Replimune®

NEXT-GENERATION ONCOLYTIC IMMUNOTHERAPY

November 2021

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, 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 Corporate Overview

Proprietary oncolytic immunotherapy platform

- Intended to maximally activate a systemic immune response against a patient's cancer
- Intended to establish Replimune's products as the second cornerstone of immuno-oncology

RP1 in numerous clinical trials with focus on establishing a major skin cancer franchise

- Registration directed development based on compelling efficacy and safety profile
  - CERPASS study in (anti-PD1 naive) advanced cutaneous squamous cell carcinoma (CSCC) enrolling
    - Potentially registrational study in CSCC solid organ transplant recipients enrolling
    - Anti-PD1 failed CSCC study enrolling
  - IGNYTE study in anti-PD1 failed melanoma enrolling

RP2/3 optimized for superior immune stimulation, intended to treat immunologically 'cold' tumors

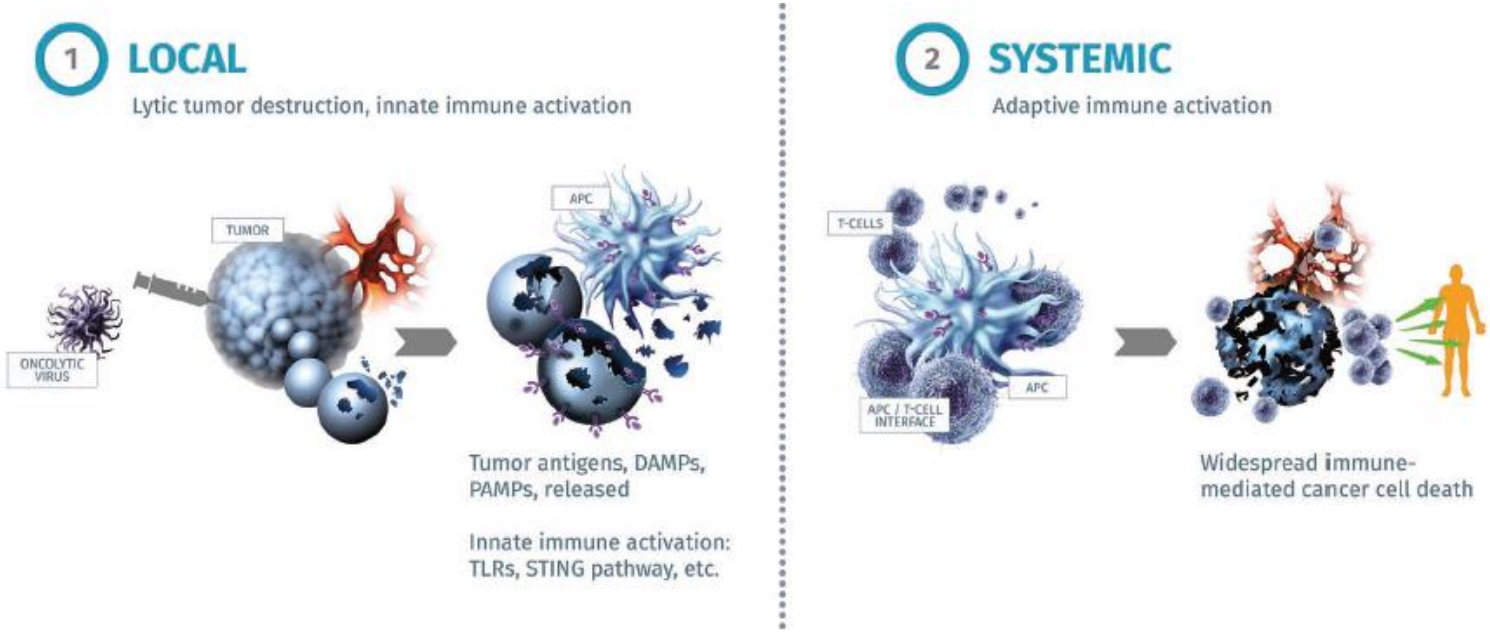
- RP2 – Durable single agent & combination with nivolumab activity demonstrated in heavily pre-treated immune insensitive & anti-PD1 failed tumors
- RP3 – Single agent dosing underway
- Phase 2 studies with focus on treating patients with liver metastases from prevalent tumor types planned

Company positioned for long term growth supporting a new pillar of oncology

- Commercial scale manufacturing facility operational; GMP production underway
- Commercial planning activities underway
- Well capitalized to deliver with cash, cash equivalents and short-term investments of ~$436m as of September 30th 2021, expected to fund current operational plan into H2 2024, excluding any confirmatory trials

Oncolytic immunotherapy

- The use of viruses that selectively replicate in & kill tumors to treat cancer
  - Highly inflammatory: Activates both innate and adaptive immunity
  - Systemically activates the immune system against the tumor antigens released
  - Can be ‘armed’ with additional genes to augment the natural properties of the virus with additional mechanisms of action
  - Off-the-shelf
- Single agent T-VEC is clinically validated & FDA approved



Practical and comprehensive activation of an anti-tumor immune response

Our platform offers ***significant potential advantages compared to competing approaches***, including cell-based therapies and personalized cancer vaccines

	Replimune's Immulytic platform	Cell-based therapy (including TILs)	Personalized cancer vaccines
"Off the shelf" – no patient-specific manufacturing	✓	✗	✗
Commercially attractive COGS	✓	✗	✗
Efficacy from multiple immune modalities – both innate & adaptive immunity stimulated	✓	✗	✗
Attractive safety profile, with limited high-grade side effects	✓	✗	✓
Applicable to nearly all patients with solid tumors – not limited by surface markers or mutations	✓	✗	✗

Replimune's best-in-class platform

1. Optimized to infect, replicate in, and kill tumor cells – intended to maximize tumor destruction & immunogenic cell death (immunogenic 'Signal 1')
   - Potent clinical HSV strain selected from comprehensive screen for anti-cancer lytic activity
   - Modifications for selective replication in tumors sparing healthy tissue (ICP34.5 deleted for selectivity, US11 upregulated)
   - Fusogeneic protein (GALV-GP R-) increases killing & immunogenic cell death 10-100 fold
2. Further armed with immune activating transgenes intended to maximize T cell co-stimulation ('Signal 2') & systemic immune activation (including through induction of inflammatory cytokines: 'Signal 3')

programs:		RP1	RP2	RP3
RH018A viral strain	Optimized tumor infectivity and lytic activity, engineered for selective replication	✓	✓	✓
GALV-GP R-	Increased tumor killing & immunogenic cell death	✓	✓	✓
GM-CSF	DC expansion & maturation	✓	✓	
Anti-CTLA-4	APC/T-cell feedback loop blocking		✓	✓
CD40L	APC maturation, T-cell co-stimulation, inflammatory cytokine release (IFN-γ)			✓
4-1BBL	T-cell co-stimulation, NK-cell ADCC, APC maturation, inflammatory cytokines release (IL-2, IL-8, IL-12, IFN-γ)			✓

Replimune's fusion-enhanced backbone virus described in Thomas et al *JITC* 2019 (7)

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

Replimune®

CRITERIA	RP1	RP2	RP3
Payload	GALV-GP R-, GM-CSF	GALV-GP R-, anti-CTLA-4, GM-CSF	GALV-GP R-, anti-CTLA-4, CD40L, 4-1BBL
Target	Immunologically responsive tumor types, including anti-PD1 failed	Less immunologically responsive tumor types	Less immunologically responsive tumor types (anticipated further improved activity as compared to RP2)
Proposed indication(s)	Skin (CSCC, ant-PD1 failed melanoma, anti-PD1 failed CSCC, other NMSCs, etc)	Prevalent tumor types with focus on liver mets e.g. colon, breast, lung, Various more superficial tumors e.g., H&N Other solid tumors including I-O resistant e.g. uveal melanoma Decision as to whether to initially enter RP2 and/or RP3 into Ph2 Q1 2022	
Incidence/commercial opportunity	++	++++	
Monotherapy activity	+	+++	Ongoing
Safety	+++	+++	Ongoing
Injection location	Superficial, nodal & visceral		
Systemic activity	Clear systemic effects seen in responding patients – uninjected tumors responding, responses generally highly durable		Ongoing
Other considerations	Optimally design for more I-O sensitive tumors with excellent safety in combination	Increased I-O systemic activity with good safety in combination	Maximized for I-O systemic activity/potency

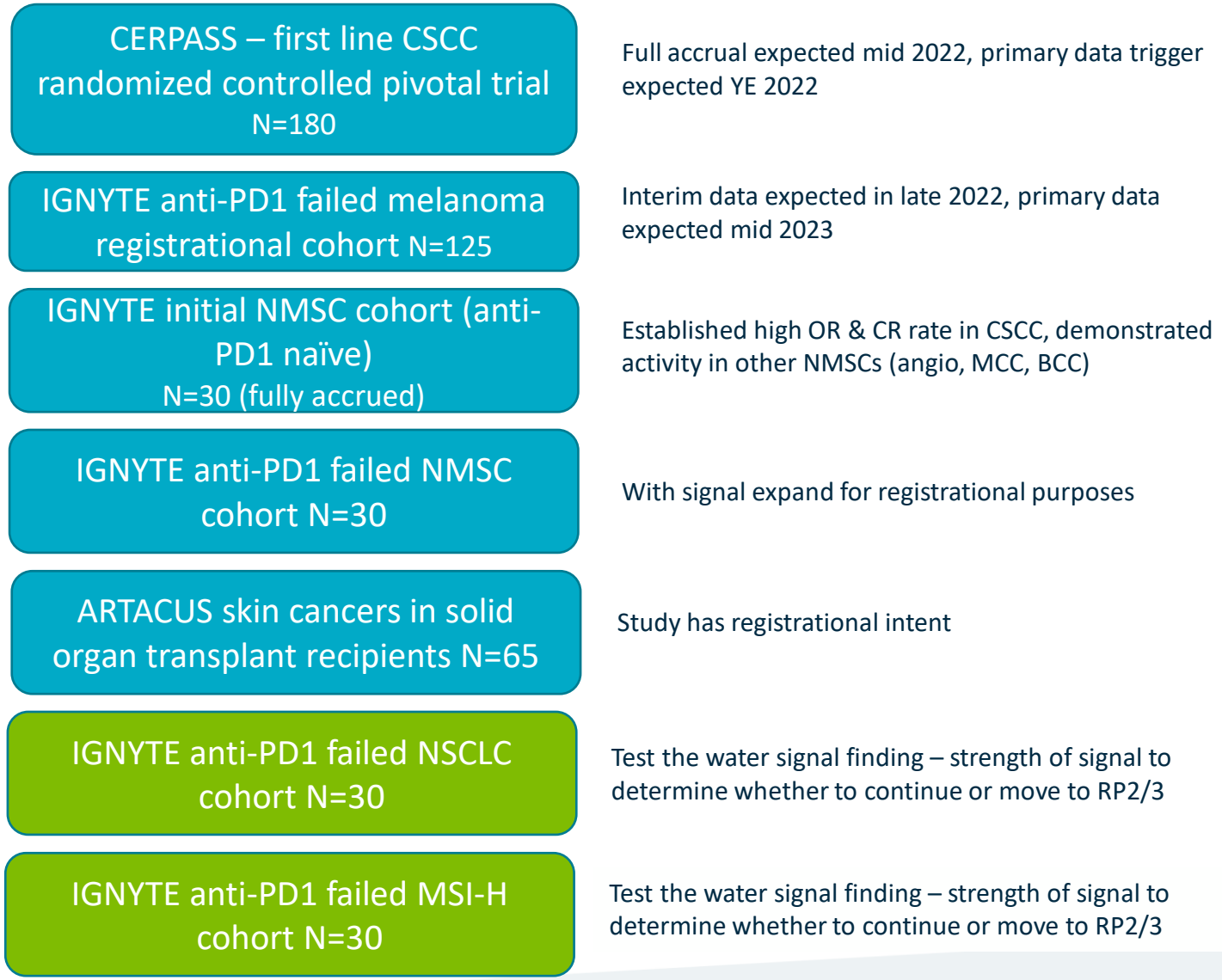
Replimune Pipeline

* Under a clinical trial collaboration & supply agreement with BMS for the supply of Opdivo – full commercial rights retained by Replimune
# Under a clinical trial collaboration agreement with Regeneron; 50:50 sharing of clinical trial costs – full commercial rights retained by Replimune
^ Planned – RP2 includes expansion in uveal melanoma; which anti-PD1 TBD
^^ Planned – To include specific cohorts of patients of tumor types where liver metastases are common; which anti-PD1 TBD

