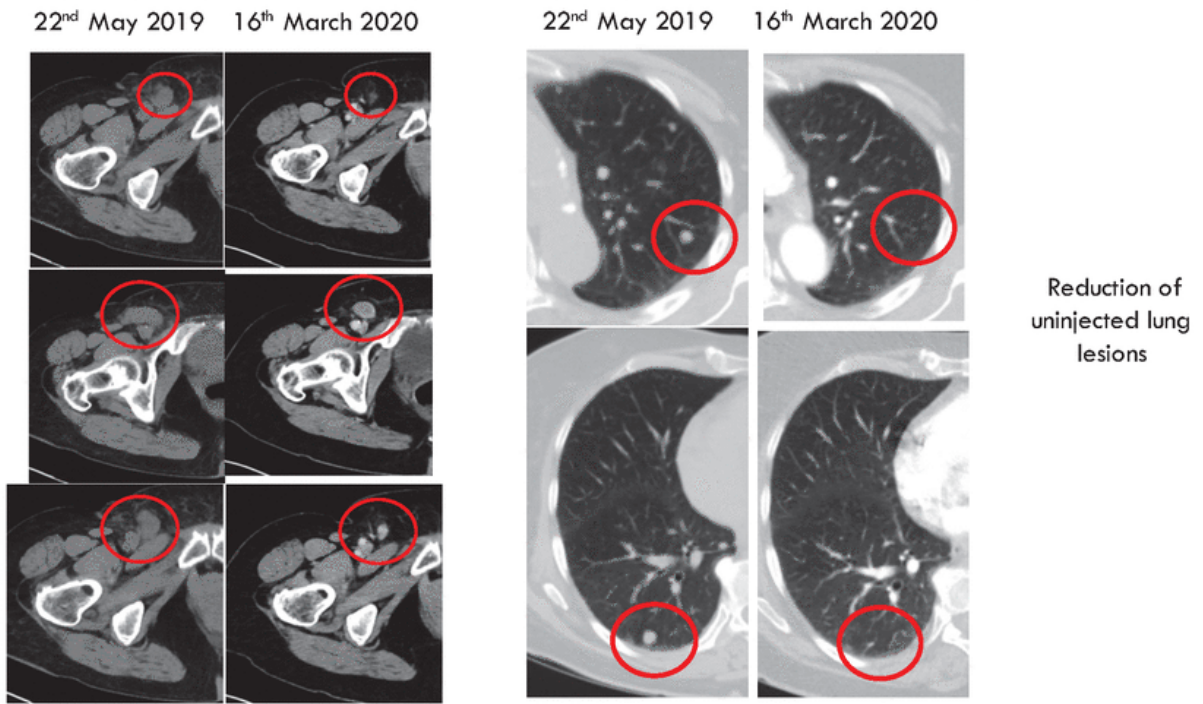
16<sup>th</sup> March 2020



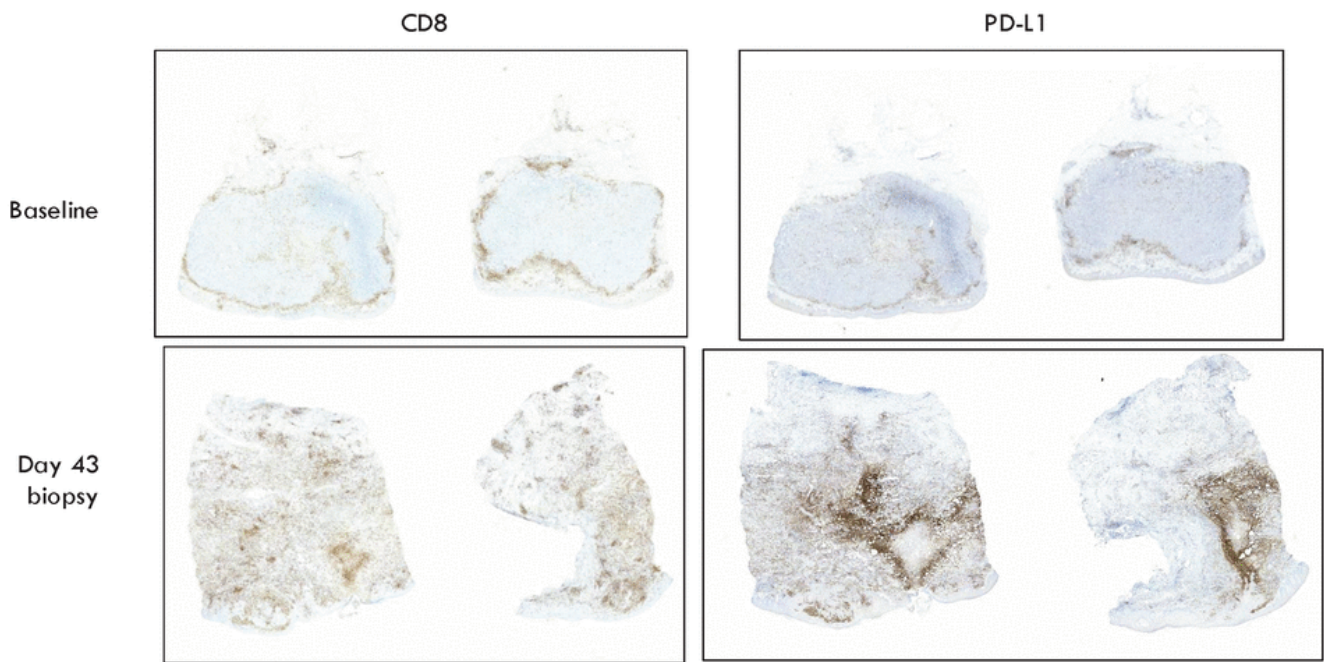
- Baseline disease in the thigh, groin & lungs
- Tumors in the thigh flattened after the first dose of RP1, i.e. prior to Opdivo & extensive oedema rapidly reduced



