



# Igniting a Systemic Immune Response to Cancer

May 2023



## 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, timing and sufficiency 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, statements regarding our expectations about our cash runway, 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, the ongoing military conflict between Russia and Ukraine and the impact on the global economy and related governmental imposed sanctions, 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.

# Replimune overview



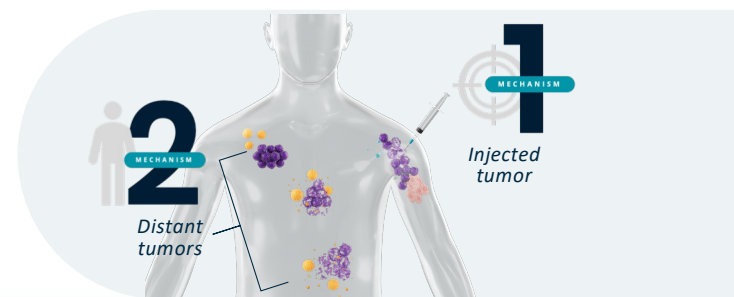
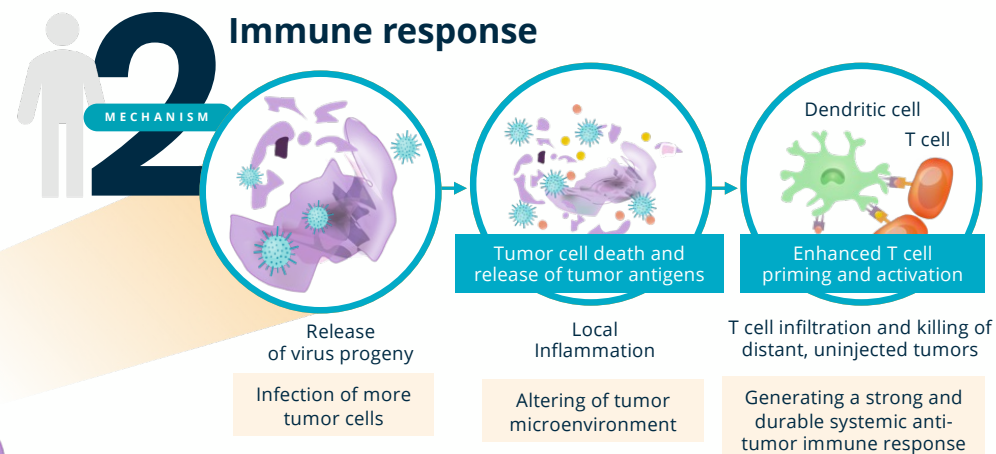
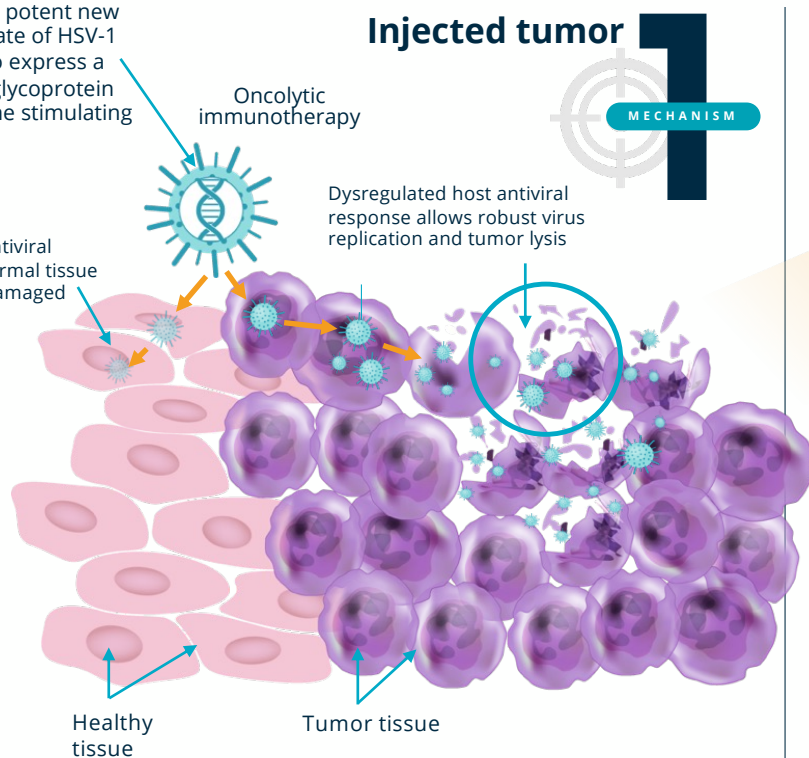
- Industry leader in tumor directed oncolytic immunotherapy (TDOI)
  - Potential to be a cornerstone treatment in immuno-oncology; 3 wholly owned programs (RP1-3)
- RP1 data supports the emergence of a major skin cancer franchise; two registrational studies ongoing
  - 211 patient 1L CSCC randomized controlled study fully enrolled; primary analysis Q3 2023
    - 47% CR rate / 65% ORR with strong durability in prior study
  - 141 patient study in anti-PD1 failed melanoma fully enrolled
    - 20% CR rate / 36% ORR in first 75 patients with activity across all disease stages and strong durability
- Broad mid-stage development planned with RP2/3 ; responses shown in multiple unmet need indications
  - Several potential fast to market opportunities
    - Cost sharing collaboration announced with Roche in 3L CRC and 2L HCC
- Potential for the portfolio to deliver substantial commercial revenues beginning in 2025
- Capitalized to build a fully integrated biotech company; US commercial infrastructure, in-house manufacturing
  - December 31 2022, cash & short-term investments c. \$616m

# Tumor directed oncolytic immunotherapy mechanism of action



Attenuated potent new clinical isolate of HSV-1 modified to express a fusogenic glycoprotein and immune stimulating proteins








Intact host antiviral response: Normal tissue remains undamaged





# RPx positioning: Platform designed to address a range of tumor types with an optimal balance of potency & safety



			
<b>Payloads</b>	GALV-GP R-, GM-CSF	GALV-GP R-, anti-CTLA-4, GM-CSF	GALV-GP R-, anti-CTLA-4, CD40L, 4-1BBL
<b>Target</b>	Immunologically responsive tumor types, including anti-PD1 failed	Less immunologically responsive tumor types	Less immunologically responsive tumor types (anticipated further improved compared to RP2)
<b>Intended indication(s)</b>	Skin cancers (CSCC, anti-PD1 failed melanoma, anti-PD1 failed CSCC, other NMSCs, etc)	Various solid tumors including primary liver cancers and/or those with a high prevalence of liver metastases e.g. HCC, CRC; Early disease (neoadjuvant/LA opportunities) e.g. SCCHN	
<b>Clinical activity in anti-PD1 failed patients demonstrated</b>			Ongoing
<b>Safety &amp; good tolerability demonstrated</b>			Ongoing
<b>Injection location</b>	Superficial, nodal & visceral	Superficial, nodal & visceral	Superficial, nodal & visceral
<b>Systemic activity</b>	<b><i>Clear systemic effects seen in responding patients (un-injected tumor responses, responses are generally highly durable)</i></b>		Ongoing
<b>Other design considerations</b>	Designed for more I-O sensitive tumor types with excellent safety alone & in combination	Increased I-O systemic activity, also with excellent safety alone & in combination	Designed to maximize systemic I-O activity & potency

# RP1: Establishing a major skin cancer franchise

## AGENDA



# Establishing a broad skin cancer franchise



1	<b>IGNYTE anti-PD1-failed melanoma registrational cohort</b> <i>N=125</i>	Impressive response rate in first 75 patients, 20% CR rate, 36% ORR, full data with 6 month follow up expected Q4 2023
2	<b>CERPASS – first-line CSCC randomized controlled pivotal trial</b> <i>N=211</i>	Fully accrued, primary data Q3 2023; 47% CR rate and 65% ORR in prior study (N=17) <b>Initial approval sought in anti-PD1 naïve CSCC</b>
3	<b>IGNYTE initial NMSC cohort (anti-PD1 naïve)</b> <i>N=30 (fully accrued)</i>	Demonstrated activity in other NMSCs; Commercialization in MCC, BCC, angiosarcoma likely to be based on compendia listing
4	<b>IGNYTE anti-PD1-failed NMSC cohort</b> <i>N=30</i>	With signal can expand for registrational purposes; label expansion ; 33% ORR to date (N=12)
5	<b>ARTACUS skin cancers in solid organ transplant recipients</b> <i>N=65</i>	Potential registration or compendia listing ; 33% ORR to date as monotherapy (N=6)
6	<b>Neoadjuvant CSCC</b>	<i>Study being planned: expected to capture significant high- risk patient population</i>

- RP1 establishes confidence in easy-to-administer settings
- Deep and durable responses across multiple settings in skin cancer, including high CRs in 1L CSCC
- Responses in anti-PD1-failed patients with melanoma & a range of NMSCs
- Development to provide proof-of-concept in neoadjuvant setting

# IGNYTE melanoma data: 36% ORR in first 75 patients

RP1 plus nivo in anti-PD1 failed melanoma 125 patient registration study



	N=16	N=75	N=91					
	Prior patients N=16 n(%)	Data snapshot patients N=75 n(%)	All patients N=91 n(%)	Prior adjuvant anti-PD1 only N=30 n(%)	Prior anti-PD1 other than adjuvant N=61 n(%)	Prior anti-PD1 & anti-CTLA4 N=31 n(%)	Stage IIIb/IIIc/IVa N=44 n(%)	Stage IVb/IVc N=47 n(%)
<b>Best Overall Response</b>								
CR	2 (12.5%)	15 (20.0%)	17 (18.7%)	9 (30.0%)	8 (13.1%)	2 (6.3%)	13 (29.5%)	4 (8.5%)
PR	4 (25.0%)	12 (16.0%)	16 (17.5%)	6 (20.0%)	10 (16.4%)	7 (21.9%)	7 (15.9%)	9 (19.1%)
SD	1 (6.3%)	13 (17.3%)	14 (15.4%)	7 (23.3%)	7 (11.5%)	5 (15.6%)	6 (13.6%)	8 (17.0%)
PD	8 (50.0%)	32 (42.7%)	40 (44.0%)	8 (26.7%)	32 (52.5%)	14 (43.8%)	18 (40.9%)	22 (46.8%)
<b>ORR</b>	<b>6 (37.5%)</b>	<b>27 (36.0%)</b>	<b>33 (36.3%)</b>	<b>15 (50.0%)</b>	<b>18 (29.5%)</b>	<b>9 (29.0%)</b>	<b>20 (45.5%)</b>	<b>13 (27.7%)</b>
DCR (CR+PR+SD)	7 (43.8%)	40 (53.3%)	47 (51.6%)	22 (73.3%)	25 (41.0%)	14 (45.2%)	26 (59.1%)	21 (44.7%)