RP1– developing a major skin cancer franchise

The RP1 program aims to:

1. Establish a broad skin cancer franchise for RP1
   - Initial approval in anti-PD1 naïve CSCC
   - Rapid follow on in anti-PD1 failed melanoma
   - Label expansion to skin cancer including CSCC in solid organ transplant recipients
   - Label expansion to anti-PD1 failed CSCC
   - Commercialization in MCC, BCC, angiosarcoma based on compendia listing or TBD registrational strategy
2. 'Test the water' in select other anti-PD1 failed settings
   - Signal finding – may continue with RP1 or move to RP2/3



Randomized controlled Phase 2 study in CSCC (CERPASS)

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 prior treatment with other immune modulating agents (incl CTLA-4)
- No untreated brain metastases

2:1
N=180

RP1 IT Q3W x 8 doses†
($1x10^6$ PFU/mL for one dose followed by $1x10^7$ PFU/mL for 7 doses)
+
Cemiplimab 350mg Q3W IV

Cemiplimab 350mg Q3W IV

57 weeks treatment‡

3-year survival follow up

Key Endpoints

Dual primary endpoints: CR& ORR (RECIST v1.1)
To win on both: An approximate 17% & 15% improvement for ORR & CRR, respectively is required
To win on ORR only: An approximate 19% improvement is required
To win on CRR only: An approximate 17% improvement is required
Secondary: DOR, PFS, OS, Disease-Specific Survival, safety/tolerability

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

Lead indication overview: CSCC

- The second most common skin cancer with ≈700,000 patients annually in the U.S.[1]
- Approximately 7,000-15,000 US deaths annually[1-3]
  - Most conservative addressable population
  - 80% of patients die from locoregional progression, not metastatic disease[4,5]
- Potential US market estimated at 7,000-28,000 patients annually[1-4]
- While effective, anti-PD1 therapy alone results in only a low rate of complete response

	Libtayo				Keytruda	Opdivo
Patient population	Locally advanced		Metastatic		47 locally advanced + 58 metastatic	4 locally advanced, 16 locoregional, 4 metastatic
Number of patients	33 (per label, 2018)	78 (ASCO 2020)	75 (per label, 2018)	59 (ASCO 2020)	105 (ESMO 2019)	24 (ASCO 2020)
ORR	48.5%	45%	46.7%	51%	34.3%	54.5%
CR	0%	13%	5.3%	20%	3.8%	0%

[1]Rogers et al *JAMA Dermatol* 2015 (10); [2]Clayman et al *JCO* 2005 (23); [3]Mansouri et al *J Am Acad Dermatol* 2017 (153);
[4]Schmults et al *JAMA Dermatol* 2013 (149) ; [5]Motaparthi et al *Adv Anat Pathol* 2017 (24)

Signal finding study showed compelling activity of RP1 + nivolumab in non-melanoma skin cancers, including in CSCC

Best response

Efficacy evaluable population (Patients with follow up scans or PD)

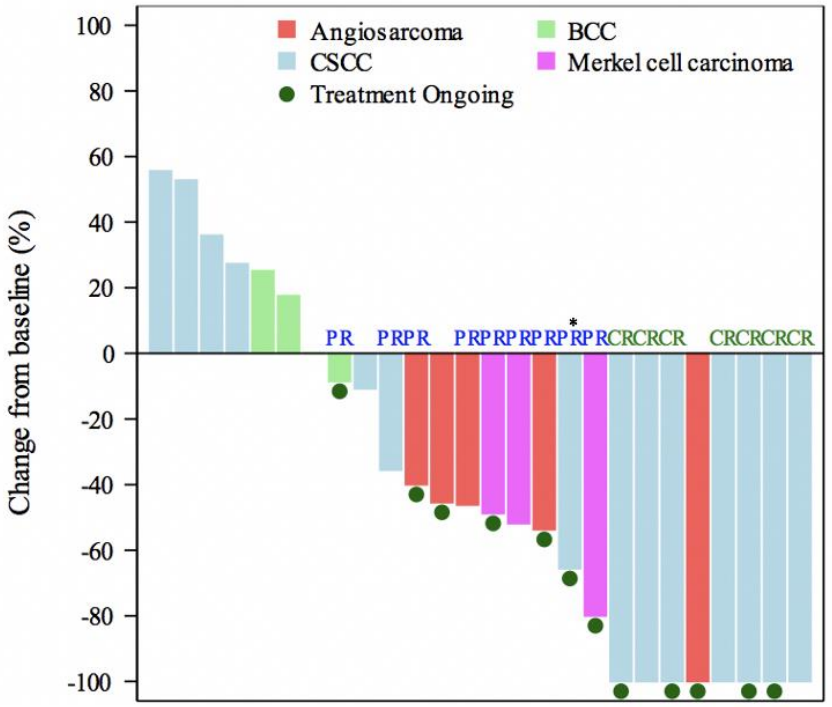
		CSCC	BCC	Merkel cell carcinoma	Angiosarcoma
Number of patients		15	4	4	5
Best overall response n (%)	**CR**	7 (46.6)	0	0	0
	PR	2* (13.2)	1 (25)	3** (75)	3** (60)
	SD	1 (6.7)	2 (50)	0	1 (20)
	PD	4 (26.7)	1 (25)	1 (25)	1 (20)
	ORR	9 (60)	0	0	3 (60)
	CR+PR+SD	10 (66.7)	3 (75)	3 (75)	4 (80)

* One PR patient awaiting formal per protocol confirmation of CR by biopsy

**One not yet confirmed

Maximum percent tumor reduction

Patients with follow up scans



* Awaiting formal per protocol confirmation of CR by biopsy

Cohort expanded from 30 to 45 patients to include patients who have failed prior anti-PD1 therapy

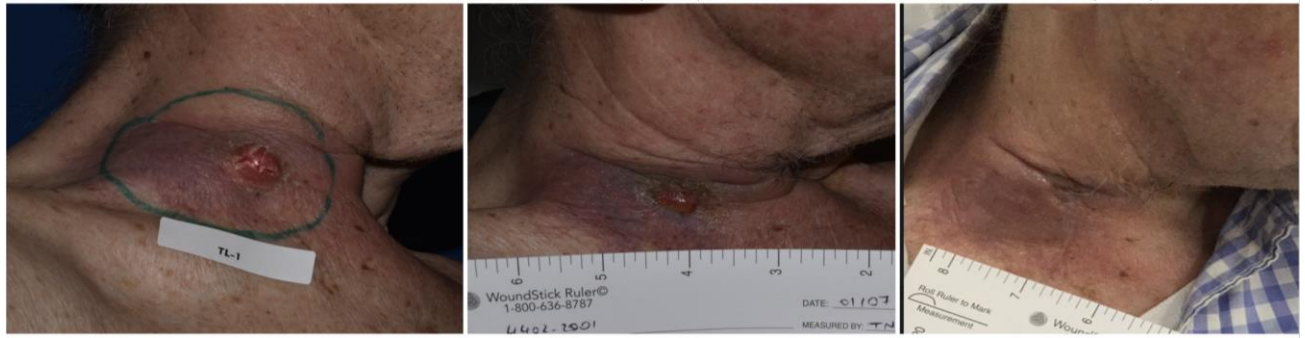
Data as of June 3 2021

Robust abscopal effects observed, with 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)

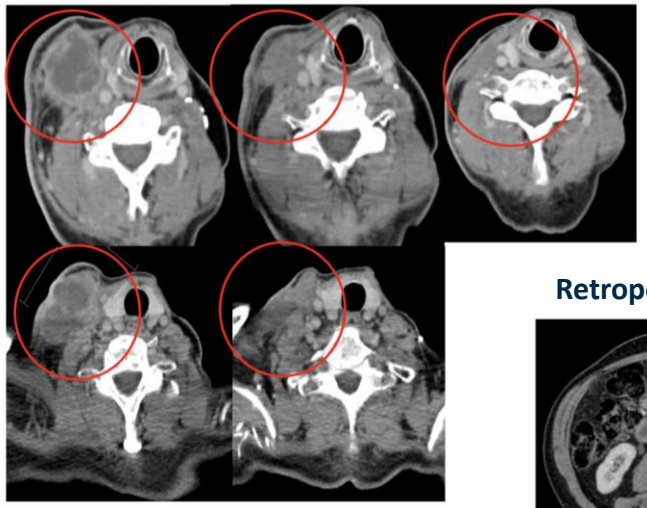


Pt 4402-2001 - CR

- 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

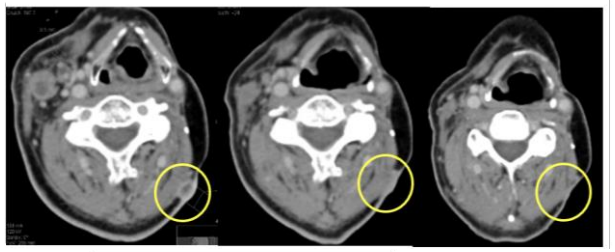
Right neck (injected)

Baseline 8 weeks 24 weeks

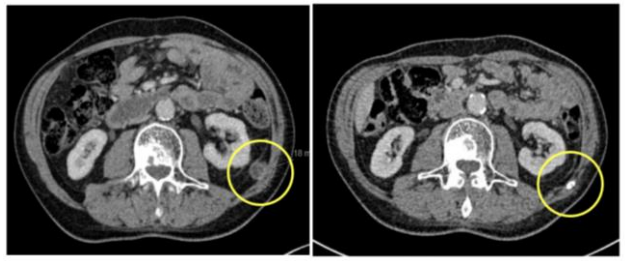


Left neck (un-injected)

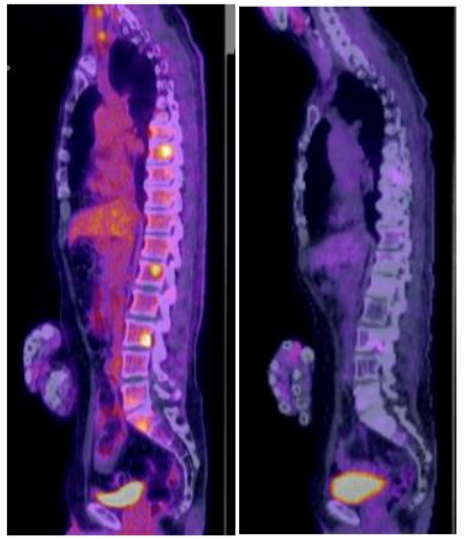
Baseline 8 weeks 16 weeks



Retroperitoneal lymph nodes (un-injected)