- Patient quality of life has also greatly improved, from being essentially immobile to being fully mobile
- Patient remains on treatment at 10 months



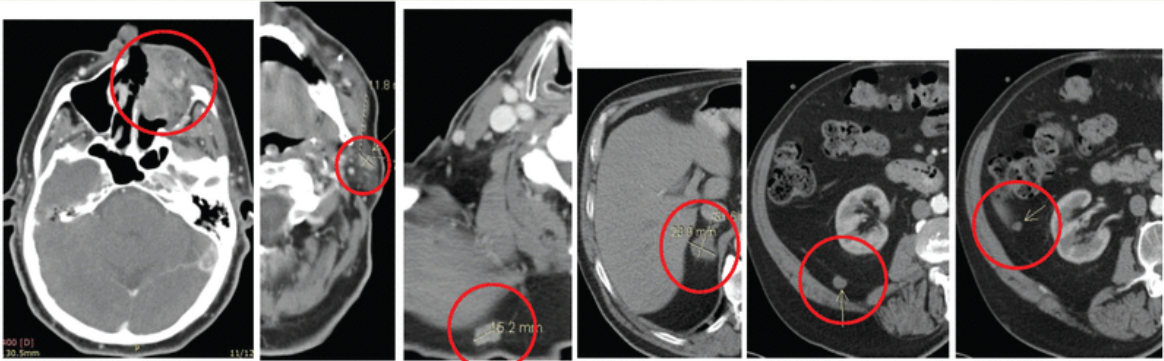




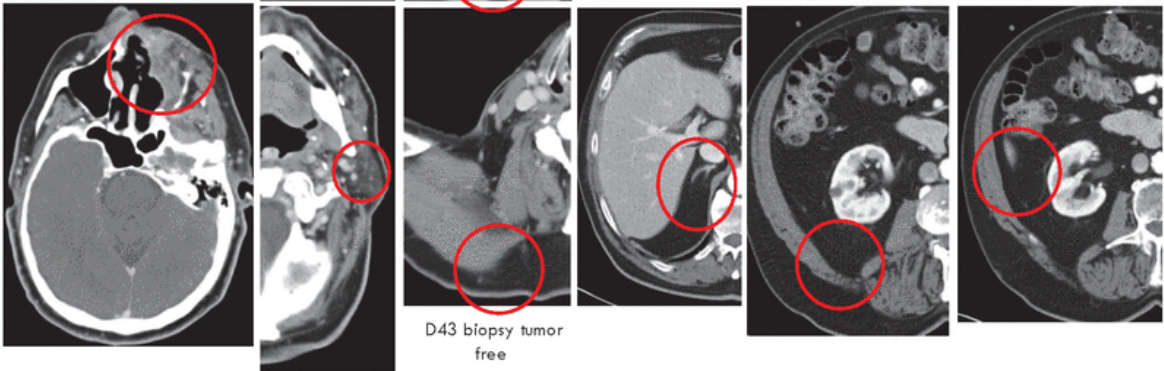
## Mucosal melanoma patients



12<sup>th</sup> Nov  
2019  
(Screening)