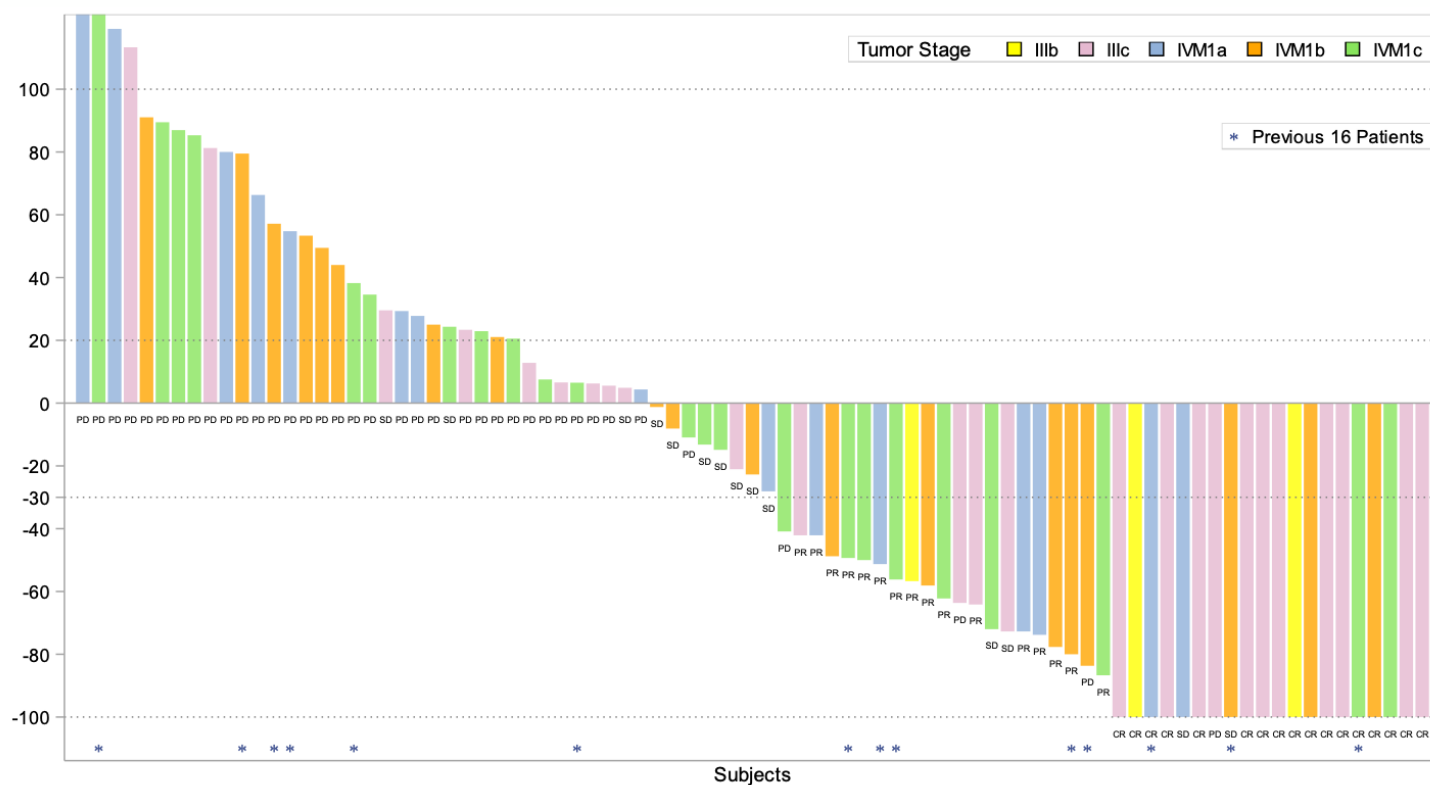
## Key Snapshot Takeaways

- Data from the 75 patient snapshot are consistent with the 16 patients enrolled into the prior melanoma cohort
  - majority of patients were primary refractory to anti-Pd1
- At least 27.7% ORR in all sub-groups analyzed
- Particularly high ORR (50%) and CR rate (30%) in patients who progressed while on prior adjuvant anti-PD1 therapy

Investigator assessed responses: The primary analysis for the 15 patient cohort will be by central review

# Waterfall plots: All patients

Maximum change in target lesions; patients with at least one follow up assessment

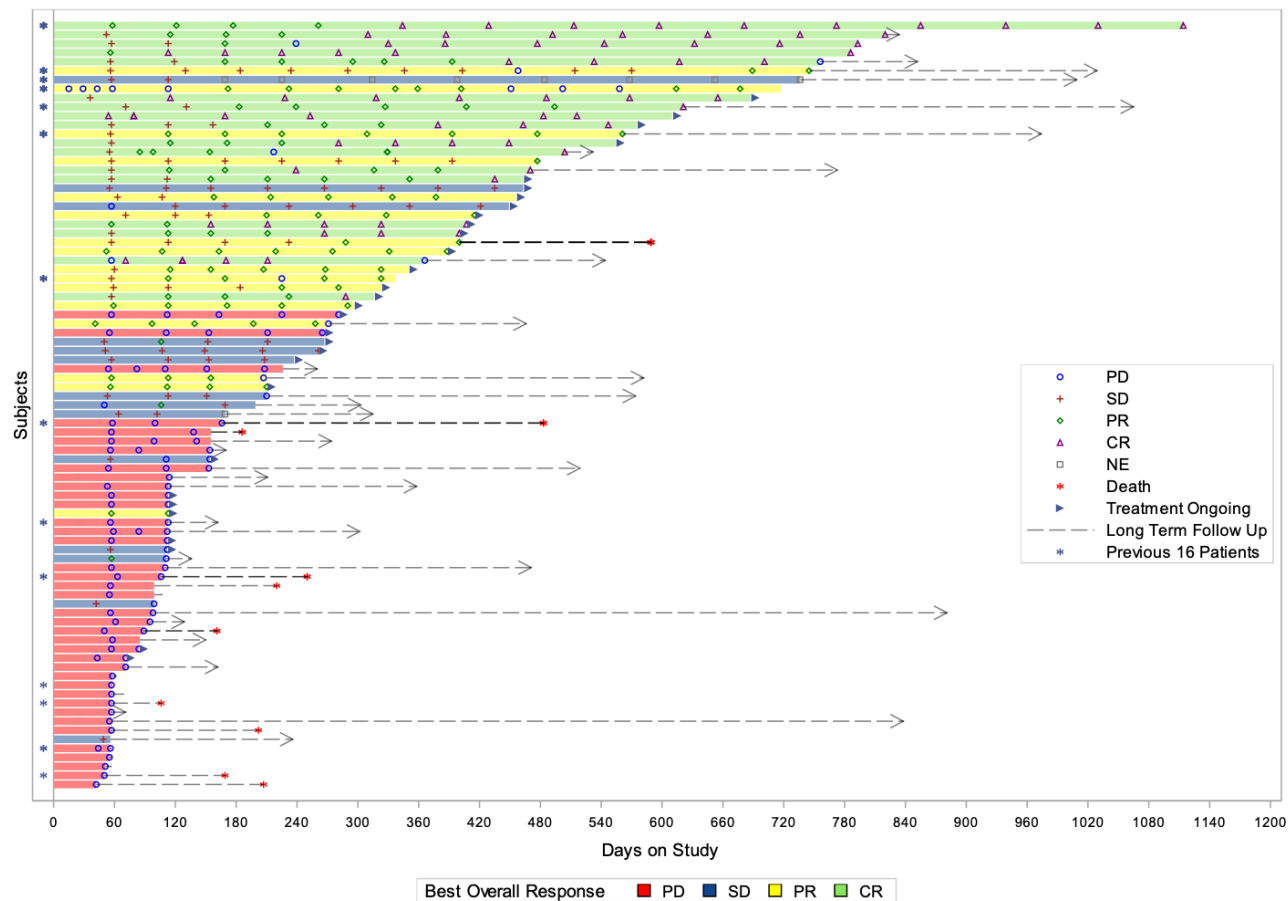


## Key Takeaways

- >50% of patients have target (RECIST) tumor reduction
- Deep responses observed
- Includes CRs in patients with Stage IV M1b/c disease

# Swimmer's plots: All patients

Patients with at least one follow up assessment



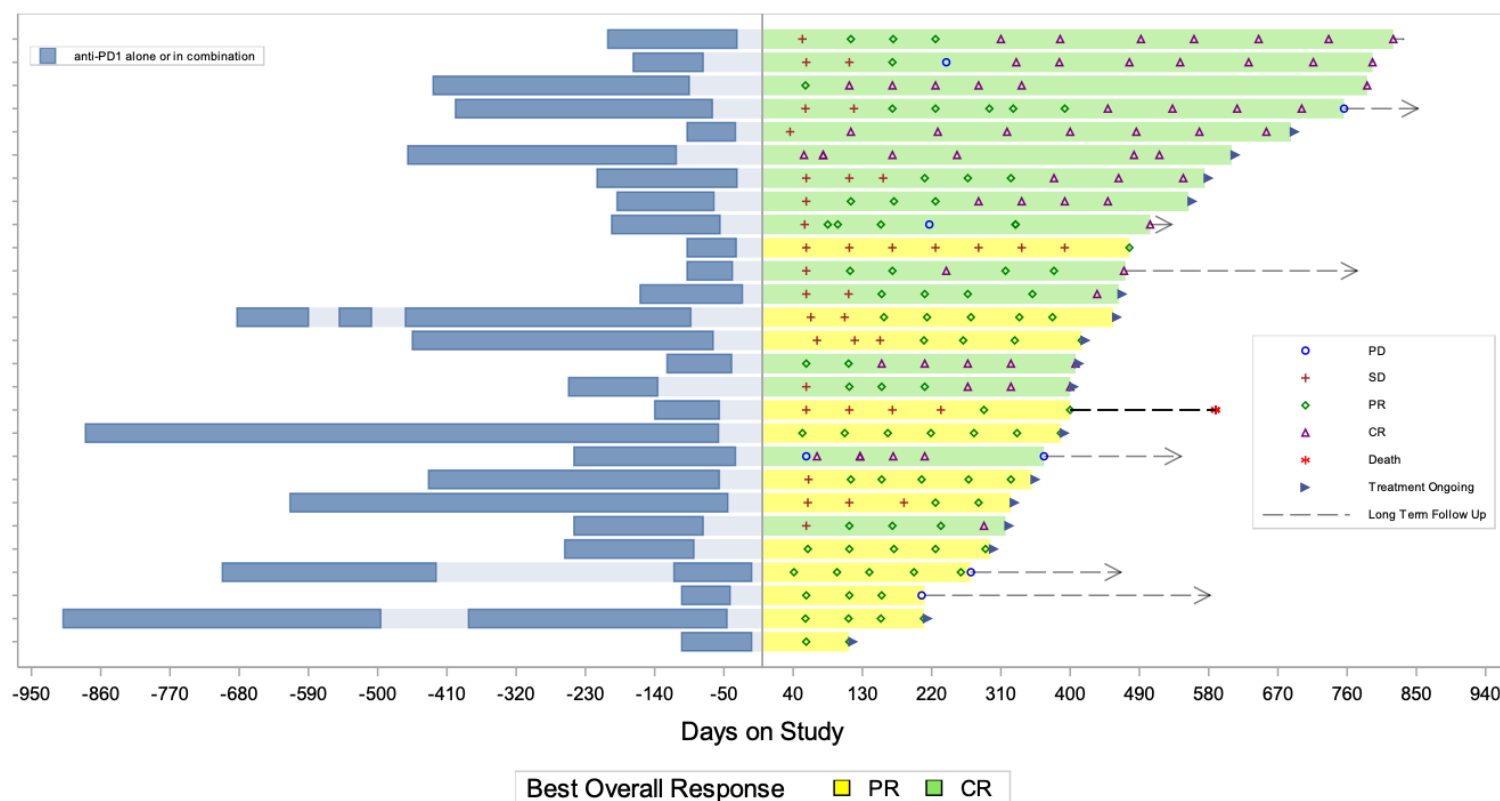
## Key Takeaway

Responses are durable, indicating systemic overall benefit

- 85% of responses are ongoing
- 59% of responders are already out over one year despite immature data



# Timing and duration of prior anti-PD1 therapy for new responding patients



## Key Takeaways

- Most responding patients progressed rapidly through prior anti-PD1 therapy
- 85% of responses are ongoing
- 59% of responders are already out over one year despite immature data