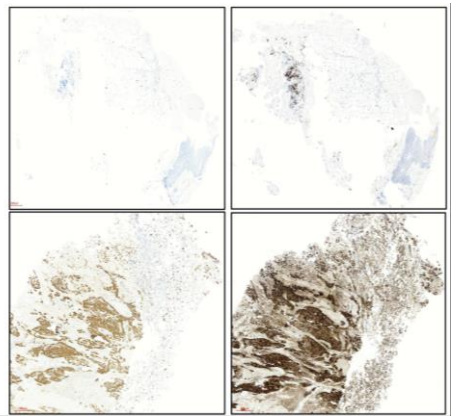
June 2018 **Feb 2020**



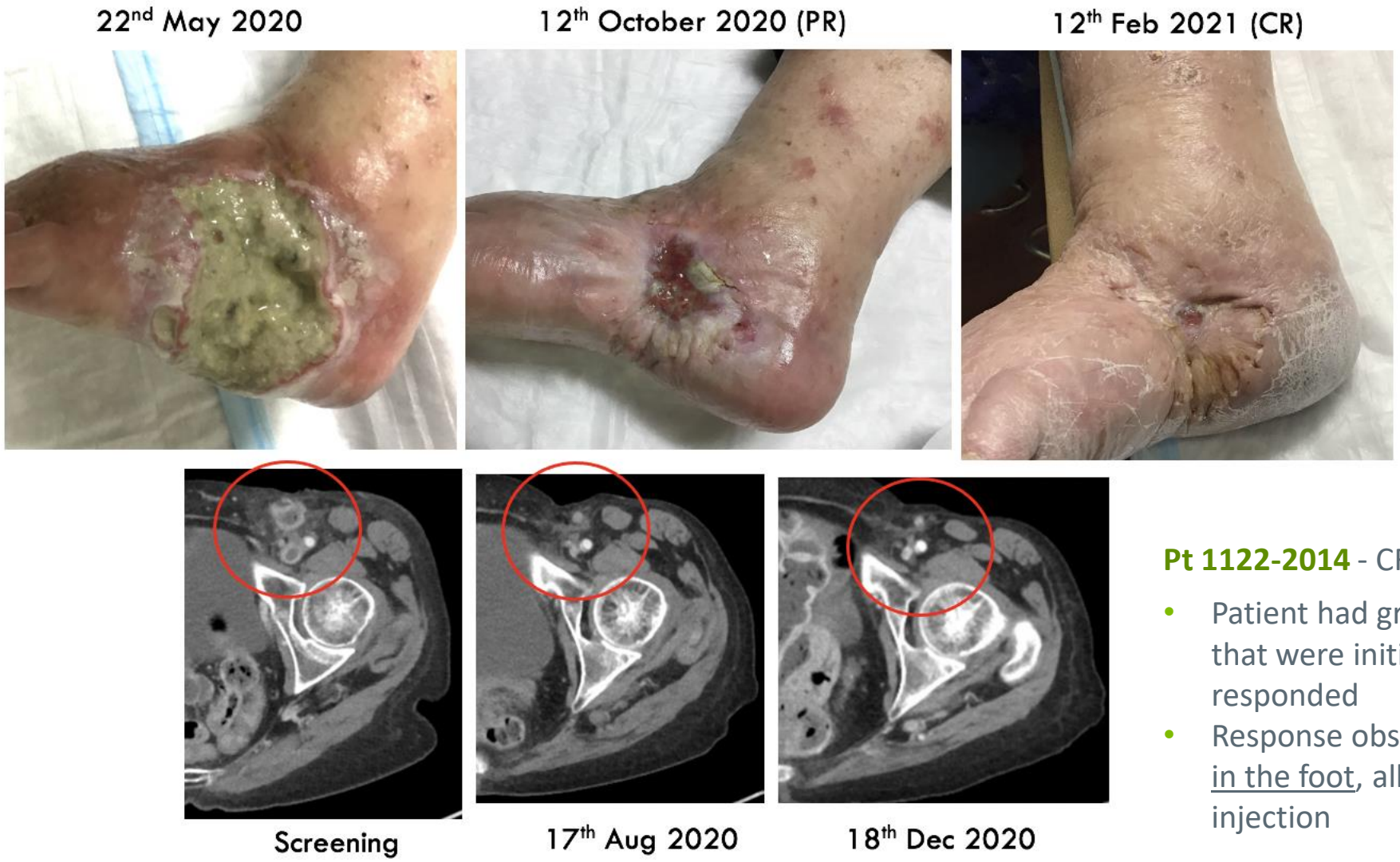
CD8 PD-L1

Baseline

Day 43



Resolution of aggressive locoregional disease



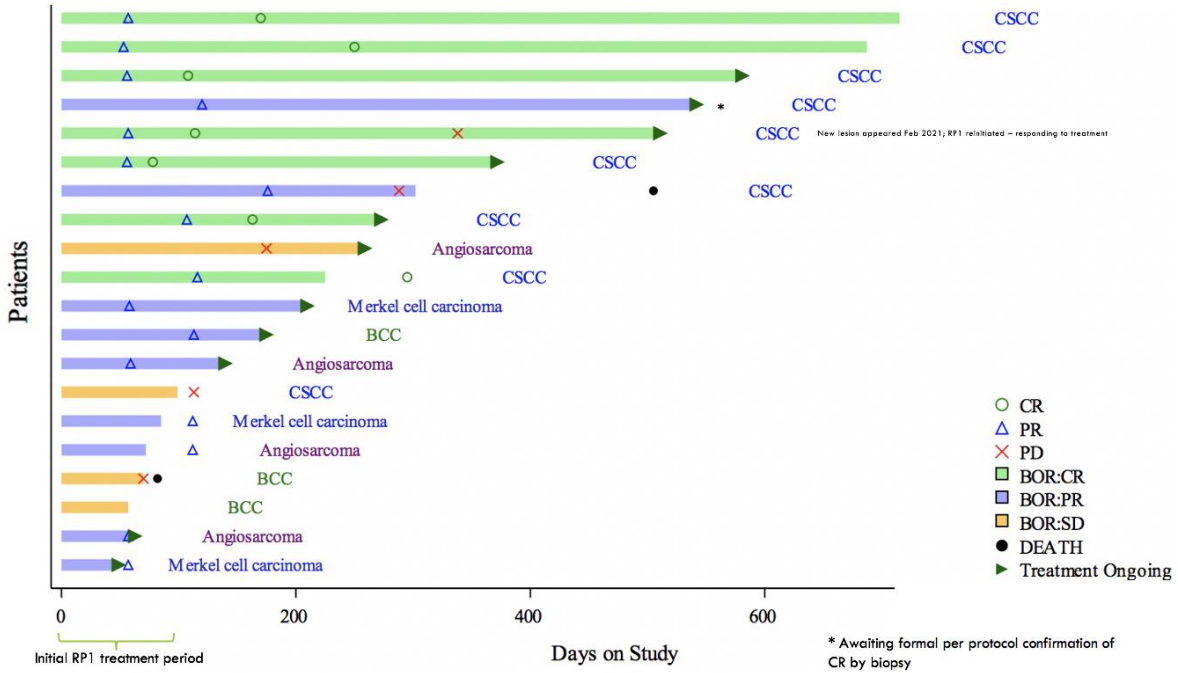
Pt 1122-2014 - CR

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

Responses in CSCC are deep & durable

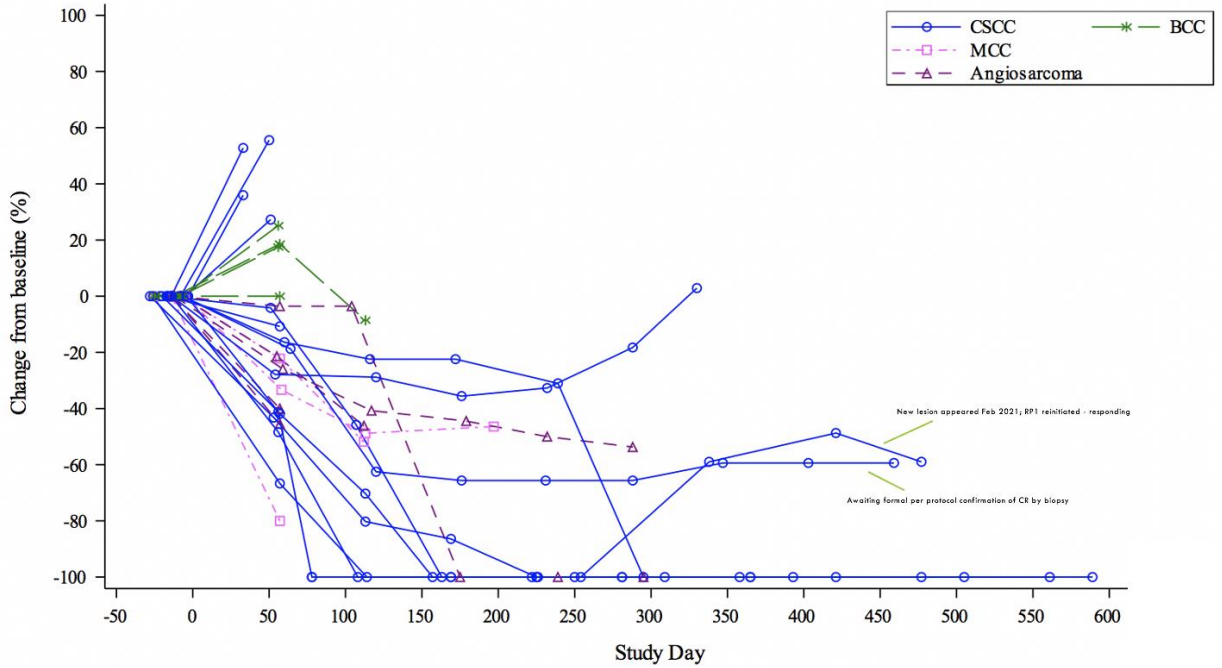
Duration of best response

Patients with a best response of at least SD



% Change from baseline in sum of tumor diameters over time

Patients with at least one follow up assessment



Based on the data to date, Replimune believes it is well positioned for success in the registration directed Phase 2 clinical trial of RP1 combined with Libtayo in CSCC

Data as of June 3 2021

Anti-PD1 failed melanoma – market opportunity

- 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[1]
- Approximately 62,000 deaths annually world-wide[2]

- High unmet medical need for patients who fail anti-PD1 based therapy
- 40-65% of all metastatic melanoma are primary refractory to initial anti-PD1 therapy[3]
- Expected response rate to continued treatment with anti-PD1 therapy following confirmed progression on single agent anti-PD1 is 6-7%[4,5]
- The expected response rate to Yervoy following failure of initial single agent anti-PD1 is 13%[6]

[1]https://seer.cancer.gov (2019 data); [2]Global Burden of Disease Cancer Collaboration *JAMA Oncol* 2019 (12); [3]Gide et al *Clin. Cancer Res* 2018 (24)
[4]Ribas et al *Lancet Oncology* 2018 (19); [5]Hodi et al *JCO* 2016 (34); [6]Pires de Sliva et al *J Clin Onc* 2020 (38)