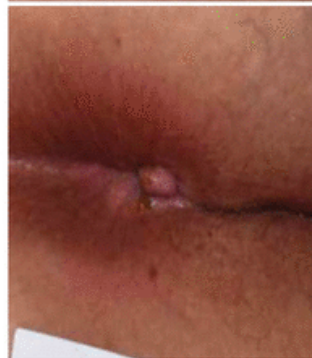
12<sup>th</sup>  
March  
2020



20<sup>th</sup> Aug  
2019  
(Screening)



15<sup>th</sup> Jan  
2020



Excision biopsy  
tumor free 1<sup>st</sup> April  
2020

## Uveal melanoma patients



Baseline (2<sup>nd</sup> Jan 2019)



24<sup>th</sup> April 2019



Baseline disease included multiple c/sc deposits up to 4cm, 5-13mm lung & liver mets, multiple intra-abdominal up to 2cm.

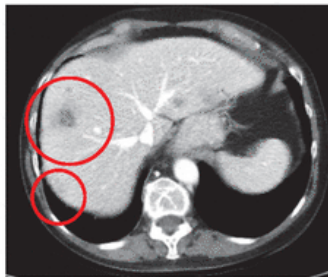
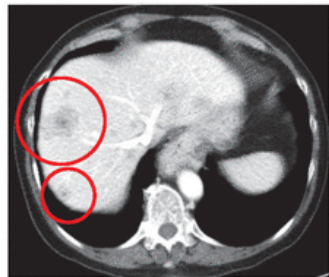
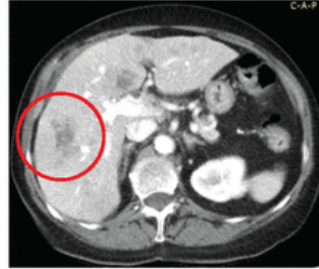
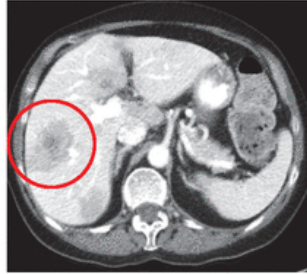
Initial response in numerous c/sc deposits, including uninjected (some biopsied showing no remaining residual tumor) and large scalp lesion. Other disease stable.

Treatment discontinued 20<sup>th</sup> Nov 2019 (new brain lesions).



25<sup>th</sup> Sept  
2019  
(Screening)

3<sup>rd</sup> April  
2020



- Patient with extensive disease in the liver
- 27.3% reduction by RECIST (unidimensional), 61% reduction by WHO (bi-dimensional)
- Treatment ongoing



## Safety of RP1 combined with Opdivo in patients with skin cancers

55

Treatment related treatment emergent adverse events (TEAEs) N=41				
Preferred term	Grade 1-2 (>15%) # (%)	Grade 3 (all) # (%)	Grade 4 (all) # (%)	Grade 5 (all) # (%)
Pyrexia	17 (41.5)	1 (2.4)	0	0
Chills	16 (39.0)	0	0	0
Influenza like symptoms	11 (26.8)	0	0	0
Fatigue	8 (19.5)	5 (12.2)	0	0
Decreased appetite		1 (2.4)	0	0
Dehydration		1 (2.4)	0	0
Hypotension		1 (2.4)	0	0
Lipase Increased		1 (2.4)	0	0
Localised oedema		1 (2.4)	0	0
Lymph node pain		1 (2.4)	0	0
Oedema		1 (2.4)	0	0
Rash		1 (2.4)	0	0
Seroconversion test positive		1 (2.4)	0	0
Total	34 (82.9)	8 (19.5)	0	0
Patients who discontinued due to TEAE		4 (9.8)		