## Patient 1121-2011:

Prior Opdivo and Keytruda, Stage IV M1c



29 JUL 2021 / Screening



20 APRIL 2022



Injected

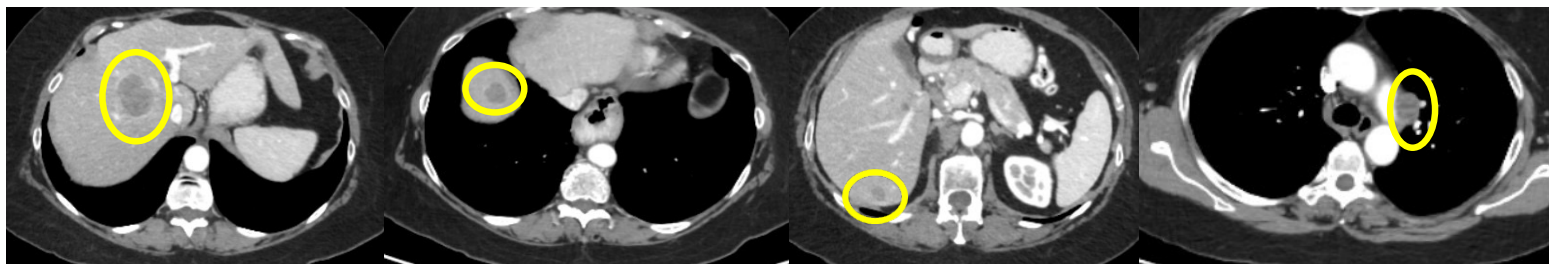


Un-injected

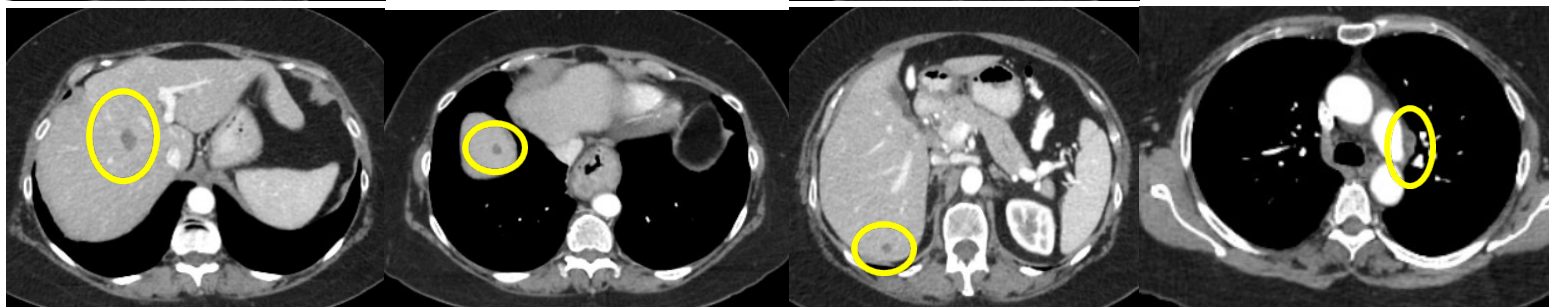
## Patient 1121-2011 Cont'd: Prior Opdivo, Keytruda: Stage IVM1c



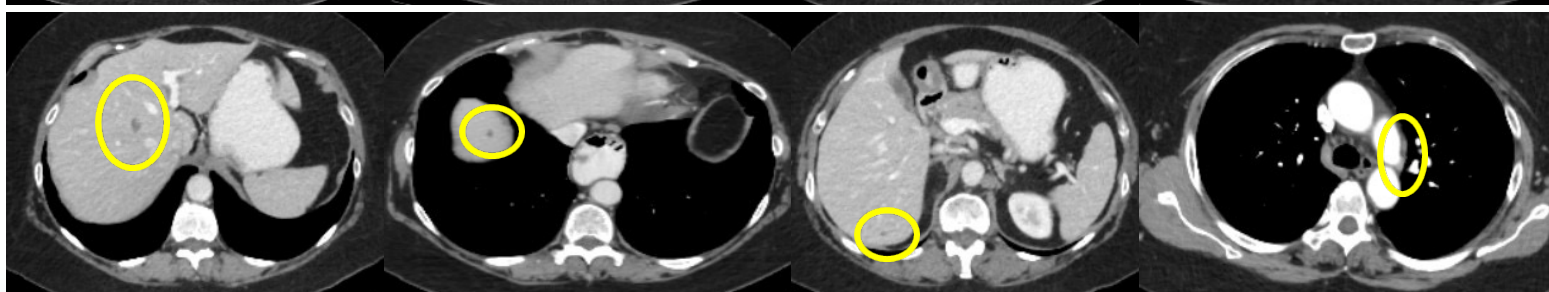
22 Jul 2021/  
Baseline



22 Sep 2021/  
Day 57



29 Dec 2021/  
Day 155



 Injected

 Un-injected

## Patient 4405-2007:

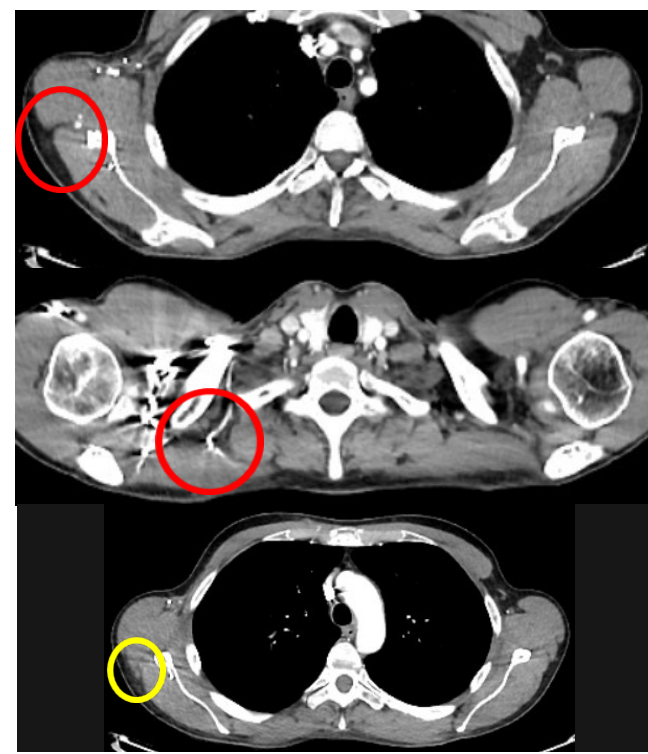
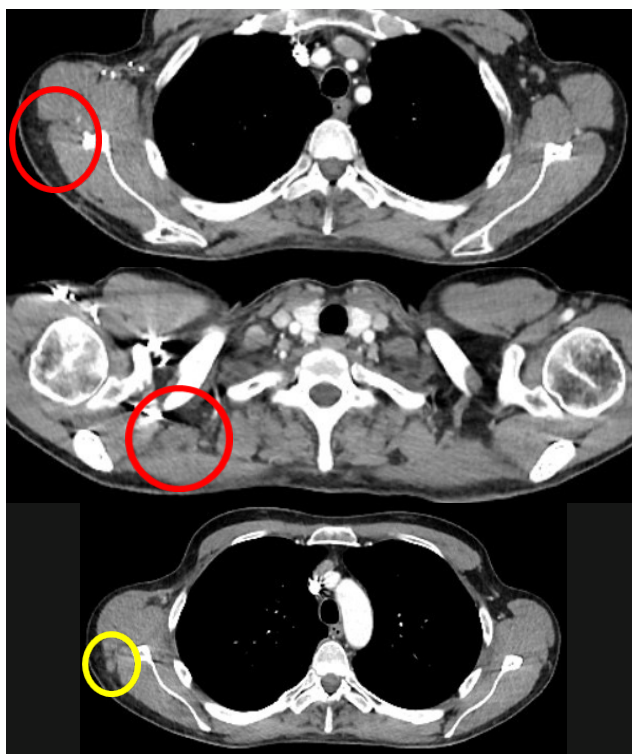
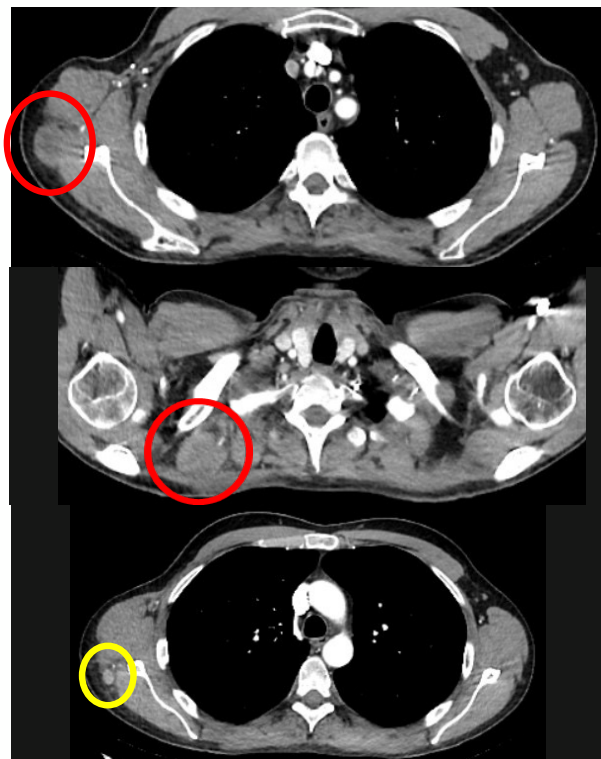
Prior Keytruda, Yervoy/Opdivo: Stage IV M1b



6 Aug 2021/Baseline

24 Jan 2022

31 Aug 2022



 Injected

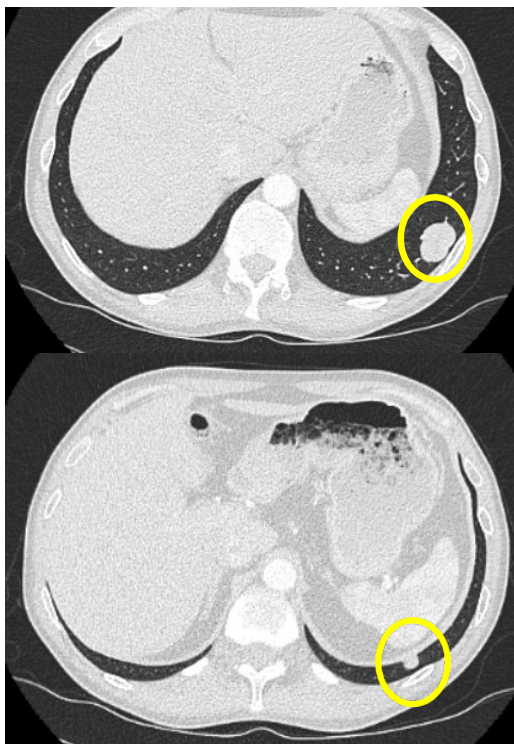
 Un-injected



## Patient 4405-2007 Cont'd: Prior Keytruda, Yervoy/Opdivo: Stage IV M1b



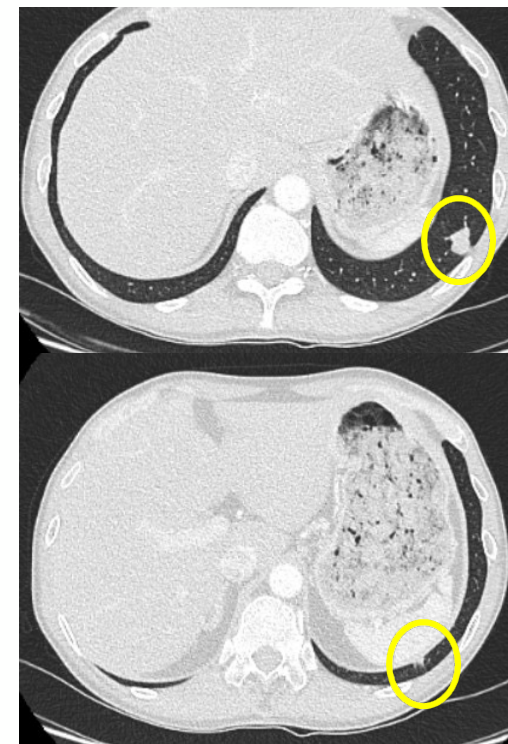
6 Aug 2021/Baseline



24 Jan 2022



31 Aug 2022



 Injected

 Un-injected

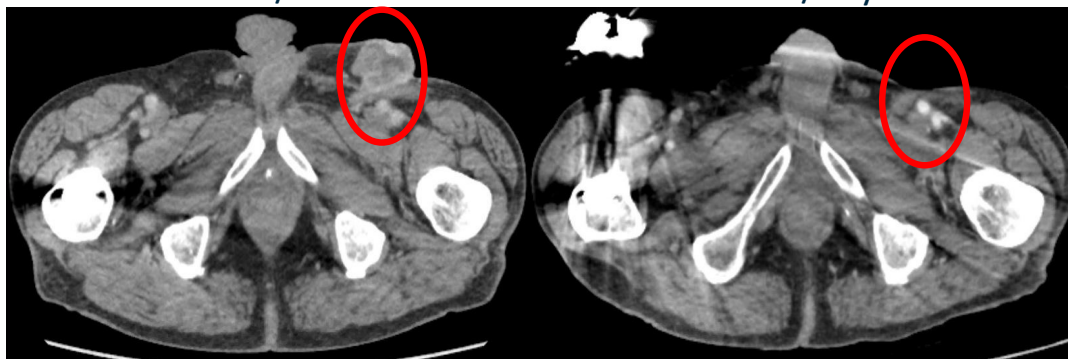
# Patient 4401-2021: Prior Tafenlar/Mekinist, Keytruda

Disease presentation type: Prior BRAF/MEK as well as progressed on anti-PD1 Stage IV M1c