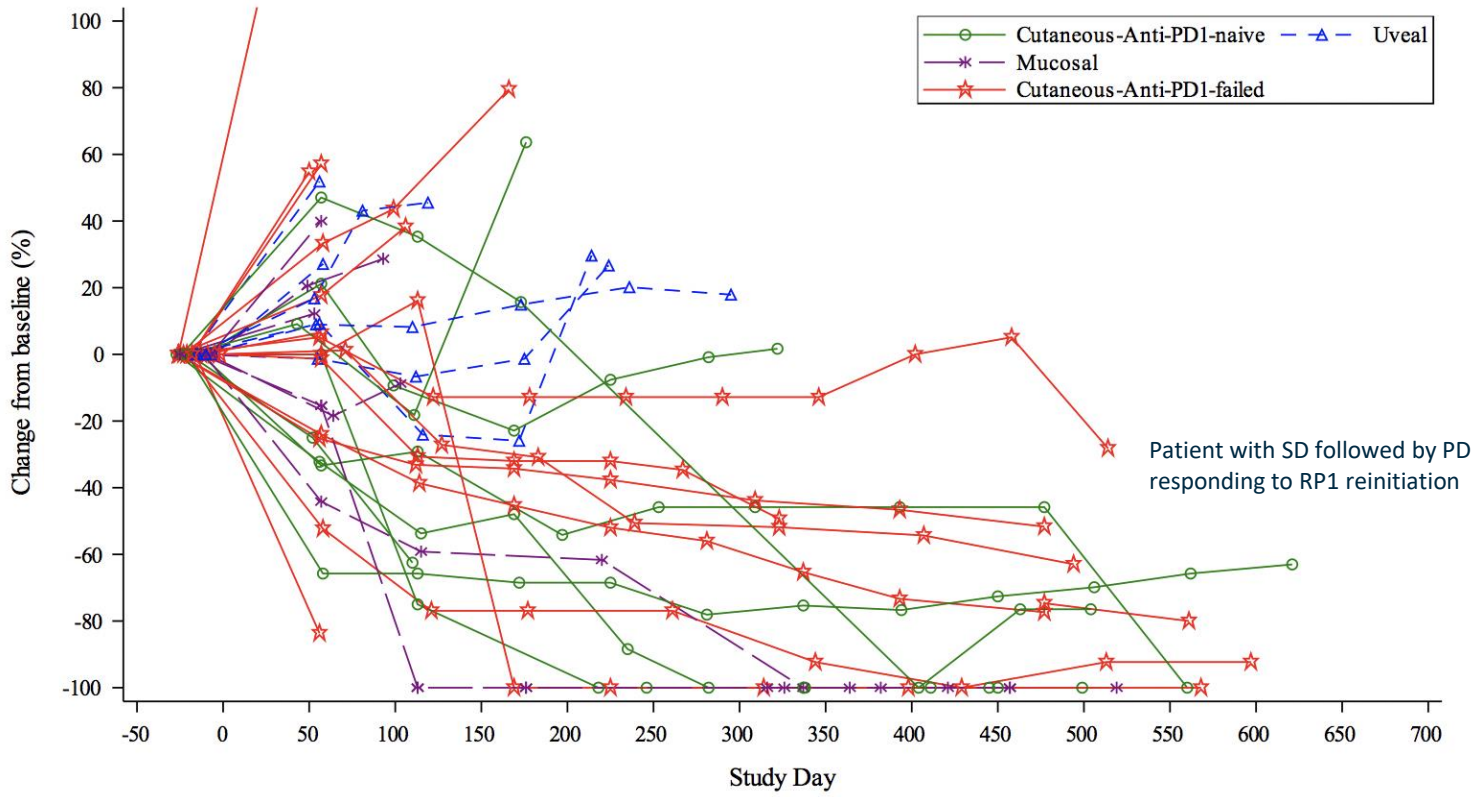
RP1 in anti-PD1 failed melanoma data

Based on May 2021 data cut of anti-PD1 failed cutaneous melanoma (N=16 patients)

- Advanced visceral disease population – **87.5% stage IVM1b/ M1c**
- Nine patients showed initial clinical benefit*
  - Five patients have met the formal criteria for response – **1 CR, 4 PR**
    - Four of which had previously failed both anti-PD1 and anti-CTLA-4 therapies
  - ORR at **31%**
  - Patients without formal response show clinical benefit from treatment
    - Ongoing surgical CR (counted as SD per study protocol definitions)
    - Ongoing CR by PET scan (no metabolic activity seen: PR by protocol definitions)
    - Ongoing SD, responding to recent reinitiation of RP1 treatment (28% reduction from baseline at latest scan)
- Responses are deep and durable – **80% ongoing at out to over 16 months**
- Clinical data supported by biomarker data, including reversal of T cell exclusion
- Activity also seen in melanoma subtypes with traditionally poor prognosis
  - Patients with uveal and mucosal melanoma who have failed prior anti-PD1 therapy

* Stable disease with evidence of anti-tumor activity

Responses are deep & durable, including for anti-PD1 failed melanoma



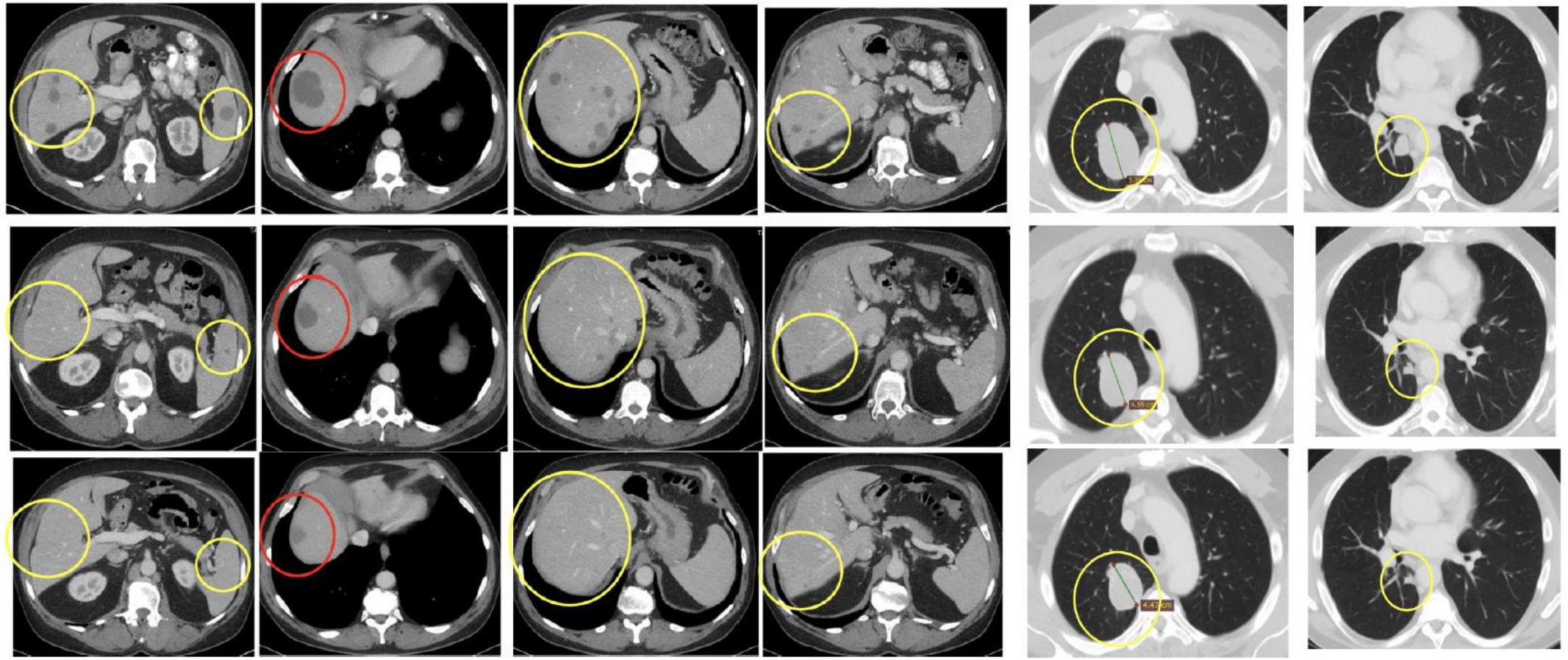
Extended clinical benefit also seen in patients with a best response of SD

Based on the data to date, Replimune believes it is well positioned for success in the registration directed 125 patient Phase 2 cohort of RP1 combined with nivolumab in anti-PD1 failed melanoma

Data as of June 3 2021

Anti-PD1/anti-CTLA-4 failed melanoma: systemic overall response

Pt 1122-2007 – PR (ongoing at 19 months from first RP1 dose)



Injected

Not injected

All lesions show no evidence of metabolic activity by PET scan

Registration-directed development in melanoma – the IGNYTE study

- Registration-directed single arm 125 patient Phase 2 cohort of RP1 combined with Opdivo in anti-PD1 failed cutaneous melanoma*
  - Patients have either failed anti-PD1 alone, or anti-PD1 in combination (including with anti-CTLA-4)
  - Confirmed disease progression required while on prior anti-PD1 therapy
  - Anti-PD1 containing therapy must be the last therapy received
  - Primary endpoint: ORR by independent central review
  - Key secondary endpoints: Duration of response, CRR, PFS, OS
- Design discussed with the FDA at a Type B meeting
  - Assuming clinically meaningful compelling data is generated, data able to be submitted for accelerated approval
  - As required for accelerated approval, a confirmatory clinical trial would also be needed to be underway at BLA filing & needed for conversion to full approval
  - Study requires an observed ORR of 22% to discount a true response rate of <15% & an observed response rate of 28% to discount a true response rate of <20%

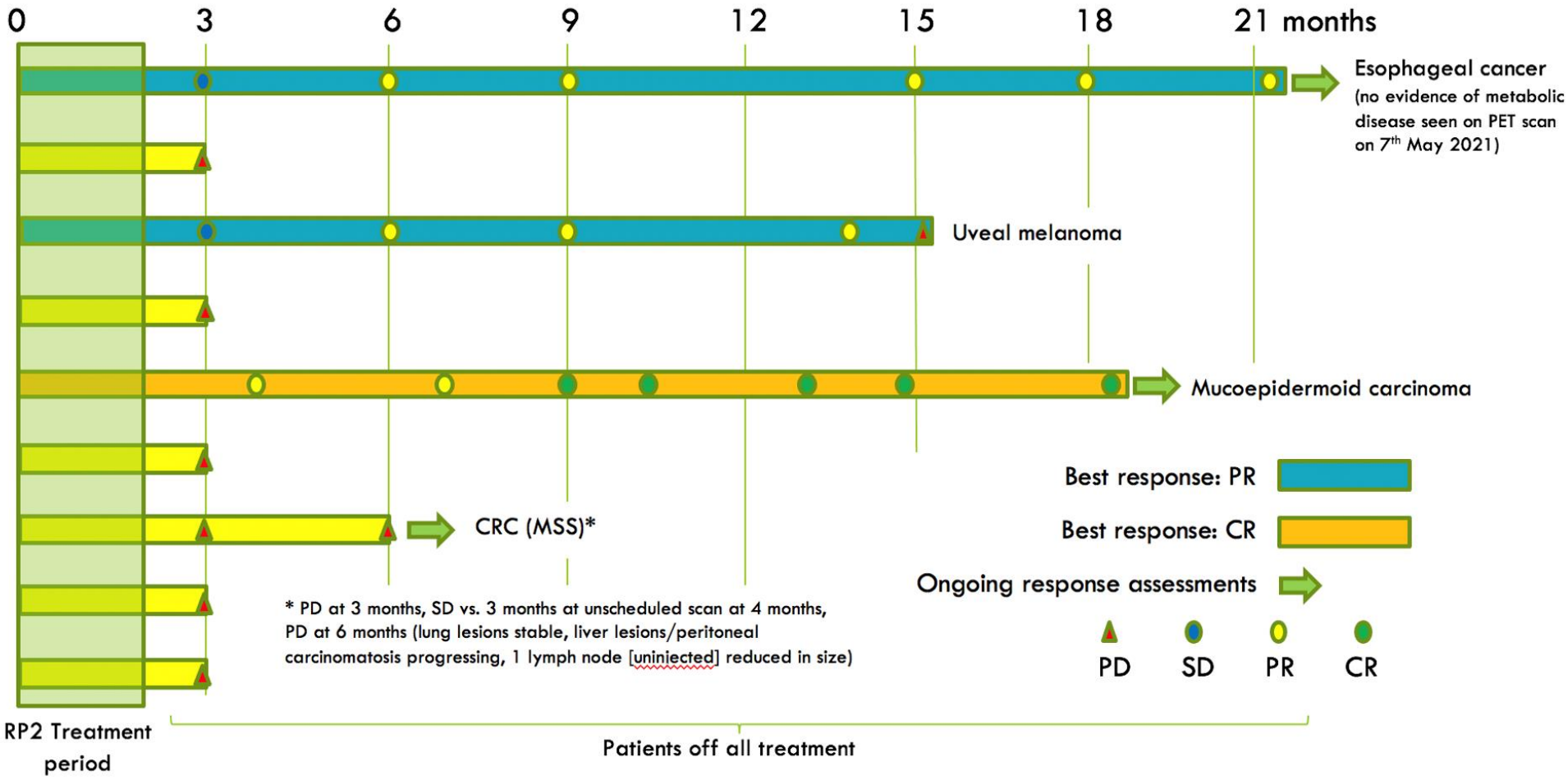
* Under a clinical trial collaboration & supply agreement with BMS for the supply of Opdivo – full commercial rights retained by Replimune