- Patients in the melanoma & NMSC phase 2 cohorts treated with RP1 combined with Opdivo as of 1<sup>st</sup> May 2020
- There continues to be a good safety profile, with most AE's being Grade 1/2 constitutional-type symptoms
- Injections into visceral tumors practical and well tolerated, with clinical activity seen

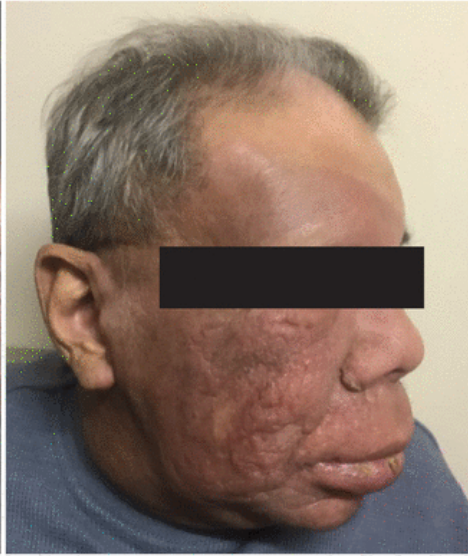
## RP1 in other tumor types

## Activity in a patient with angiosarcoma (ongoing PR)

57



6<sup>th</sup> November 2019



18<sup>th</sup> February 2020

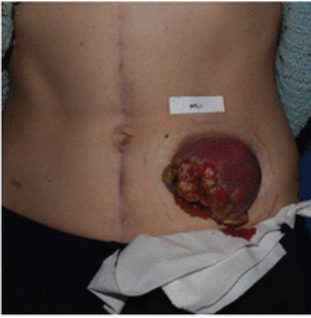
- Patient withdrew from treatment due to Opdivo side effects

 Replimune

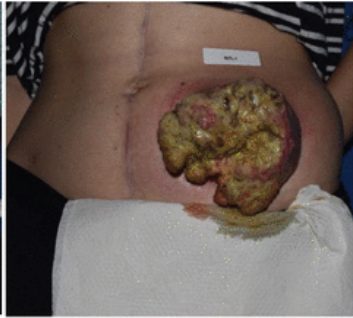
## MSI-H colorectal cancer

58

- 22 year old female with MSI-H rectal cancer
- Prior neoadjuvant FOLFOXIRI
- Treated with RP1 combined with Opdivo
- Ongoing PR
- Biopsy "No tumour present - strips of dysplastic epithelium and inflammatory exudate only"



9<sup>th</sup> October 2019



20<sup>th</sup> November 2019



15<sup>th</sup> January 2020



25<sup>th</sup> March 2020

## MSI-H colorectal cancer

59

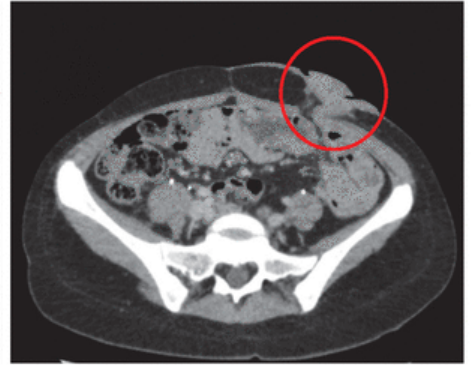
- Latest scan (March 2020) shows 87% reduction (including of uninjected abdominal disease)



4<sup>th</sup> Dec 2019 (C5)



29<sup>th</sup> Jan 2020 (C8)



25<sup>th</sup> March 2020 (C11)

## Esophageal cancer

60

- Heavily pre-treated esophageal cancer (8 prior therapies)
- Lung lesions & lesions around the esophagus.
- Treated with RP1 combined with Opdivo
- Ongoing PR at 10 months