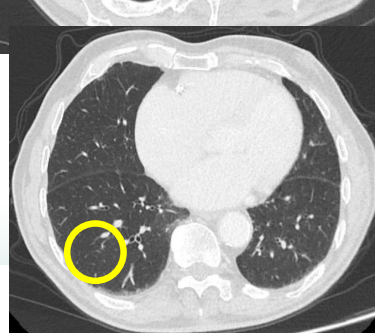
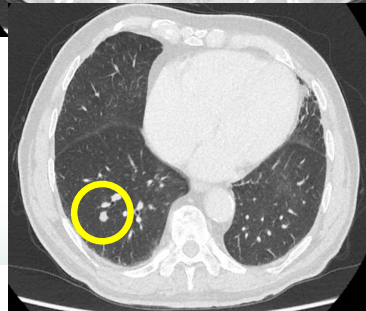
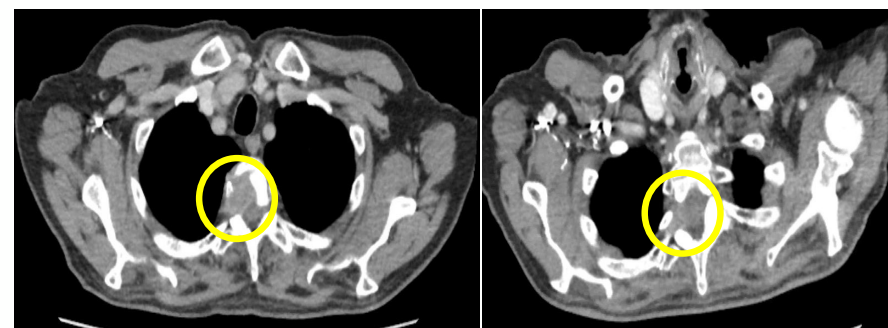
12JAN2021/Baseline

15FEB2022/Day 368



12JAN2021/Baseline

15FEB2022/Day 368



Injected

Un-injected

Data snapshot date: 3 Nov 2022

© 2022 Replimune Group Inc.

16



# Patient 3410-2001:

Prior adjuvant Keytruda: Stage IV M1a



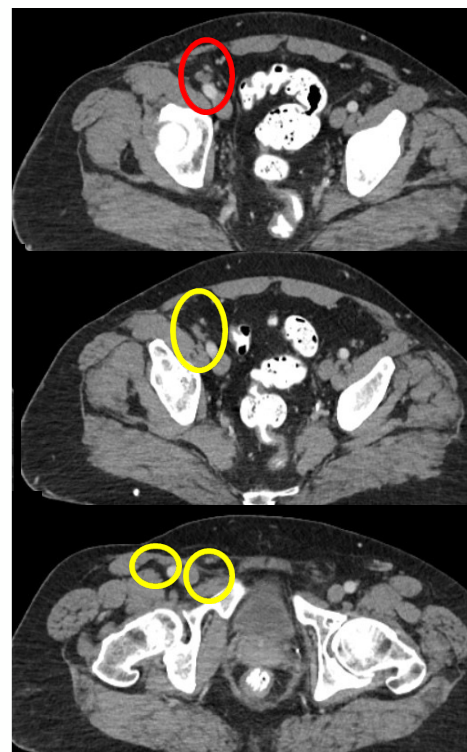
23SEP2021/Screen



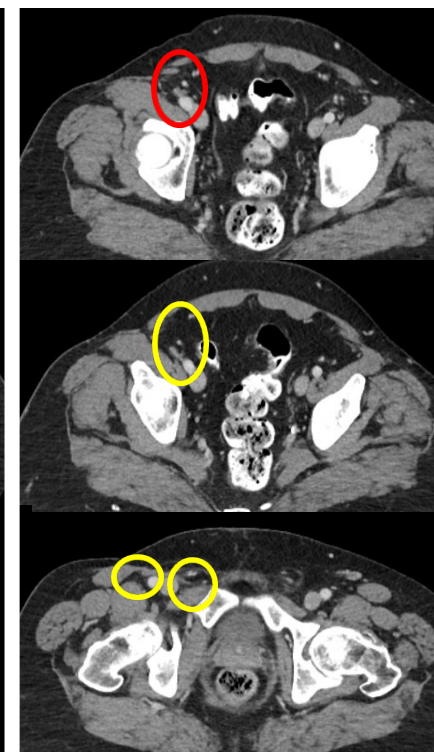
25JAN2022/Day 113



17MAY2022/Day 211



6SEP2022/Day 323



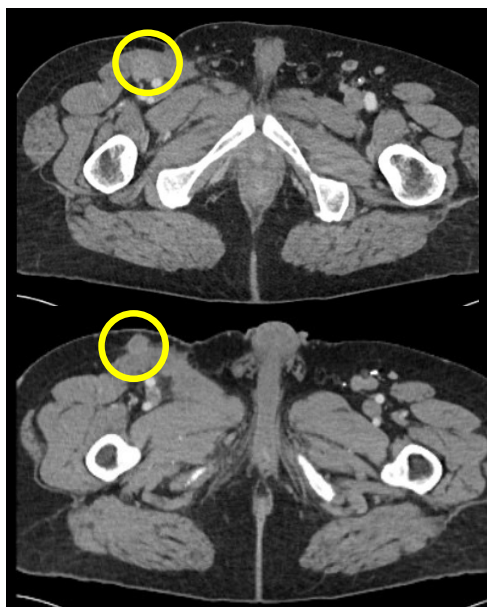
● Injected

● Un-injected

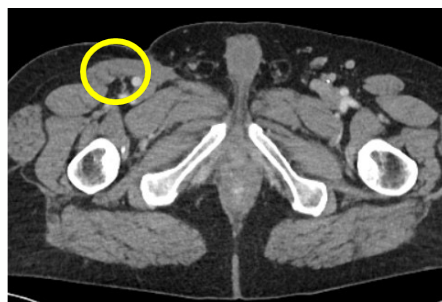
## Patient 3410-2001 Cont'd: Prior adjuvant Keytruda: Stage IV M1a



23SEP2021/Screen

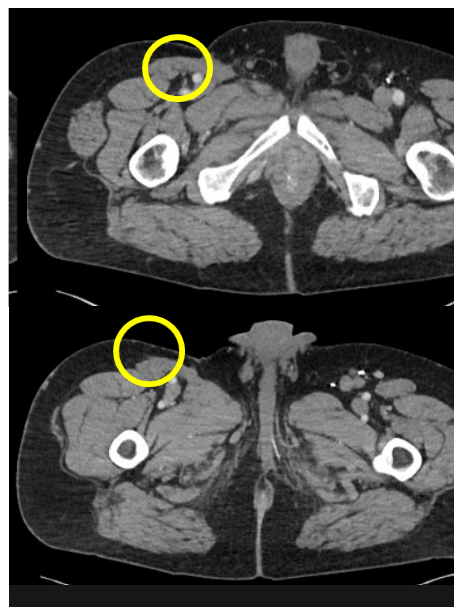


25JAN2022/Day 113



NOT IMAGED

17MAY2022/Day 211



6SEP2022/Day 323



NOT IMAGED

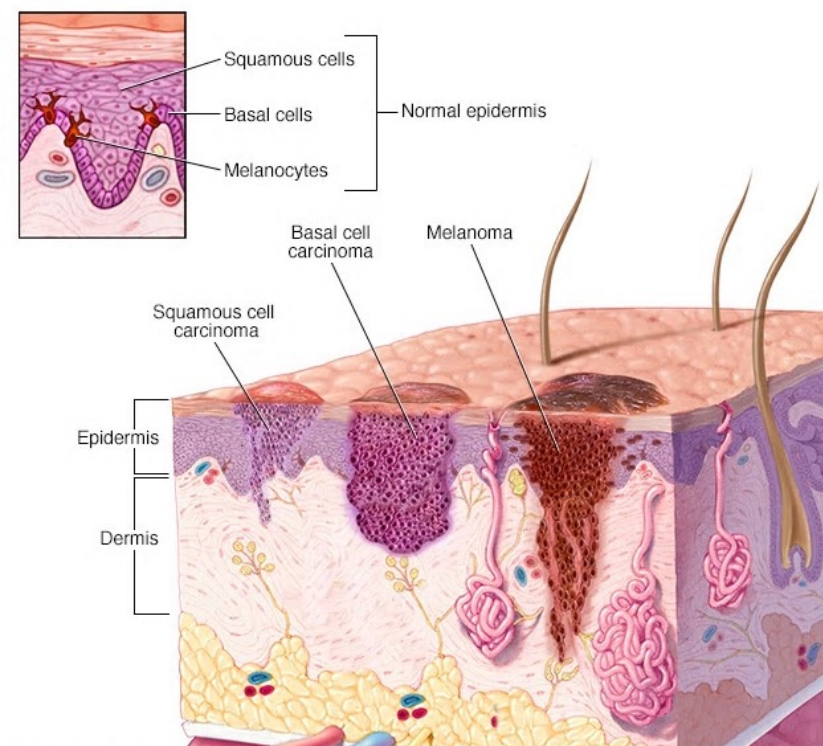
 Injected

 Un-injected

# CSCC disease characteristics, largely superficial/local issue



- Second most common skin cancer with  $\approx 700,000$  patients annually in the U.S.<sup>1</sup>, caused by exposure to ultraviolet radiation
- ~up to **10% of CSCC patients are high risk (neo-adj opportunity)**
- Approximately 7,000-15,000 US deaths annually<sup>1-3</sup>
  - **80% of patients die from locoregional progression, not metastatic disease<sup>4,5</sup>**
- **CSCC is an outward growing disease with large, painful, superficial tumors, almost all (~90%) CSCC have superficial tumors**
- Majority of systemic treated patients have **prior surgery and/or radiation**
- First systemic treatment, cemiplimab, approved in 2018 followed by pembrolizumab in 2020
- **(ORR: ~35-45%, CRR: ~5-15%)**



© 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



## High rates of CR in CSCC in IL study in combo with Nivo Replimune<sup>®</sup>

	CSCC	BCC	MCC	Angio
# of patients*	17	4	4	6
<i>Best overall response n (%)</i>				
CR	8 (47.1)	1 (25.0)	2 (50.0)	1 (16.7)
PR	3 (17.6)	0	1 (25.0)	3 (50.0)
SD	1 (5.9)	2 (50.0)	0	1 (16.7)
PD	4 (23.5)	1 (25.0)	1 (25.0)	1 (16.7)
OR	11 (64.7)	1 (25.0)	3 (75.0)	4 (66.7)
CR+PR+SD	12 (70.6)	3 (75.0)	3 (75.0)	5 (83.3)

\*Patients with follow up assessments (n=31), on study with no follow up currently for the other patient (MCC); Note: Data snapshot date: 11th March 2022