Single agent activity clearly demonstrated in traditionally ‘cold’ tumor types

- RP2 leverages Replimune’s platform to additionally express an anti-CTLA-4 antibody
- Maximizes antigen presentation to kickstart an immune response
  - CTLA-4 inhibits antigen presentation and T cell activation (Immunogenic ‘Signal 1’ & ‘Signal 2’)
  - **Local expression optimal** mechanistically, and to reduce systemic toxicity
- Well tolerated – side effects consistent with RP1
- **Compelling single agent efficacy** (N=9) in heavily pre-treated patients with immune insensitive tumor types
  - CR – Mucoepidermoid carcinoma – ongoing at 19 months
  - PR – Uveal melanoma – maintained for 15 months before PD
  - PR – Esophageal cancer – ongoing at 22 months
- **Combination data further confirms activity**
  - 30 patients so far enrolled with RP2 combined with Opdivo
  - Seven responses so far (2x uveal melanoma, 4x cutaneous melanoma, 1x SCCHN – all pts having had prior anti-PD1)
  - All but one response durable to date at out to >425 days
  - Responses seen irrespective of prior PD-L1 status

Deep and durable responses with RP2 monotherapy

Kinetics of response following treatment with single agent RP2



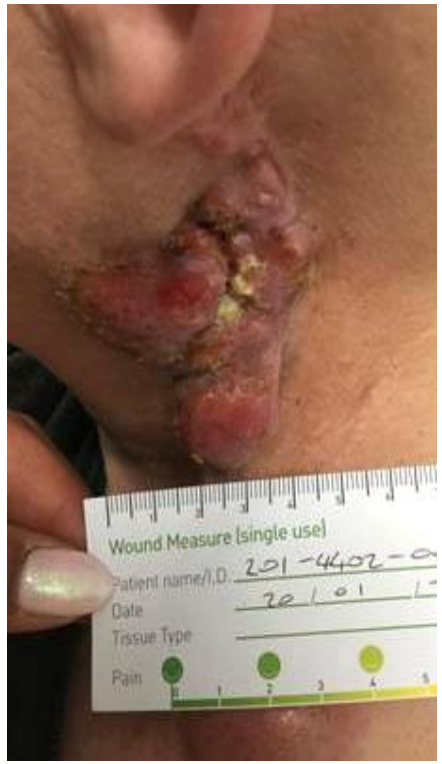
Data as of Oct 12th 2021

Ongoing CR in mucoepidermoid carcinoma following single agent RP2

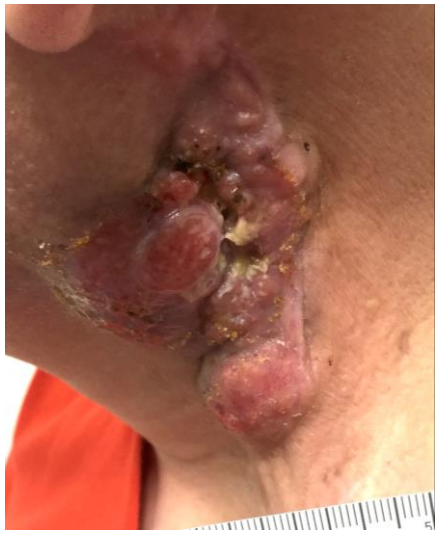
Pt 4402-0001 - ongoing CR

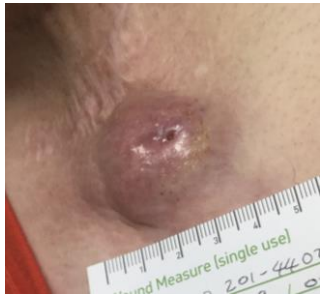
- Mucoepidermoid carcinoma of the parotid
- Prior therapies: Carboplatin/ paclitaxel, bicalutamide, ceralasertib
- Cervical lymph node & supraclavicular fossa injected

Baseline

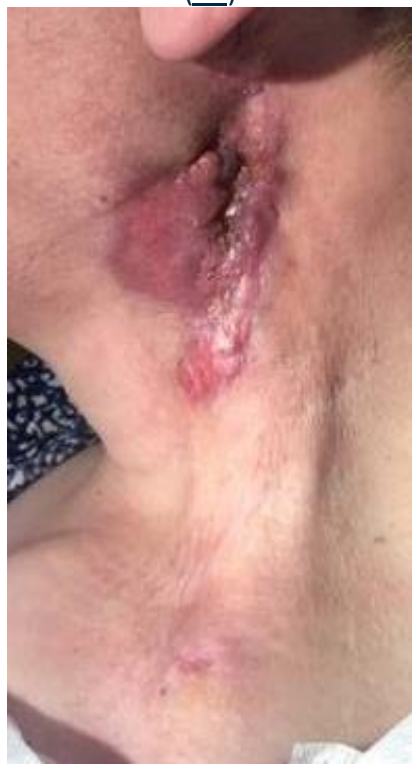


1 month

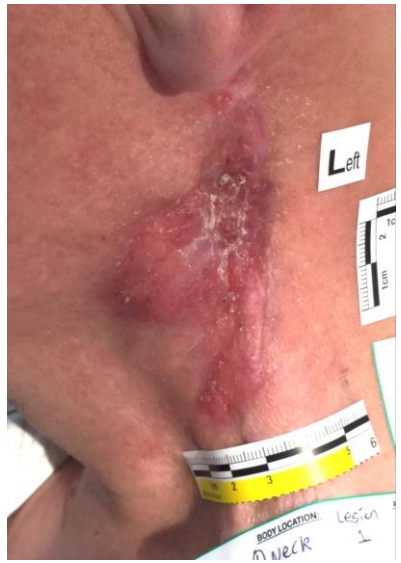


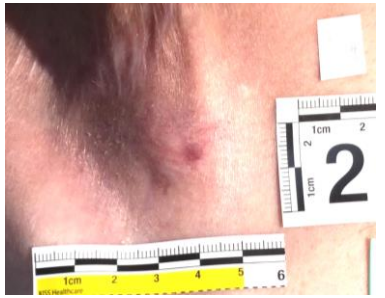


3 months
(PR)