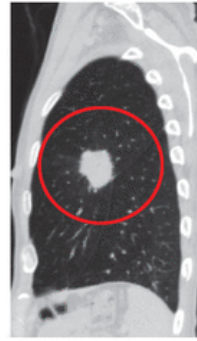
Baseline



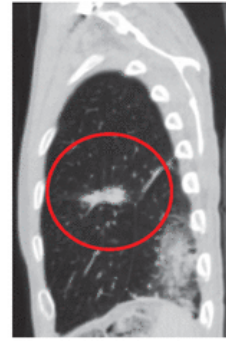
C5



C11

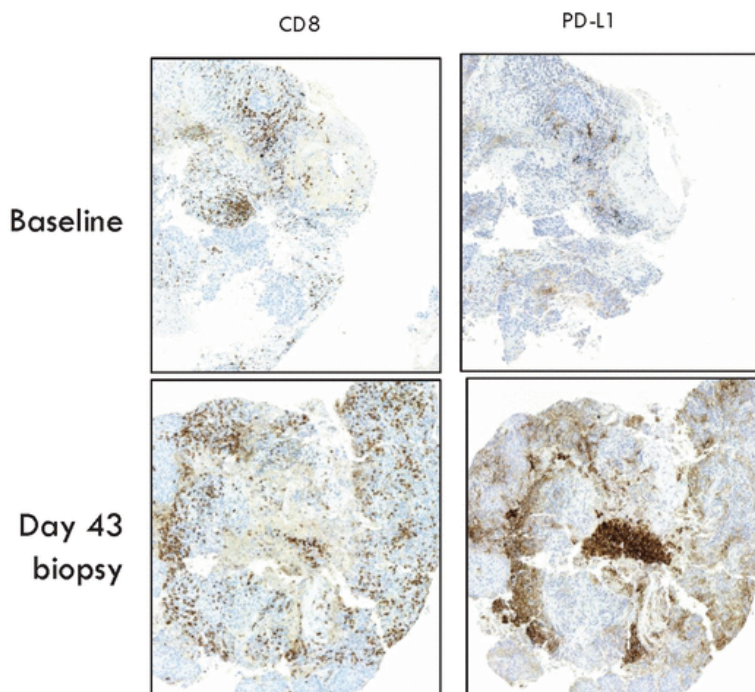


Baseline



C11

# Esophageal cancer: CD8 T cell & PD-L1 staining





## New cohort in anti-PD1 refractory NSCLC & termination of bladder cohort

62

- Due to the changing competitive landscape in bladder cancer Replimune has elected to direct resources to a new high-value target & terminate the enrollment of the bladder cancer cohort
- Anti-PD1 refractory NSCLC is an area of considerable un-met need, with no SOC/viable options
- RP1 combined with Opdivo has demonstrated the ability to shrink lung metastases
- RP1 combined with Opdivo shows activity in anti-PD1 refractory melanoma
- RP1 has been administered safely into lung tumors in multiple patients using imaging guidance
- The lung is an 'immune responsive' site
- Agreed with BMS to 'swap in' an anti-PD1 relapsed/refractory NSCLC cohort in place of the bladder cancer cohort





## **Beyond immune responsive tumor types: RP2 & RP3**

## RP2 & RP3: anti-CTLA-4 & co-stimulatory pathway agonist delivery

64

- Focus on delivery of proteins which act as the immune response is being generated
  - Systemic antibody approaches probably don't act at the right place or the right time
  - Potential for toxicity



- Delivery of anti-CTLA-4 directly into the tumor
  - Blocks Treg activation/inhibition of T cell activation at the site of immune response initiation
  - Retain the efficacy of Yervoy alone & in combination with anti-PD1 but reduce toxicity
    - Phase 1 trial alone & combined with Opdivo underway – initial data expected late 2020



- Delivery immune co-stimulatory pathway activating ligands
- RP3 encodes anti-CTLA-4, CD40L & 4-1BBL
  - CD40L: Broadly activates both innate & adaptive immunity
  - 4-1BBL: Promotes the expansion of cellular & memory immune responses
  - Phase 1 trial alone & combined with anti-PD1 expected to initiate this year



## Conclusions from today's data: "Building the Second Cornerstone of IO"

65

- **RP1 - CSCC**
  - Significant expected commercial opportunity
  - Clear path to market
  - Frequency of CRs provides clear differentiation to anti-PD1 alone
  - Biomarkers (CD8 T cells & PD-L1) supportive
- **RP1 - Anti-PD1 refractory melanoma**
  - Significant expected commercial opportunity
  - Clear activity in Yervoy/Opdivo failed patients, including with extensive visceral disease
  - Biomarkers (CD8 T cells & PD-L1) supportive
  - Activity also seen in mucosal & uveal melanoma patients
- **RP1 - Early indications of activity seen beyond skin cancers**
- **Clinical testing of RP1 combined with Opdivo in anti-PD1 refractory NSCLC planned**