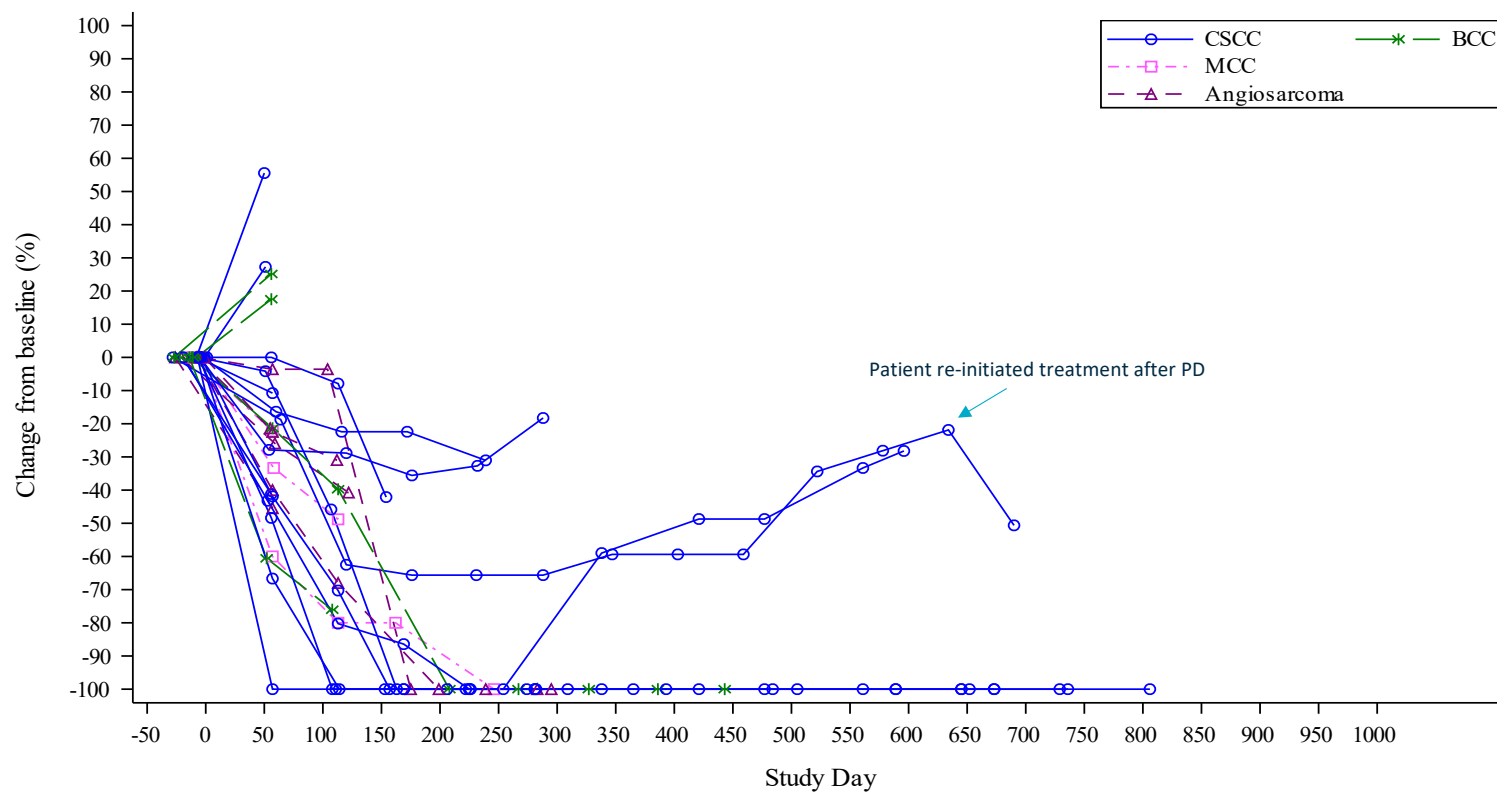
© 2022 Replimune Group Inc.

20



# Anti-PD1 naïve NMSC: Deep/durable responses in CSCC

A high frequency of durable responses continues to be observed







## Example complete resolution of aggressive locoregional disease



22<sup>ND</sup> MAY 2020



12<sup>TH</sup> OCT 2020 (PR)

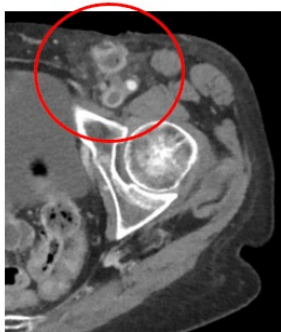


12<sup>TH</sup> FEB 2021 (CR)



### Pt 1122-2014 - CR

- Patient had groin node metastases that were initially injected & responded
- Response observed in **distant tumor in the foot**, allowing for subsequent injection



SCREENING



17<sup>TH</sup> AUG 2020



18<sup>TH</sup> DEC 2020



Injected



Un-injected





# Robust effects observed, with complete resolution of uninjected metastases, including bone



June 16, 2019  
(baseline)



July 1, 2019  
(post 1 dose RP1, no Opdivo)

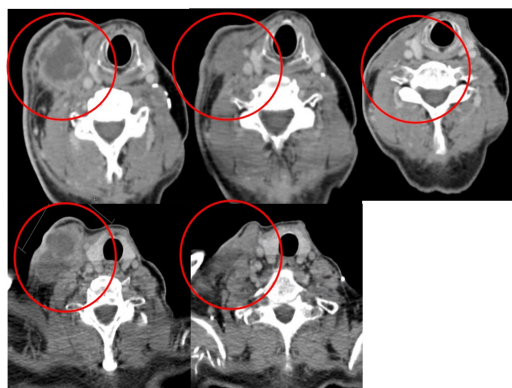


July 16, 2019  
(post 2 doses RP1, 1 dose Opdivo)



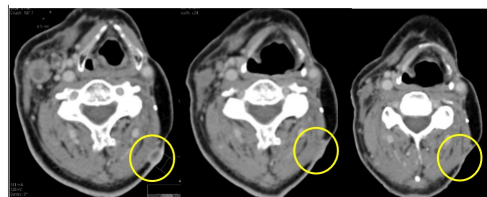
## Right neck (injected)

Baseline 8 weeks 24 weeks

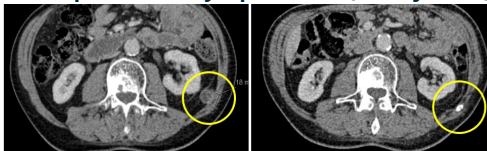


## Left neck (un-injected)

Baseline 8 weeks 16 weeks



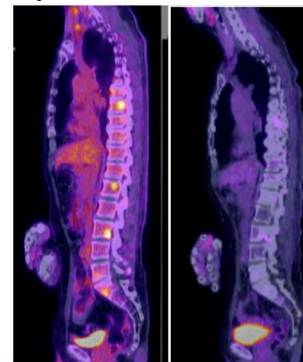
## Retroperitoneal lymph nodes (un-injected)



## Pt 4402-2001 - CR

- Recurrent CSCC of the neck (bilateral)
- Previously treated with cisplatin-based chemoradiation & six cycles of carboplatin/5-FU
- Both the large injected tumor & the contralateral tumor in the neck reduced before first Opdivo dose
- Resolution of bone metastases

June 2018 Feb 2020

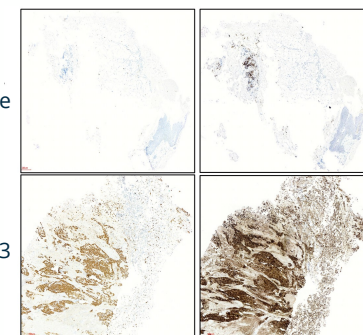


CD8

PD-L1

Baseline

Day 43



Red circle Injected

Yellow circle Un-injected

# Increasing CRs: An opportunity to transform the CSCC market



## CSCC Characteristics

- Large, outward, fast-growing tumors
- Disease can cause social isolation — disfiguring, painful, oozing
- **Directly tackling the problem** via tumor injection

## Market Research / KOL Feedback

- Despite CPIs impressive outcomes, there is still need for improvement in ORR, and particularly CR
- RP1 profile seen as compelling especially **doubling CRs vs. SOC** with good tolerability

*"CRs are very important in this setting, as they usually lead to long-term survival and also have a huge impact on the patient's quality of life"*

*KOL in market research*

## Future Market Impact

- Potential to change existing mindset and treatment approach to treat more earlier stage patients
- **Driving CRs key to success in neoadjuvant** allowing many more patients to be treated and cured



**Ability to see a fast (even prior to CPI admin), deep and durable response**  
*5 months*

*Latest response ; PR - still on study with potential for CR*





# Registrational randomized controlled Ph2 study in CSCC (CERPASS)

Top line primary analysis data expected in H1 2023



## Key Eligibility Criteria:

- Locally-advanced/metastatic CSCC
- ECOG PS 0 or 1
- No active autoimmune disease
- No prior treatment with a PD-1/PD-L1 inhibitor
- No untreated brain metastases

2:1  
N=211

**RP1 IT Q3W x 8 doses<sup>†</sup>**  
( $1 \times 10^6$  PFU/mL for one dose followed by  $1 \times 10^7$  PFU/mL for 7 doses)

+

**Cemiplimab 350mg Q3W IV**

**Cemiplimab 350mg Q3W IV**

57 weeks treatment<sup>‡</sup>

3-year  
survival  
follow up

## Key Endpoints

- **Dual independent primary endpoints: Complete Response Rate & Overall Response Rate**
  - Approx. 15% absolute difference in CRR and/or ORR required
- Secondary endpoints: DOR, PFS, OS, disease-specific survival, safety/tolerability

<sup>†</sup>First dose of RP1 to be given as monotherapy with cemiplimab to be given with second dose of RP1  
<sup>‡</sup>57 weeks treatment for the combination arm; treatment duration for cemiplimab-only arm is 54 weeks

# RP1 Commercial Opportunity

## AGENDA

# RP1: A significant skin franchise opportunity

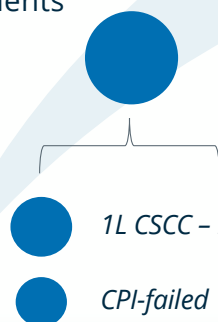


## Aiming to transform skin cancer care with RP1

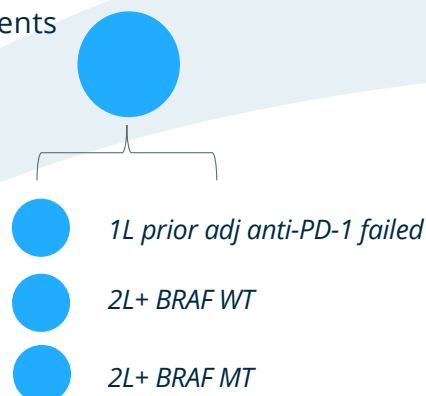
- RP1 + anti-PD1 intended to improve on SOC
- Address high unmet need anti-PD-1 failed settings
- Provides opportunity for cure in early-stage patients

Potential for approx. 10K additional advanced CSCC patients with transformational results (e.g., higher CR rates are seen)

★ **Advanced CSCC\***  
11K patients



★ **Anti-PD1-failed melanoma\*\***  
13K patients



**Neo-adjuvant skin cancers\*\*\***  
~45K patients

**~80K**  
US patient opportunity

\*RP1 + cemiplimab/nivolumab or RP1 mono

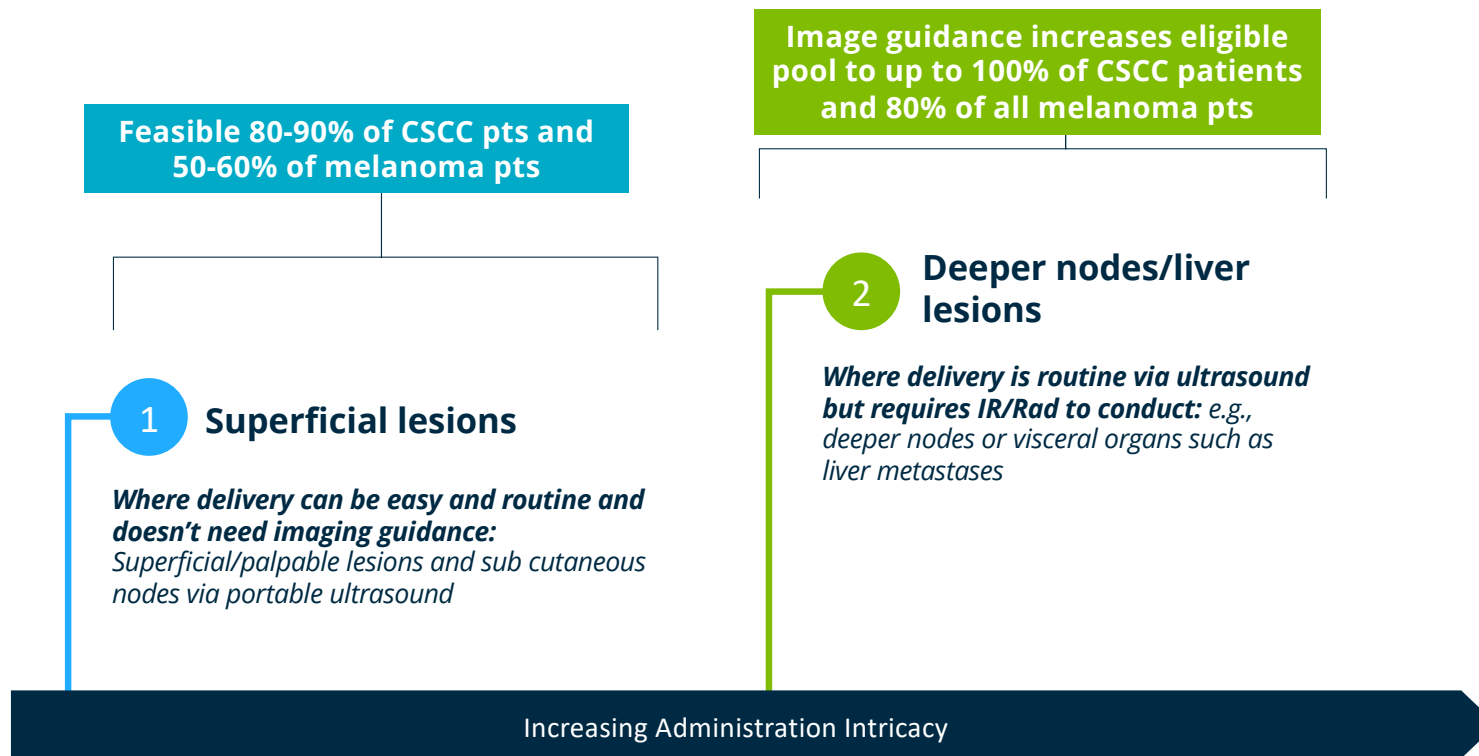
\*\*RP1 + nivolumab

\*\*\*Neoadjuvant CSCC (est 30K pts) and melanoma (est. 15K pts)