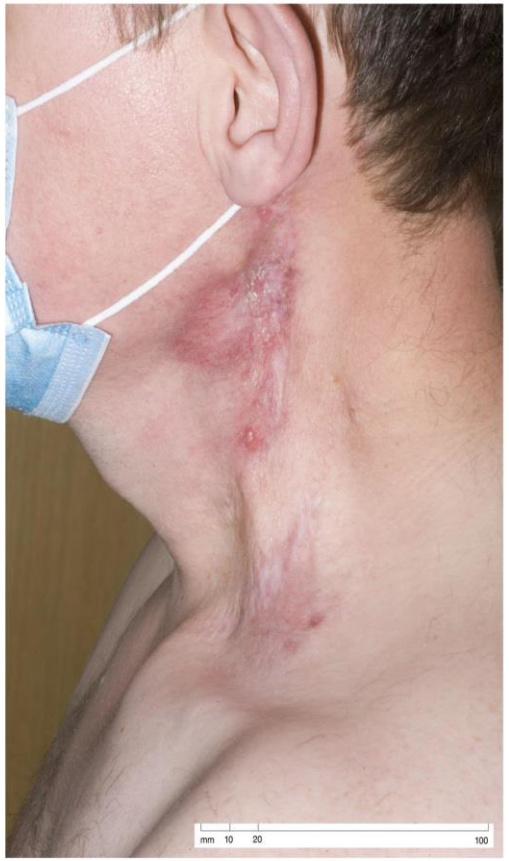
4 months



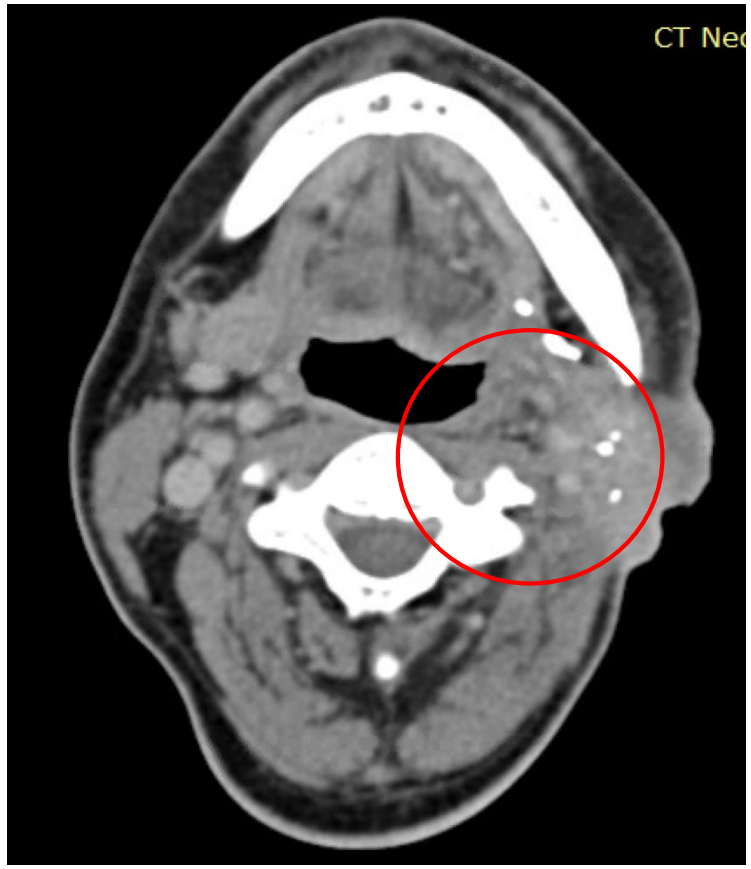


Ongoing CR in mucoepidermoid carcinoma following single agent RP2

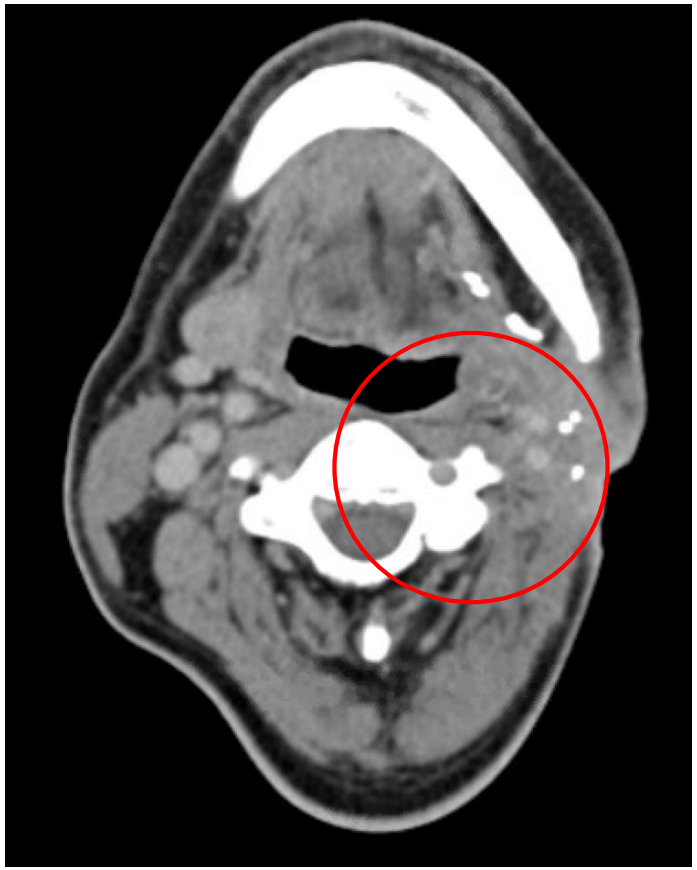
6 months



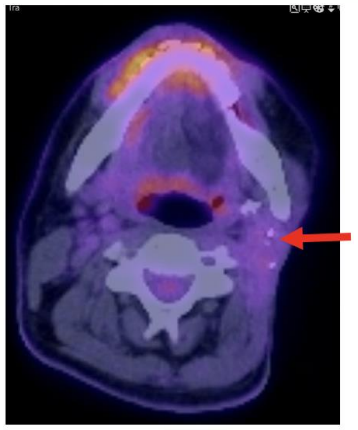
Screening

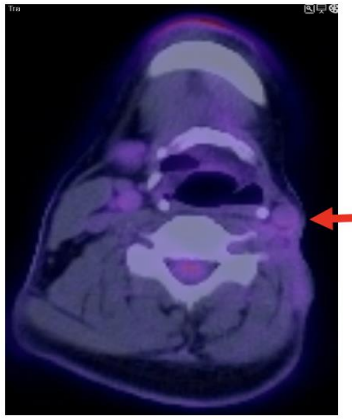


5 months



8 months
(PET scan to confirm CR)

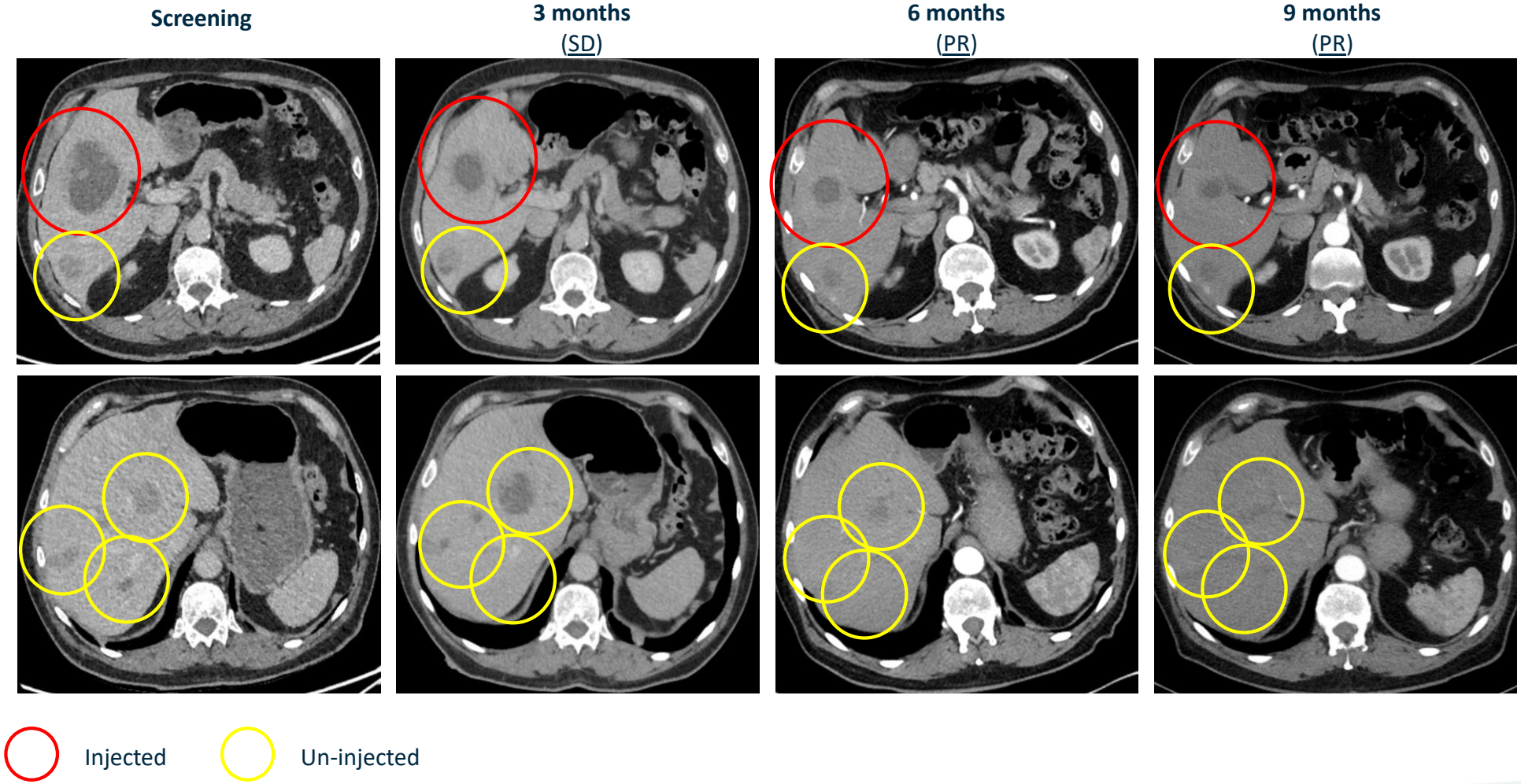




PR in ipi/nivo failed uveal melanoma following single agent RP2

Pt 4401-0003 - PR

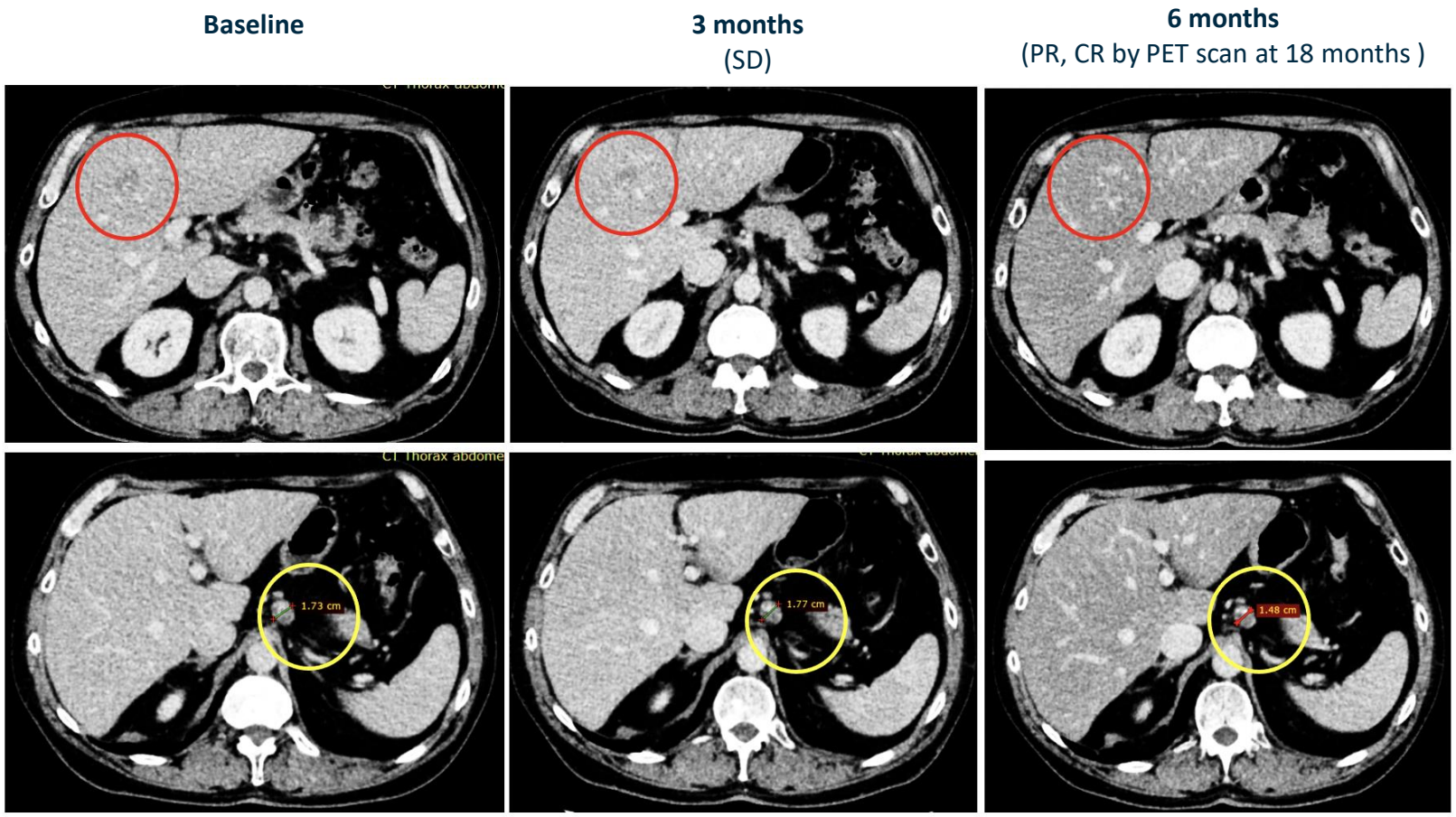
- Uveal melanoma
- Extensive liver metastases (others not shown)
- Prior therapies: Ipilimumab/ nivolumab
- Patient progressed at 15 months



Ongoing PR in anti-PD-L1 failed esophageal cancer following single agent RP2

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 combined with Opdivo provides responses in advanced, heavily pre-treated phase 1 patients

Tumor type	All	Cutaneous melanoma (failed anti-PD1 +/- anti-CTLA-4)	Uveal melanoma	SCCHN	Other (NPC, thyroid, salivary, sarcoma, sarcomatoid, chordoma)
# of patients	30	9	8	3	10
Best response					
PR	7	4	2*	1**	0
SD	10	2	3	0	5
PD	13	3	3	2	5
Current ORR	23.3%	44.4%	25%	33%	0%