## Looking ahead: Targeted milestones for the remainder of 2020\*

66

- **RP1 - CSCC**
  - Complete recruitment of 30 patient NMSC cohort with Opdivo
  - Present data from first patients dosed in single agent transplant study
  - Plan for neoadjuvant study
- **RP1 - Anti-PD1 refractory melanoma**
  - Discuss potential path to market with FDA
  - Report mature data set from 30 patient completed cohort with Opdivo
- **RP1 - Finalize planning for anti-PD1 refractory NSCLC cohort**
- **RP2 - Initial data from phase 1 trial of RP2 alone & combined with nivolumab**
- **RP3 - Phase 1 clinical trial to initiate**

\*COVID-19 has impacted & is expected to continue to impact accrual & therefore the number of patients from whom data is expected to be available during 2020, with average expected length of follow up also expected to be reduced.



## **Replimune Provides RP1 Data Update from its Phase 2 Cohorts in Melanoma and Non-Melanoma Skin Cancer that Strongly Support Replimune's Ongoing Registration-Directed Clinical Trials with RP1**

*Multiple Complete Responses Observed in Advanced Cutaneous Squamous Cell Carcinoma*

*High Rate of Deep Responses in Anti-PD-1 / Anti-CTLA-4 Refractory Melanoma*

*Announces Intention to Commence Clinical Development in Anti-PD-1 Refractory Non-Small Cell Lung Cancer*

**Woburn, MA, June 3, 2020** – Replimune Group, Inc. (Nasdaq: REPL), a biotechnology company developing oncolytic immuno-gene therapies derived from its Immulytic™ platform, today announced new interim data presented from the Phase 2 part of its Phase 1/2 clinical trial of RP1 in combination with Opdivo® that continues to provide strong support for its lead indications of cutaneous squamous cell carcinoma (CSCC) and anti-PD-1 refractory melanoma.

“CSCC is a significant commercial opportunity that we believe has the potential to drive substantial value for the company. The number of complete responses (CRs) observed is highly suggestive that our combination approach with RP1 can provide better patient outcomes compared to anti-PD-1 therapy alone, where CRs are infrequent,” said Philip Astley-Sparke, CEO of Replimune. “In anti-PD-1 refractory melanoma, we believe we also have a strong efficacy signal and are optimistic that our currently-enrolling 125 patient cohort could generate data to support regulatory approval, pending feedback from the U.S. Food and Drug Administration (FDA) and other regulatory agencies. We are also excited to be moving to evaluate RP1 in anti-PD-1 refractory non-small cell lung cancer (NSCLC), given the large unmet need in this tumor type. We believe we have established clinical proof of principle with RP1 in immune-responsive tumor types and in anti-PD-1 refractory cancers, and now have a solid foundation upon which to establish our product candidates more broadly as the second cornerstone of immuno-oncology.”

**New interim clinical data in CSCC from the enrolling 30 patient non-melanoma skin cancer cohort evaluating RP1 in combination with Opdivo continues to strongly support the Company's registration-directed clinical trial of RP1 in combination with Libtayo®**

Overall, four of seven evaluable patients have ongoing CRs and six of seven have an ongoing CR or partial response (PR) (compared to one out of five patients and two out of five, respectively, as presented at the Society for the Immunotherapy of Cancer meeting in November 2019). The data continues to demonstrate that RP1 in combination with Opdivo is well-tolerated, demonstrates immune activation and continues to drive deep and durable responses in patients with CSCC. Furthermore, the number of CRs observed to date in advanced CSCC patients with aggressive disease treated with RP1 in combination with anti-PD-1 provides clear differentiation versus anti-PD-1 therapy alone, which we believe provides the Company strong validation of its clinical development plan.

---

“The data in patients with CSCC treated with RP1 in combination with Opdivo has continued to strengthen since it was last presented at the SITC conference in November 2019, with PRs converting to CRs, providing patients with the potential for cure, and with further responses observed, including CRs,” said Professor Kevin Harrington, PhD, Professor in Biological Cancer Therapies at The Institute of Cancer Research, London, and Consultant Clinical Oncologist at The Royal Marsden NHS Foundation Trust in the UK. “RP1 in combination with anti-PD-1 therapy therefore appears to be highly active for the treatment of CSCC, both in patients with advanced loco-regional disease, which is the main cause of death in patients with CSCC, and in patients with distant metastatic disease, with the potential to provide a highly effective new therapeutic option for these patients.”