Note: CSCC US treated patient population for 2029 based on multiple sources including IQVIA claims, primary market research, and company data. Melanoma US treated patient population for 2029 based on CancerMPact® Patient Metrics, Cerner Enviza (available from [www.cancermpect.com](http://www.cancermpect.com) Accessed 11 Oct 2022), with adjustments to future 2L+ treatment rates based on primary market research

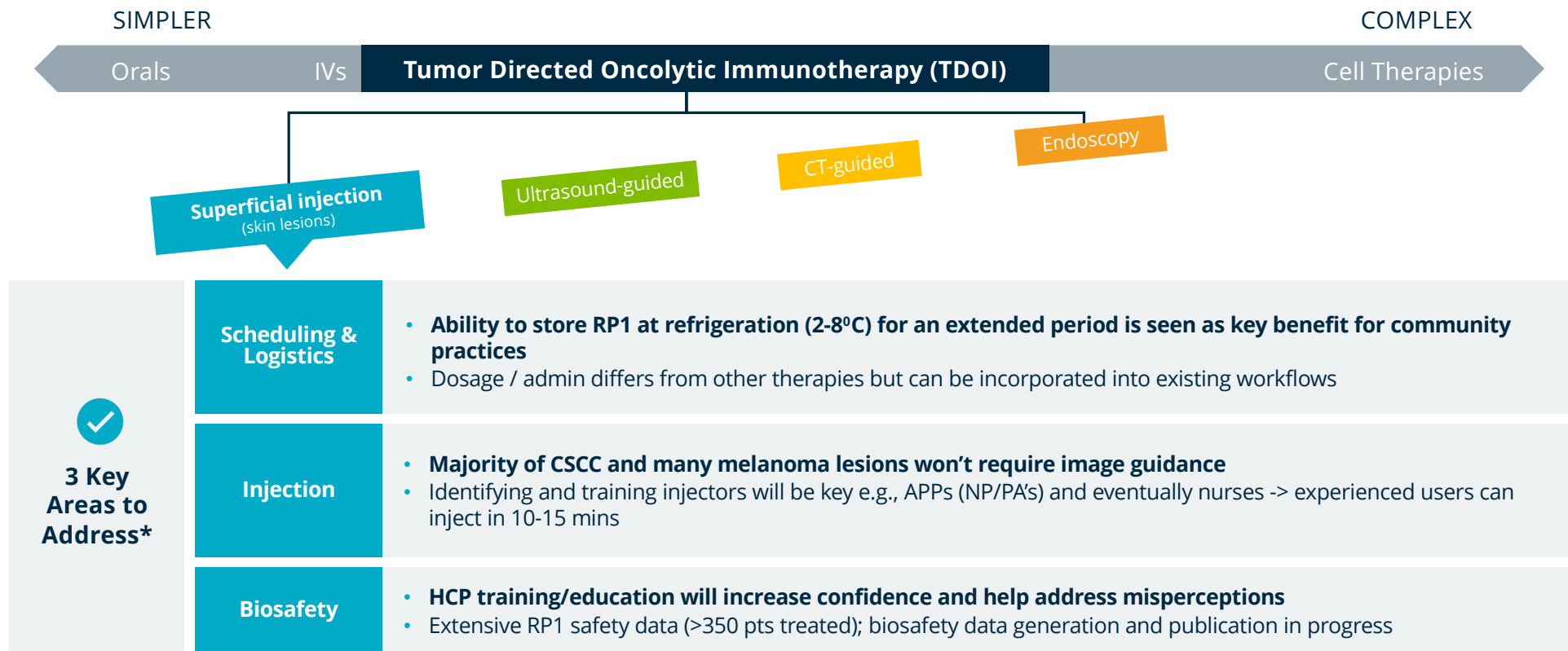
© 2022 Replimune Group Inc.

# RP1: Initial launch in skin cancers maximizes the chance of commercial success due to high unmet need & tumor directed administration feasibility





# Superficial skin lesion injections are feasible and can routinely be incorporated across the majority of practice settings



# Investment in manufacturing to support full commercialization



## Commercial scale in-house manufacturing established

- 63,000 square foot state-of-the-art facility for GMP manufacturing
  - *RP1-3 technology transfer from CMO successfully completed*
  - *RP1 released to clinic post comparability analysis*
  - *RP1 BLA consistency lot runs underway*
- Scale expected to be sufficient to cover global commercialization of all Replimune's product candidates at full capacity
- Commercially attractive cost of goods & 'off the shelf' product practicality



# RP2/3 Update

## AGENDA



## RP2 & RP3 leverage Replimune's platform to express additional potent immune stimulators

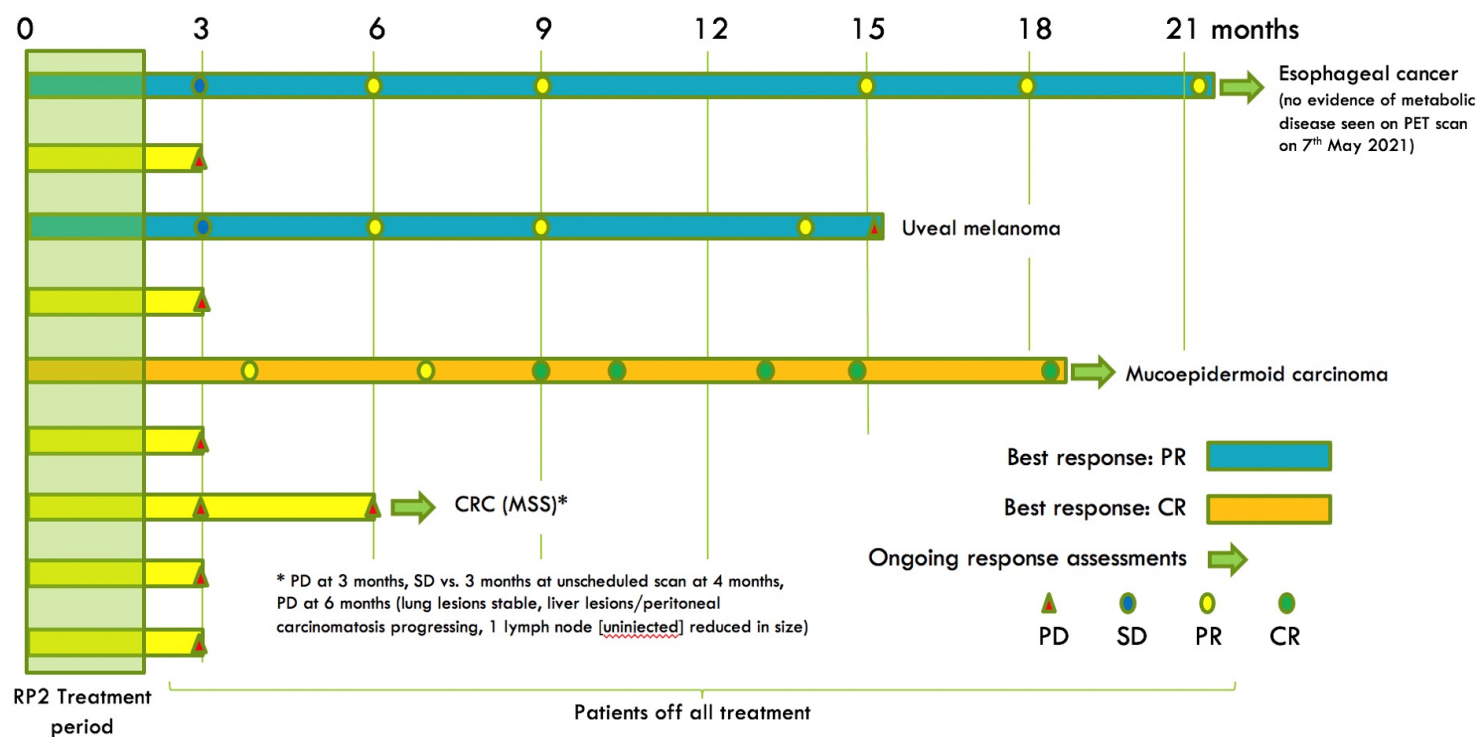


- Focus on the delivery of molecules which function at the time & place of immune activation, i.e. in tumors & draining lymph nodes
- Delivered mechanisms are clinically validated:
  - *Anti-CTLA-4 – ipilimumab, tremelimumab*
  - *CD40L, 4-1BBL – agonistic antibodies against CD40 & 4-1BB (CD137) have shown clinical activity*
- The RP1 backbone maximizes antigen presentation & T cell activation to kickstart an immune response
  - *CTLA-4 inhibits the effectiveness of antigen presentation and T cell activation (immunogenic 'Signal 1' & 'Signal 2')*
  - *CD40L & 4-1BBL provide immune co-stimulation (immunogenic 'Signal 2') needed for full immune activation — this leads to the expression of inflammatory cytokines – immunogenic 'Signal 3'*
- **Local expression of each of anti-CTLA-4, CD40L & 4-1BBL optimal**, both mechanistically, and to reduce systemic toxicity

# Single agent activity demonstrated in traditionally 'cold' tumor types



## Kinetics of response following treatment with single agent RP2





# Ongoing CR in mucoepidermoid carcinoma following monotherapy RP2



Baseline



1 month



3 months (PR)



4 months

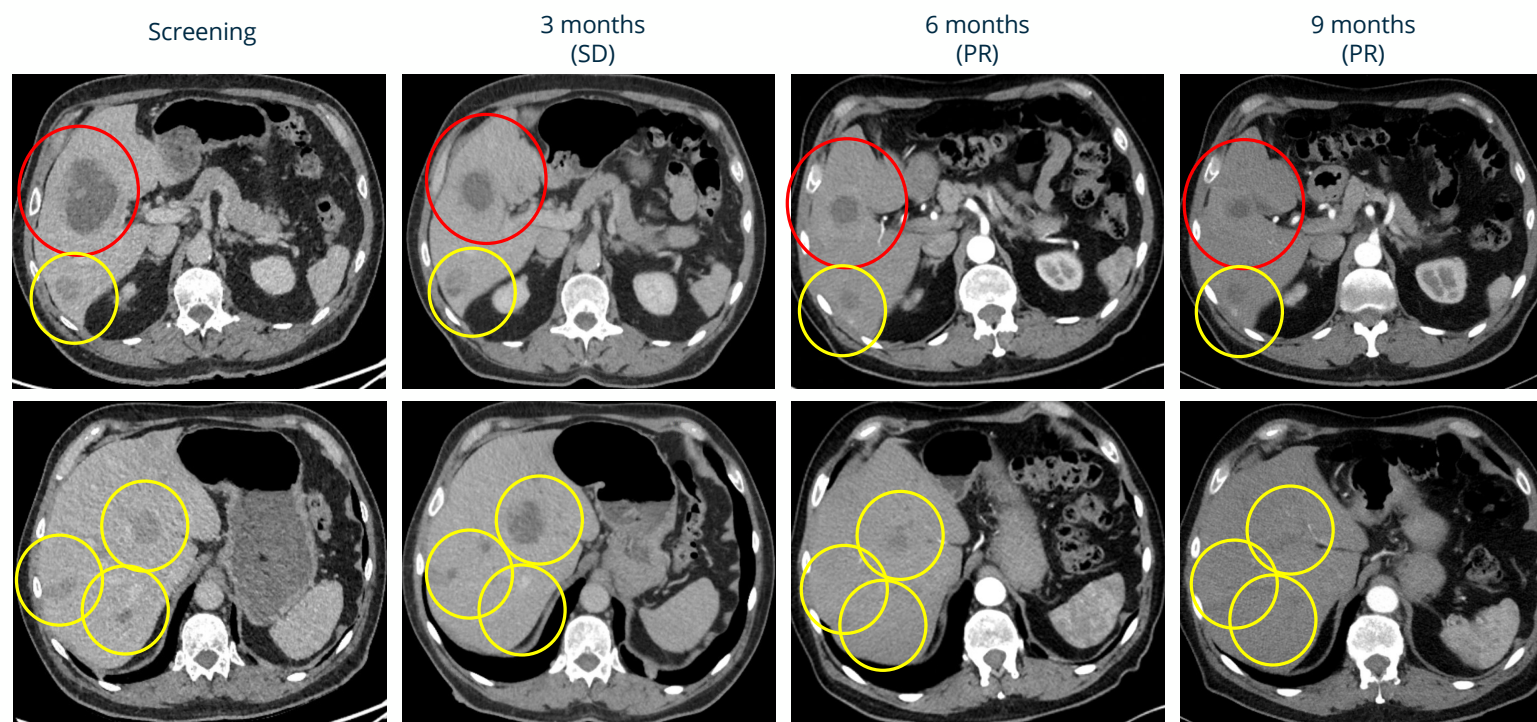


## Pt 4402-0001 - ongoing CR

- Mucoepidermoid carcinoma of the parotid gland
- Prior therapies: carboplatin/ paclitaxel, bicalutamide, ceralasertib
- Cervical lymph node & supraclavicular fossa lesions injected