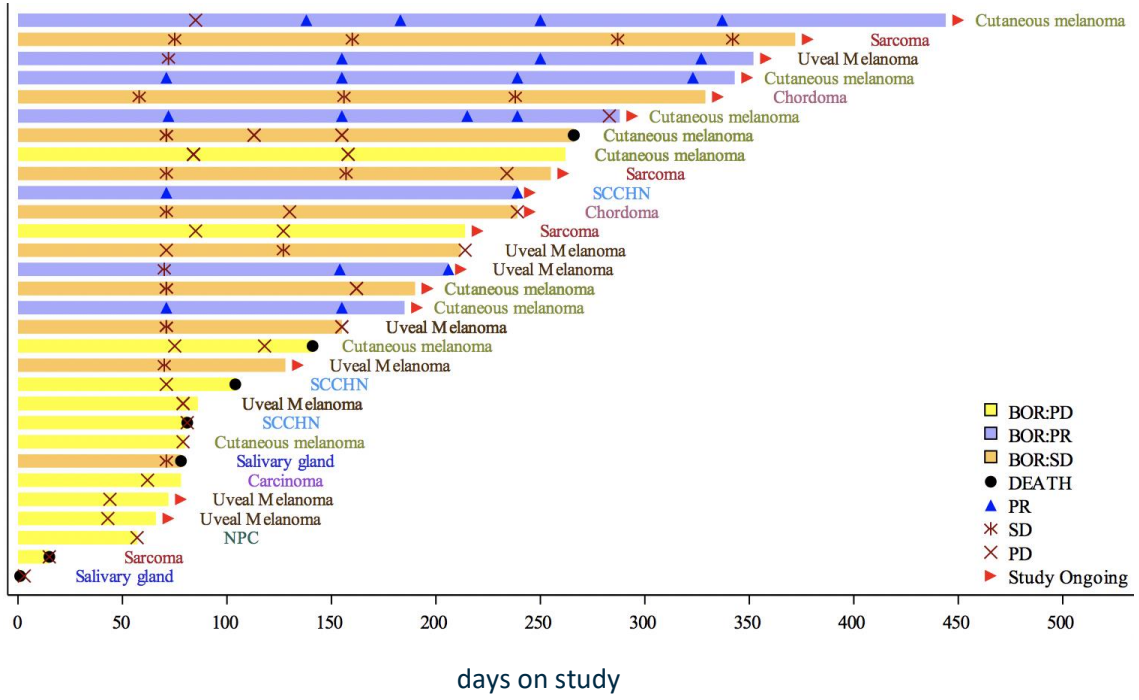
*Nivolumab and ipilimumab/pembrolizumab failed
**Prior nivolumab, 5-FU/cisplatin, radiotherapy

Data as of Oct 12th 2021

RP2 + nivolumab provides deep and durable responses

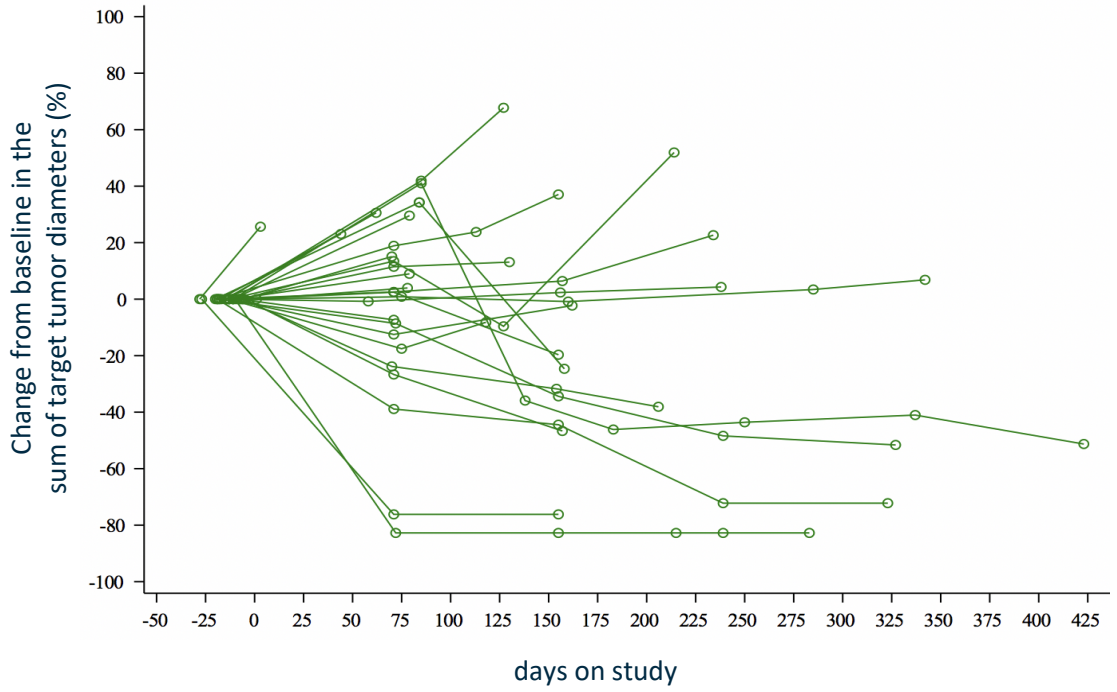
Duration of best response

Patients with a best response of at least SD



Change in tumor size

Patients with at least one follow up assessment

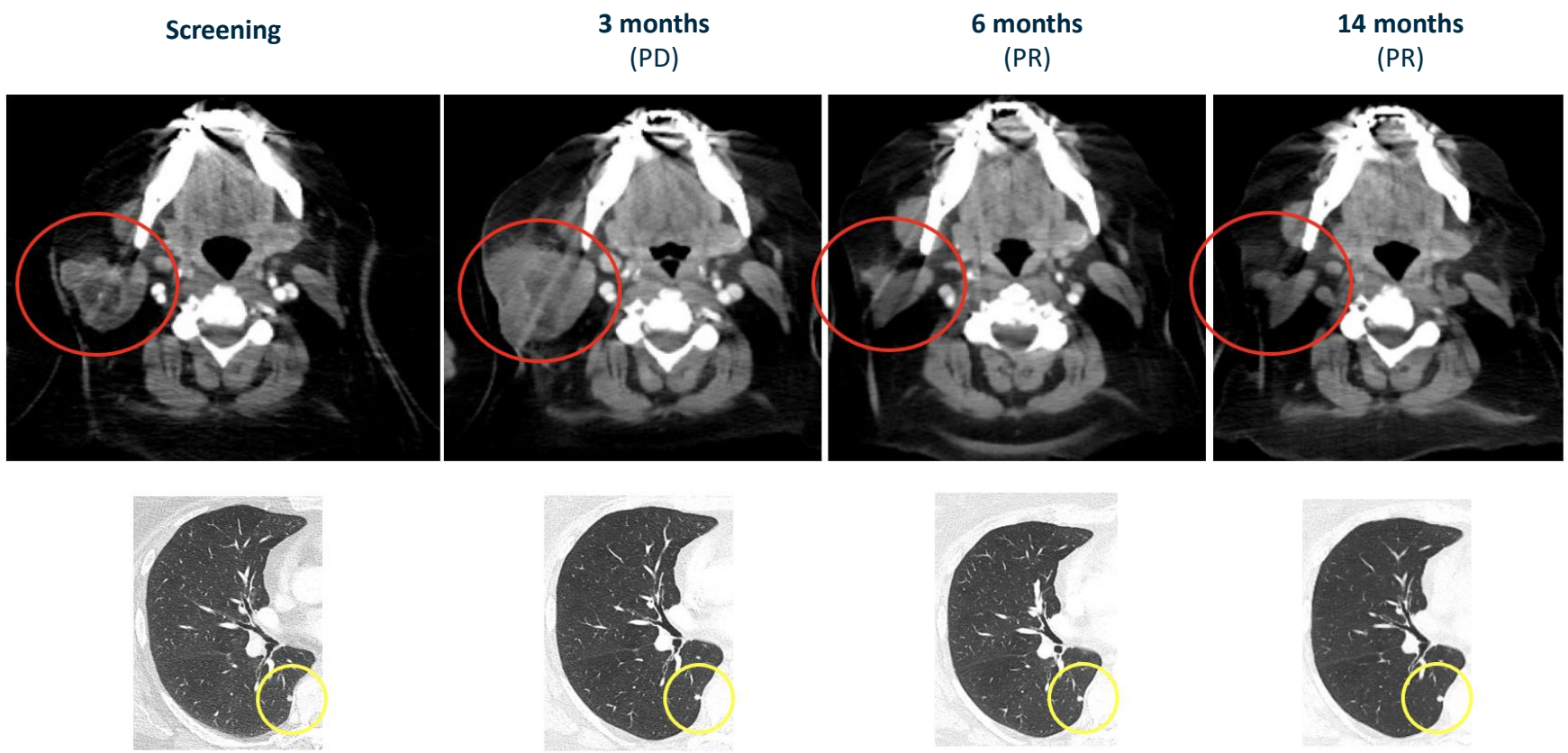


Data as of Oct 12th 2021

Example patient with anti-PD1 failed melanoma: Response following initial pseudo-progression

Pt 4403-0004 - PR

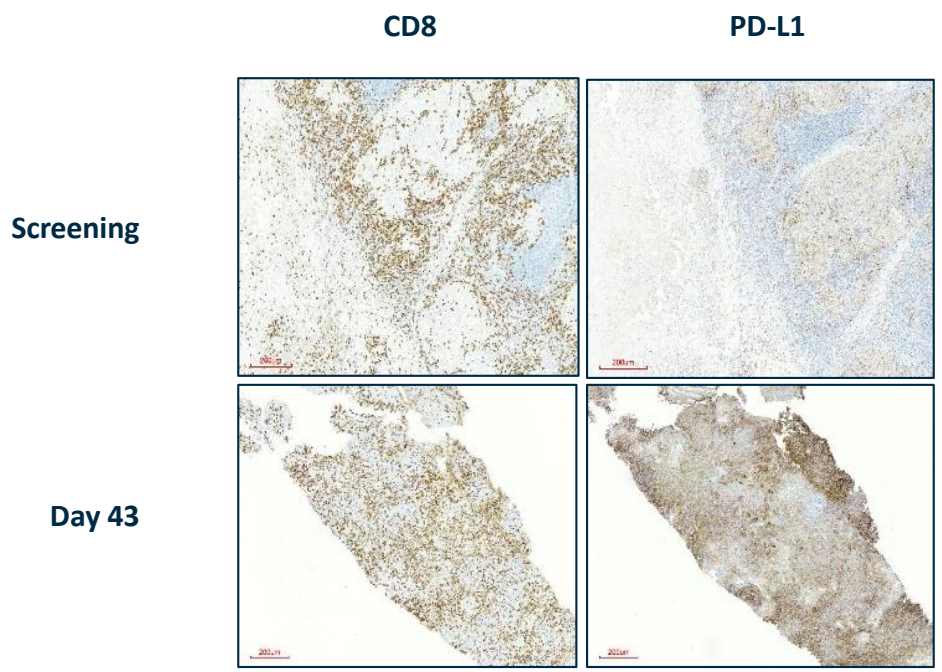
- Cutaneous melanoma
- Extensive liver metastases (others not shown)
- Small lung & brain lesions stable since baseline
- Prior therapies: nivolumab, dabrafenib, trametinib
- Had been off work for three years & in significant pain: Now off all pain meds & back at work