The Company’s registration-directed Phase 2 clinical trial (CERPASS) in CSCC is a multi-center, randomized, controlled clinical trial intended to enroll approximately 240 patients. The primary objective is to compare the response rate following treatment with RP1 in combination with Libtayo versus Libtayo alone. Libtayo is an anti-PD-1 therapy developed by Regeneron and Sanofi and was approved by the FDA last year for the treatment of patients with metastatic or locally advanced CSCC who are not candidates for curative surgery or radiation. This clinical trial is being conducted under the Company’s collaboration agreement with Regeneron. Multiple clinical trial sites in the United States and Australia are open for enrollment. Additional clinical trial sites in these and other countries will be added, with recruitment expected to take approximately 18 to 24 months.

A clinical trial of single-agent RP1 in organ transplant recipients with CSCC is also open for enrollment. This clinical trial is intended to enroll approximately 30 patients and assess the safety and efficacy of RP1 in liver and kidney transplant recipients with recurrent CSCC. Anti-PD-1 therapy is not indicated for solid organ transplant recipients due to the risk of rejection of the transplanted organ.

**New interim clinical data in anti-PD-1 refractory melanoma from the fully accrued 30 patient melanoma cohort testing RP1 in combination with Opdivo continues to strongly support the Company’s registrational approach**

Overall, 36 melanoma patients have been treated in the Phase 1/2 clinical trial of RP1 in combination with Opdivo, of which there were 6 patients in the Phase 1 expansion cohort and 30 patients in the Phase 2 cohort. Sixteen anti-PD-1 refractory cutaneous melanoma patients have been treated. An additional eight patients with anti-PD-1 naïve cutaneous melanoma and 12 patients with uveal or mucosal melanoma (both anti-PD-1 naïve and refractory) have also been enrolled. Initial results from this immature data set (the final patient was enrolled in January 2020) in the anti-PD-1 refractory cutaneous melanoma patients showed:

- Five patients so far have met the formal criteria for response; four of which had previously failed both anti-PD-1 and anti-CTLA-4 therapies
- Two further patients remain on treatment with the opportunity for response
- The minimum final objective response rate (ORR) for these patients will therefore be 31%

The majority of melanoma patients treated with anti-PD-1 therapy have primary resistance, or acquire resistance to checkpoint blockade drugs following initial response. The clear activity of RP1 in anti-PD-1 refractory patients, including in patients with extensive visceral disease, represents a new potential therapeutic option for these patients. Based on the initial efficacy data with RP1 in melanoma, the Company initiated a registration-directed 125-patient cohort of anti-PD-1 refractory melanoma in the Phase 2 clinical trial of RP1 in combination with Opdivo in the first quarter of 2020. The additional cohort is being enrolled under an expansion of the clinical trial collaboration and Opdivo supply agreement with Bristol Myers Squibb (BMS).

Clinical data from the additional patients with anti-PD-1 naïve cutaneous melanoma, mucosal melanoma and uveal melanoma are also supportive of the clinical activity of RP1 in combination with Opdivo. This includes eight patients with anti-PD-1 naïve cutaneous melanoma, six patients with mucosal melanoma and six patients with uveal melanoma.

- Anti-PD-1 naïve cutaneous melanoma (N=8): Four patients so far have met the formal definition of response with two further patients remaining on treatment with the opportunity for response
- Mucosal melanoma (N=6): Two patients (one anti-PD1 naïve, one having had prior anti-PD-1) have met the formal definition of response
- Uveal melanoma (N=6): Two patients with extensive liver disease are responding to treatment, both refractory to combined Opdivo and Yervoy<sup>®</sup>, one so far having a 27.3% reduction by RECIST criteria uni-dimensional measurement and 61% reduction by WHO criteria bi-dimensional measurement

“Responses to RP1 in combination with Opdivo in patients with difficult to treat melanomas who have failed both anti-PD-1 and anti-CTLA-4 would not have been expected for those receiving a second line of anti-PD1 alone,” said Mark Middleton, Professor of Experimental Cancer Medicine in the Department of Oncology, consultant Medical Oncologist at the Oxford Cancer and Haematology Centre and Head of the Department of Oncology at the University of Oxford. “The clinical activity of RP1 in combination with Opdivo in these patients appears robust, with the overall safety profile suggesting no additional toxicities compared to anti-PD1 therapy alone.”