## Example patient with liver metastases treated with RP2 monotherapy – uveal melanoma



### Pt 4401-0003 - PR

- Uveal melanoma
- Extensive liver metastases (others not shown)
- Prior therapies: Ipilimumab/ nivolumab
- Patient progressed at 15 months

 Injected                       Un-injected



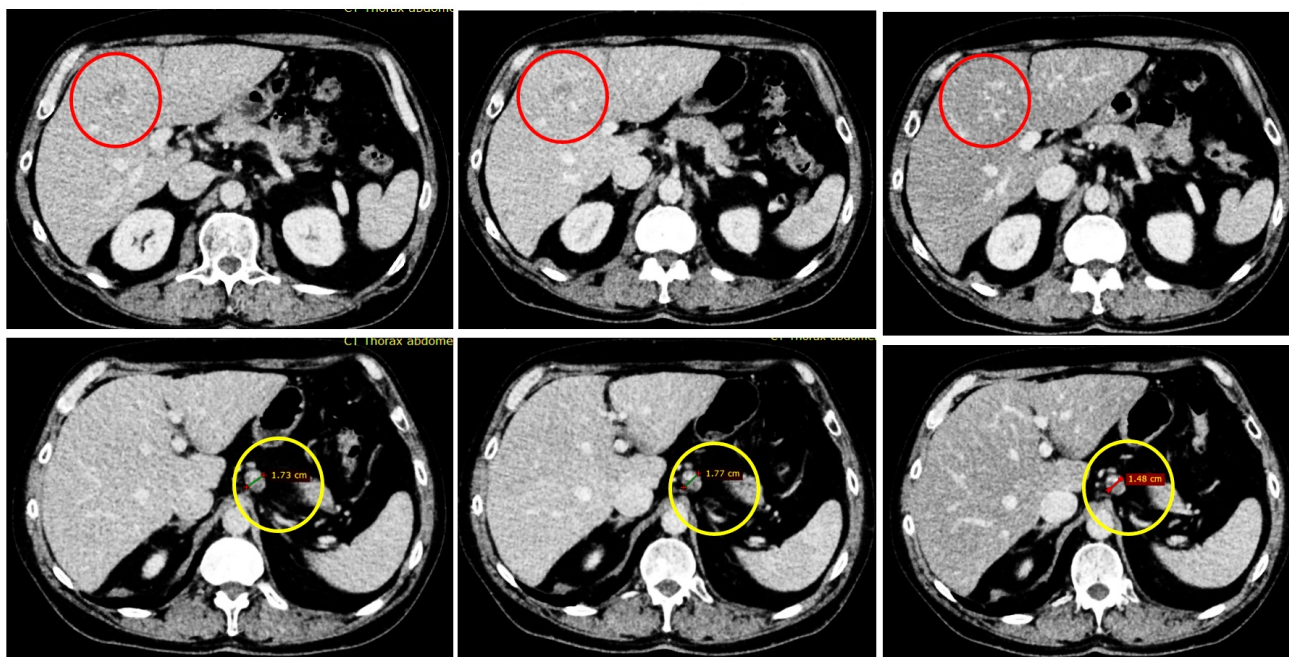
## Example patient with liver metastases treated with RP2 monotherapy – esophageal cancer



Baseline

3 months  
(SD)

6 months  
(PR, CR by PET scan at 18 months )



### Pt 4401-0001 - ongoing PR

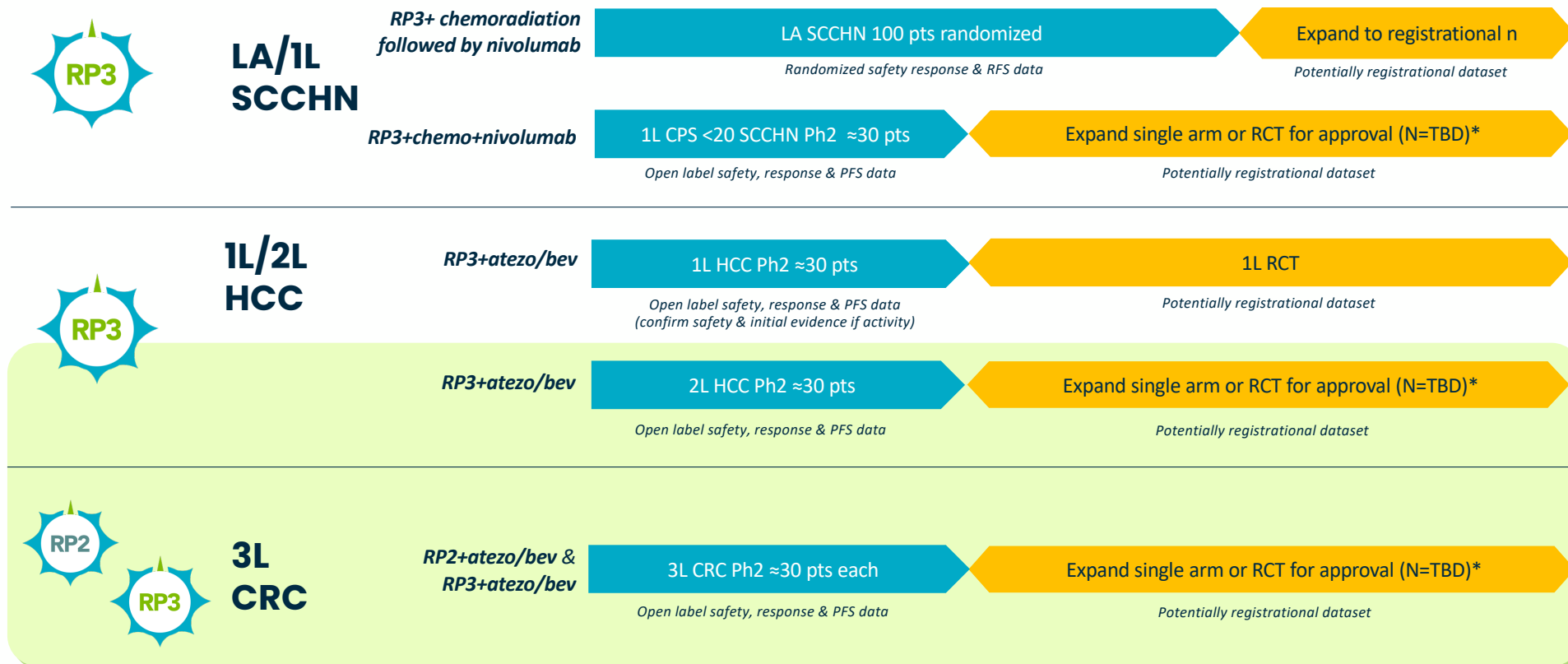
- Esophageal cancer
- Liver & abdominal lymph node metastases
- Prior therapies: Durvalumab (anti-PD-L1), M6620 (ATR kinase inhibitor), capecitabine, oxaliplatin, cisplatin, chemoradiation
- Liver lesion injected

○ Injected

○ Un-injected

# RP2 vs. RP3 positioning and ph2 development plan

## Liver/liver mets driven post Roche collaboration



Highlighted green box=potential FTM opportunities

\*Pending FDA discussion; Note: Replimune has a clinical trial collaboration & supply agreement with BMS for the supply of Opdivo in its clinical trial program with RP2/3

© 2022 Replimune Group Inc.

37

# Unmet need in liver cancer/liver mets remains



## Unmet need<sup>1</sup>

- Liver is a common site of metastasis across tumor types
- Patients with liver mets have a poor prognosis
- IO has a particularly poor outcome in pts with liver mets
- Liver mets are often the primary driver of mortality

## Scientific rationale<sup>2</sup>

- Liver metastases are associated with the antigen-specific elimination of T cells from the circulation by macrophages
  - *Leads to systemic loss of T cells and diminished immunotherapy efficacy*

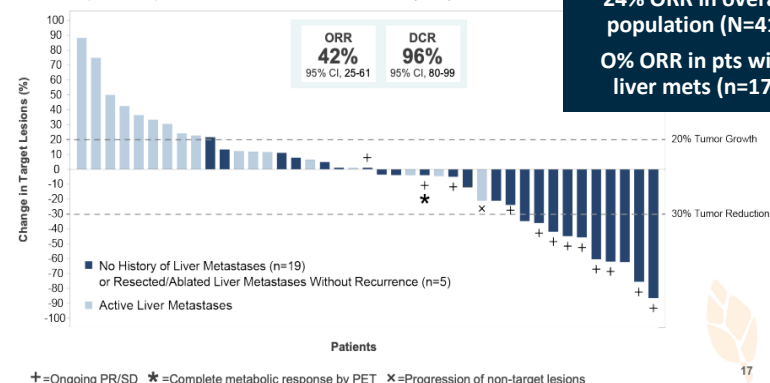
## "OI" rationale/feasibility

- RPx MOA - powerful direct tumor killing & systemic immune activation
  - *Relief of organ (liver) symptoms & systemic disease control*
- Liver/liver mets are routinely injected by ultrasound and IR/Rads already play a key role in patient management

## Agenus: 2L+ MSS CRC – Botensilimab (CTLA4)+PD-1 EMSO 2022

### Exploratory Analysis by Liver Involvement

Enriched responses in patients without active liver metastases (n=24)



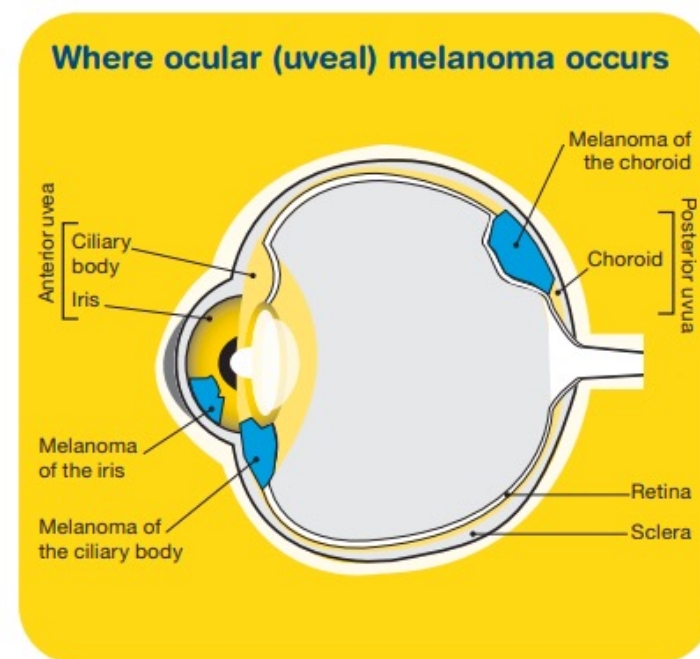
<sup>1</sup>SEER 2021 Estimated Deaths. From SEER Cancer Stat Facts by indication; Riihimaki et al Cancer Med 2018

<sup>2</sup>Yu et al Nat Med Jan 2021; IR=interventional radiologists, Rads=radiologists

## RP2: Uveal melanoma; proxy for treating immune insensitive disease with liver mets



- Ocular or “uveal” melanoma is a rare cancer with approx. 1,000 cases in the US per year<sup>1</sup>
  - *Originates from melanocytes and can occur in several eye locations*
  - *The historic median OS is approx. 12 months<sup>1</sup>*
- Uveal melanoma **behaves quite differently from skin melanoma**
  - **Mostly metastasizes to the liver** (approx. 70-90% of cases) and once this occurs only about 10% of these patients survive beyond a year
  - **A difficult to treat tumor where CPIs have previously demonstrated limited activity<sup>2,3,4</sup>**
  - Kimmtrak (tebentafusp) is the 1st approved agent in uveal melanoma in HLA-A\*02:01-positive adult patients (approx. 50% of the total population)\*
- **Unmet need for uveal melanoma patients remains high, including improved efficacy/tolerability, effective options for HLA negative patients, and options for Kimmtrak and anti-PD1 failed patients**



<sup>1</sup>Carvajal RD et al. Br J Ophthalmol 2017; <sup>2</sup>Nathan P et al. N Engl J Med. 2021;385(13):1196-1206; <sup>3</sup>PelsterMS et al. J Clin Oncol. 2021;39(6):599-607; <sup>4</sup>Lukzky J et al SMR 2022;  
\* Versus investigator's choice, pembrolizumab, ipilimumab, or dacarbazine



# Uveal melanoma patients treated with RP2

4 out of 14 patients for whom the outcome is known responded (28.6%) – all anti-PD1 failed



Patient #	RP2 monotherapy or combination w/ nivolumab	Prior therapies	Sites of disease	Best response	Current status
4401-0002	Monotherapy	Iplimumab+ nivolumab, temozolomide , selumetinib+ vistusertib , carboplatin	Lung, liver, abdomen, chest, lymph nodes, subcutaneous, bone	PD	Died
<b>4401-0003</b>	<b>Monotherapy</b>	<b>Iplimumab+ nivolumab</b>	<b>Liver</b>	<b>PR to 15 months</b>	<b>Died post PD</b>
4401-0007	Monotherapy	Iplimumab+ nivolumab , <u>intratumoral</u> AGI-134	Liver, kidney, head and neck, peritoneal, intramuscular, subcutaneous, bone	Not done (non-evaluable)	Died
4401-0014	Combination	None	Liver	SD	Died
<b>4402-0007</b>	<b>Combination</b>	<b>Nivolumab</b>	<b>Orbital mass, bone (pelvis, vertebral), cheek</b>	<b>PR</b>	<b>Ongoing PR (CR by PET scan reported by investigator) at 21 months from first dose</b>
4401-0021	Combination	Selumetinib+paclitaxel, pembrolizumab, ipilimumab, melphalan intrahepatic chemoperfusion	Liver, GI lymph nodes, abdominal wall, leg,	SD	Died
4401-0022	Combination	Iplimumab, dacarbazine	Liver	Not captured	Died
<b>4402-0014</b>	<b>Combination</b>	<b>Ipilimumab , pembrolizumab</b>	<b>Retroperitoneal, SCF</b>	<b>PR</b>	<b>Ongoing PR at 12 months from first dose</b>
4403-0014	Combination	IMCGP100	Liver	PD	Died
4403-0015	Combination	IMCGP100 , nivolumab+ ipilimumab	Lung, liver, vertebra	SD	Patient withdrew consent
4401-0026	Combination	Iplimumab+ nivolumab , chemosaturation	Liver	PD	Lost to follow-up
<b>4403-0017</b>	<b>Combination</b>	<b>Ipilimumab +nivolumab</b>	<b>Liver</b>	<b>PR</b>	<b>Ongoing PR at 9 months from first dose</b>
4402-0018	Combination	None	Liver	SD	In follow up
4402-0019	Combination	Ipilimumab , pembrolizumab	Liver, perirenal	PD	In Follow-up
4403-0018	Combination	Nivolumab+ ipilimumab	Liver	SD	On treatment
4403-0019	Combination	Ipilimumab+ nivolumab	Liver	Not done yet	On treatment
3412-0001	Combination	Ipilimumab+nivolumab, IL-2, carboplatin, paclitaxel	Liver, lung	Not done yet	On treatment

Legend: **Green** = responding patients **Yellow** = patients ongoing on treatment for whom the outcome isn't yet known

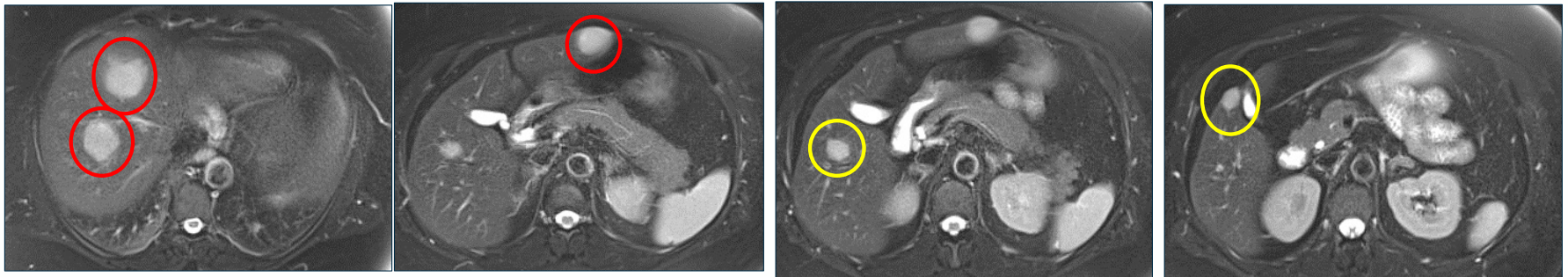
© 2022 Replimune Group Inc.

# Patient 201-4403-0017: Uveal melanoma

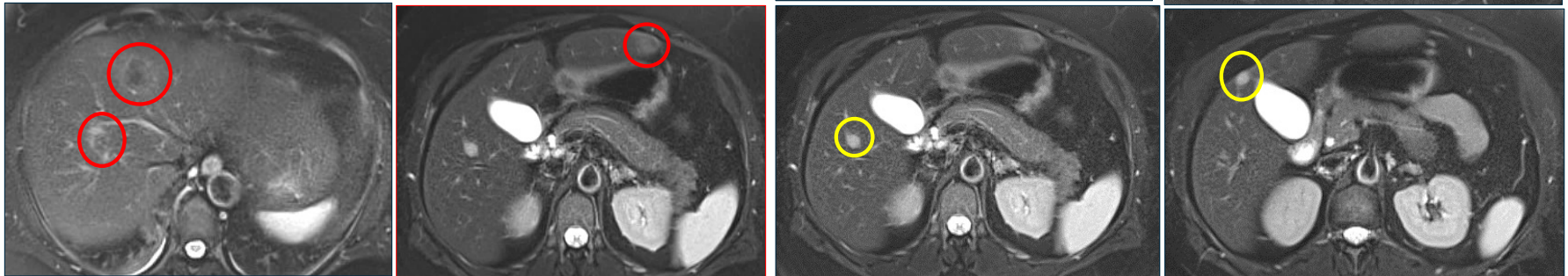
Yervoy/Opdivo failed – PR (RP2+Opdivo)



24th Dec 2021  
(Screening)



5th Sept 2022

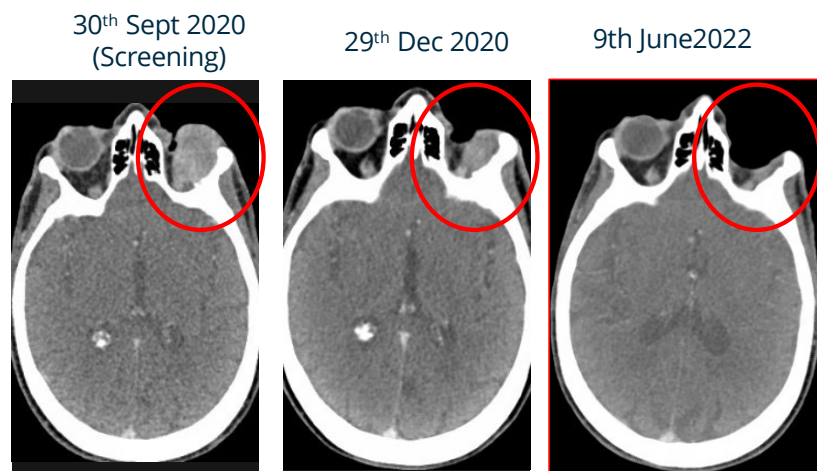


○ Injected

○ Un-injected

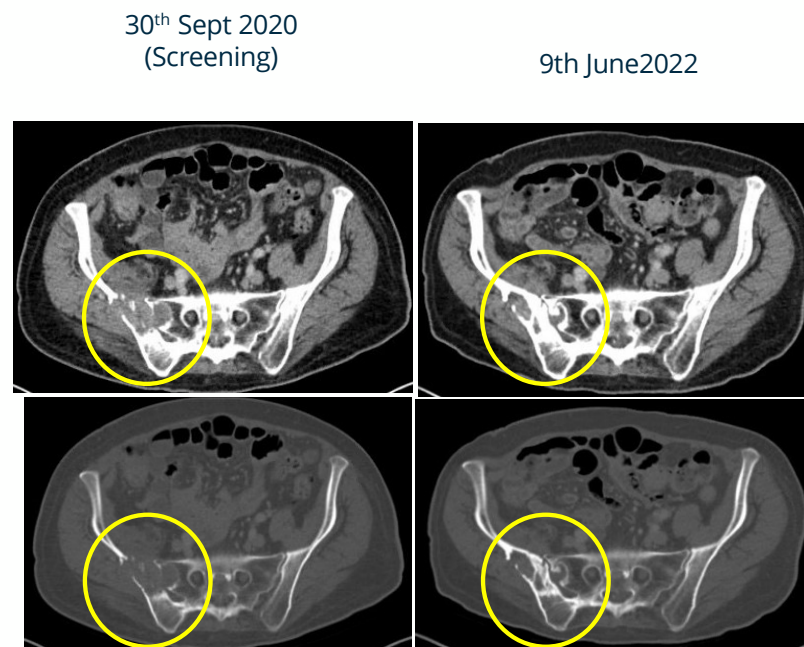
# Patient 201-4402-0007: Uveal melanoma

Opdivo failed – PR (RP2+Opdivo)



19<sup>th</sup> Oct 2020 (Baseline)

27<sup>th</sup> Jan 2021



## Notes:

- Ongoing metabolic CR at 21 months

○ Injected

○ Un-injected

# Overall summary



## Major skin cancer franchise planned with RP1

- Strong data to date in multiple skin cancers in both the PD1 naïve and failed setting
  - **Anti-PD1 failed data presented to date potentially transformative in anti-PD1 failed melanoma**
  - *CERPASS registrational data in CSCC expected Q3 2023*
- Scale manufacturing in place
  - *To serve worldwide market at attractive COGS*
- Commercial planning ramping up for intended US launch in H2 2024\*



## RP2/3 mid-stage pipeline

- *Focused on easily injected tumor types with high commercial value, such as SCCHN, HCC, & CRC*
- *Fast routes to randomized controlled trials or expansion of single arm trials for approval*



## Strong cash position to execute on our vision

- *Cash and Investments of \$616m as of December 31, 2022 \*\**
- *Availability of \$200M non-dilutive debt facility*

## With catalyst rich 2023

- *RP1 CERPASS primary read out*
- *ARTACUS update*
- *RP1 NMSC anti-PD1 failed update*
- *RP1 anti-PD1 failed full read out*
- *RP2/3 further Phase 1 expansion data*
- *RP2/3 Phase 2 trial initiations*

• Subject to submission & approval of a BLA  
\*\*. Unaudited estimate





# THANK YOU

## MISSION

To enable tumor directed oncolytic immunotherapy (TDOl) to become a cornerstone in the treatment of cancer

## VISION

To deliver **transformational** results for patients **across cancers** using tumor directed oncolytic immunotherapy to induce a powerful and durable systemic anti-tumor immune response resulting in **quality survival** and a **chance for a cure**