The data from this clinical update can be found in the presentation linked [here](#).

Based on the emerging data indicating that RP1 can be safely administered to tumors in the lung and that evidence of activity, including in anti-PD1 refractory disease, has been observed in patients with lung metastases of other tumor types, the Company announced its intention to enroll a thirty patient cohort of patients with anti-PD1 refractory NSCLC in the Phase 2 clinical trial of RP1 in combination with Opdivo, subject to approval of a protocol amendment by the regulatory authorities. The Company also announced that it plans to terminate the enrollment of the cohort of patients with metastatic bladder cancer in light of changes to the competitive landscape.

#### **Investor event and webcast information**

Replimune will host a virtual investor event today, Wednesday, June 3, 2020 at 8:00 a.m. ET. The webcast and accompanying slides will be available under “[Events and Presentations](#)” in the [Investors and Media section](#) of the company’s website at [www.replimune.com](http://www.replimune.com). Alternatively, audience members may listen to the call by dialing (833) 651-0806 from locations in the United States and (918) 922-6072 from outside the United States. The conference ID number is 4268503. An archived webcast recording of the event will be available on the website for approximately 30 days.



## **About CSCC**

CSCC is the second most common form of skin cancer and is estimated to be responsible for at least 7,000 deaths each year in the United States. It currently accounts for approximately 20% of all skin cancers in the United States, with the number of newly diagnosed cases expected to rise annually. When CSCC invades deeper layers of the skin or adjacent tissues, it is categorized as locally advanced. Once it spreads to other distant parts of the body, it is considered metastatic. Libtayo<sup>®</sup> is the only approved therapy in the United States and Brazil, and conditionally approved therapy in the European Union and Canada, for the treatment of locally advanced or metastatic CSCC.

## **About Melanoma**

Melanoma is a form of skin cancer characterized by the uncontrolled growth of pigment-producing cells (melanocytes) located in the skin. Metastatic melanoma is the deadliest form of the disease and occurs when cancer spreads beyond the surface of the skin to other organs. The incidence of melanoma has been increasing steadily for the last 30 years. In the United States, 91,270 new diagnoses of melanoma and more than 9,320 related deaths are estimated for 2018. Globally, the World Health Organization estimates that by 2035, melanoma incidence will reach 424,102, with 94,308 related deaths. Melanoma is mostly curable when treated in its very early stages; however, survival rates are roughly halved if regional lymph nodes are involved.

## **About RP1**

RP1 is Replimune's lead Immulytic<sup>™</sup> product candidate and is based on a proprietary new strain of herpes simplex virus engineered 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 to develop the next generation of oncolytic immuno-gene therapies for the treatment of cancer. Replimune is developing novel, proprietary therapeutics intended to improve the direct cancer-killing effects of selective virus replication and the potency of the immune response to the tumor antigens released. Replimune's Immulytic<sup>™</sup> platform is designed to maximize systemic immune activation, in particular to tumor neoantigens, through robust viral-mediated immunogenic tumor cell killing and the delivery of optimal combinations of immune-activating proteins to the tumor and draining lymph nodes. The approach is expected to be highly synergistic with immune checkpoint blockade and other approaches to cancer treatment. Replimune intends to progress these therapies rapidly through clinical development in combination with other immuno-oncology products with complementary mechanisms of action. For more information, please visit [www.replimune.com](http://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 the advancement of our clinical trials, our plans to initiate new clinical trials, our goals to develop and commercialize our product candidates, our expectations regarding commercialization of our product candidates, our expectations regarding the size of the patient populations for our product candidates if approved for commercial use, patient enrollments in our existing and planned clinical trials and the timing thereof, our expectations with respect to our own in-house manufacturing capabilities, 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 of operating our in-house manufacturing facility, the timing and scope of regulatory approvals, 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 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.

### **Investor Inquiries**

Chris Brinzey  
Westwicke, an ICR Company  
339.970.2843  
chris.brinzey@westwicke.com

### **Media Inquiries**

Arleen Goldenberg  
Verge Scientific Communications  
917.548.1582  
agoldenberg@vergescientific.com