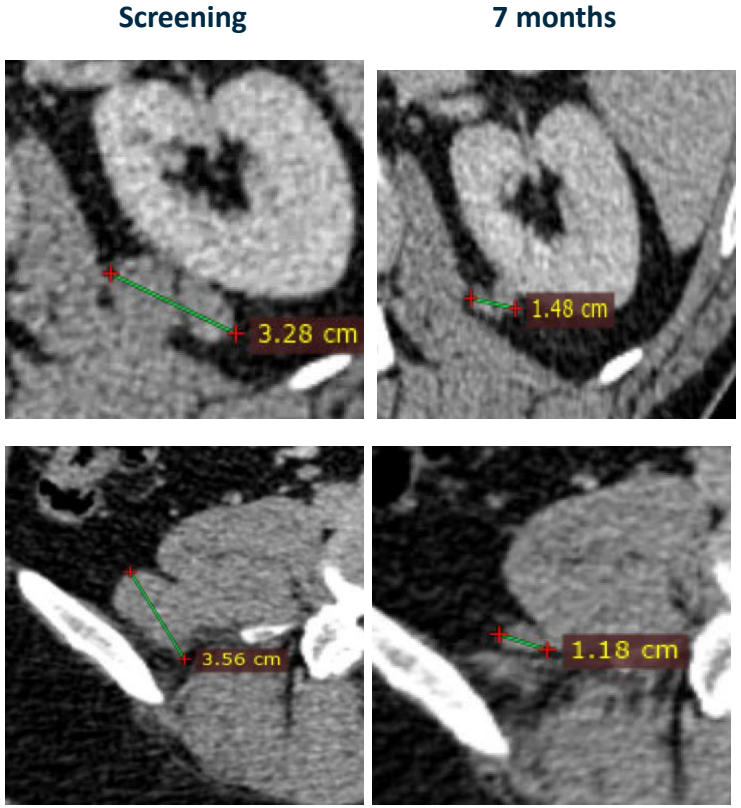
Ongoing partial response following deep nodal injection in ipi/pembro failed uveal melanoma

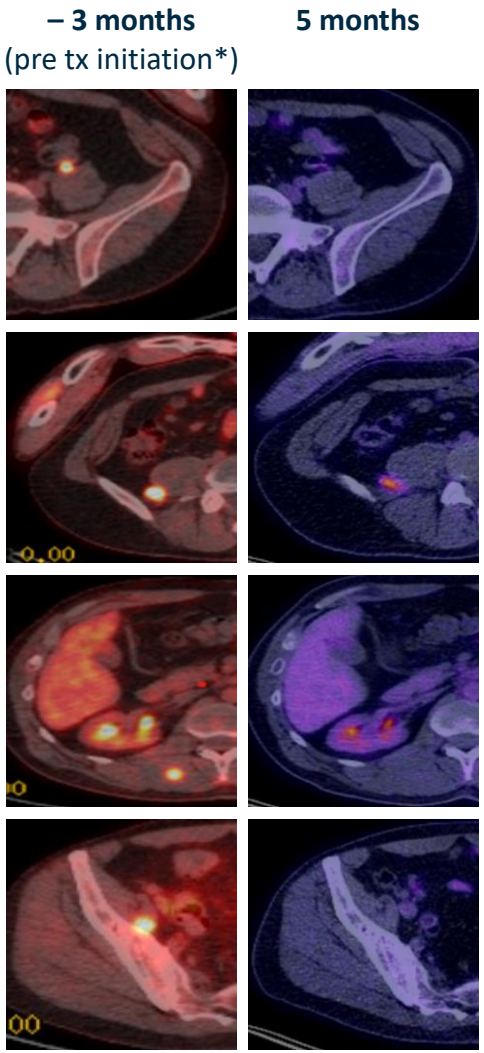
Pt 4402-0014 - PR

- Uveal melanoma
- Deep nodal lesion injected
- Prior therapies: ipilimumab, pembrolizumab



Discordant CD8 & PD-L1 staining at baseline changing to concordant staining at day 43





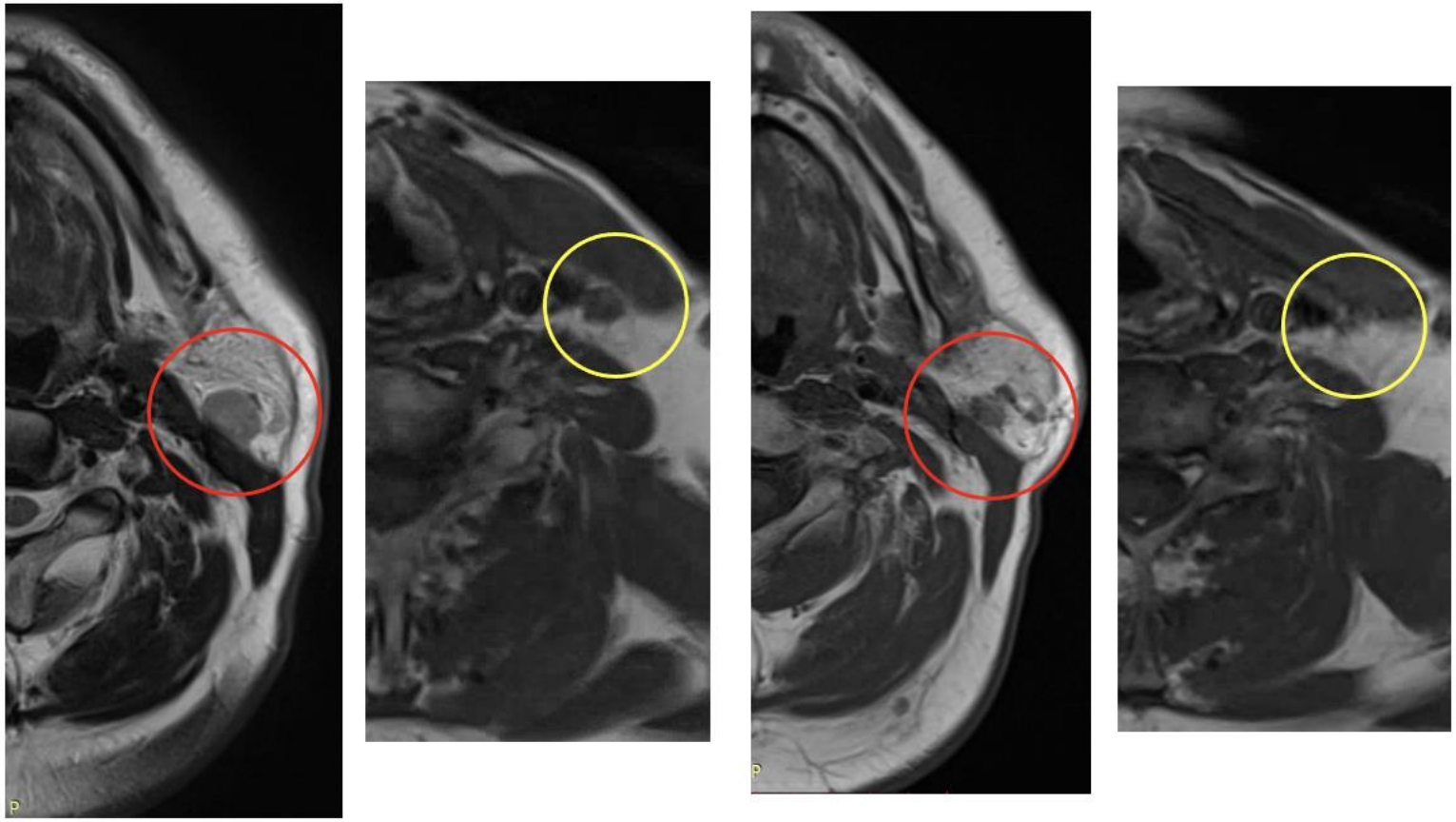
*No intervening therapy for patient in 3 months prior to screening, RP2 initiation

Ongoing PR in anti-PD1 failed head & neck cancer

Pt 4403-0011 - PR

- Squamous cell carcinoma of the head and neck
- Prior therapies: 5-FU/cisplatin, radiation, Opdivo

Screening | **2 months** (PR)

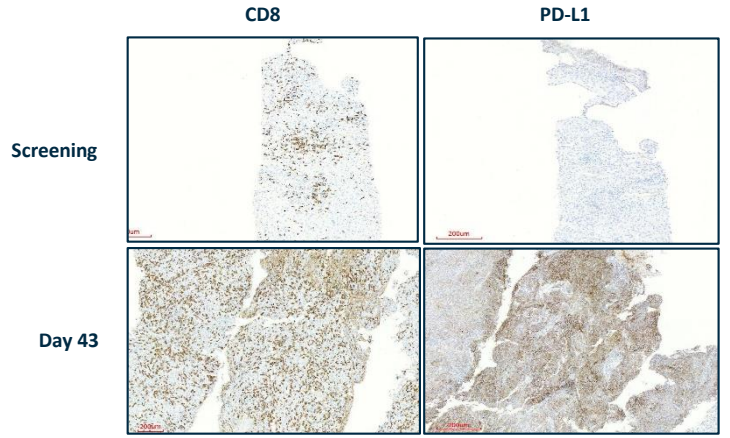


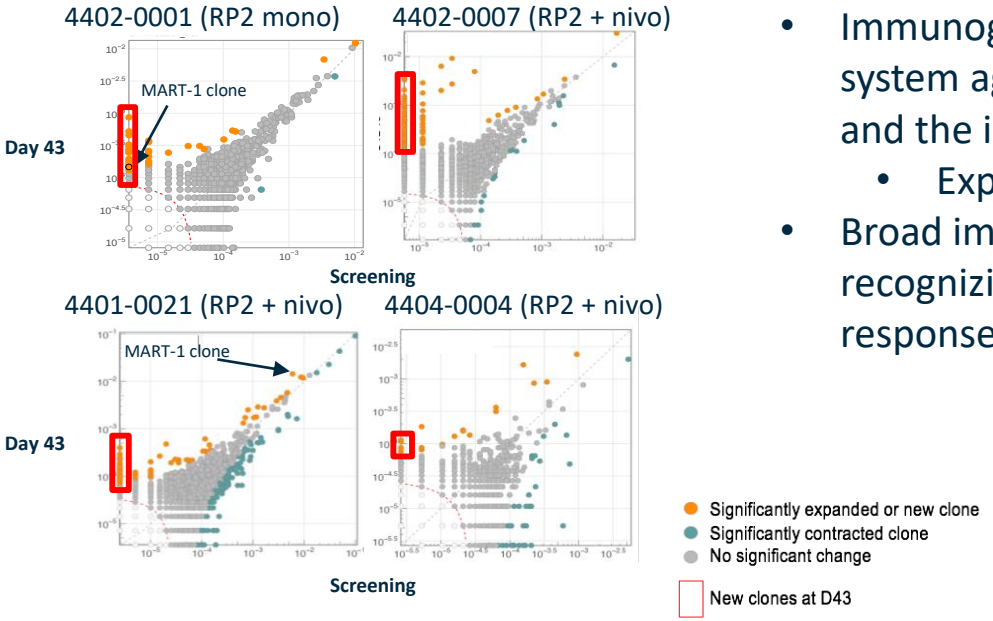
Injected | Un-injected

RP2: Reshaping the tumor microenvironment & immune activation

- Pre and post treatment biopsies show robust influx of CD8+ T cells into the tumor
- Increases in PD-L1 indicates potent immune activation and suggests benefit is likely to be increased in combination with anti-PD1 therapy

RP2 modifies the tumor micro-environment to turn 'cold' tumors 'hot'





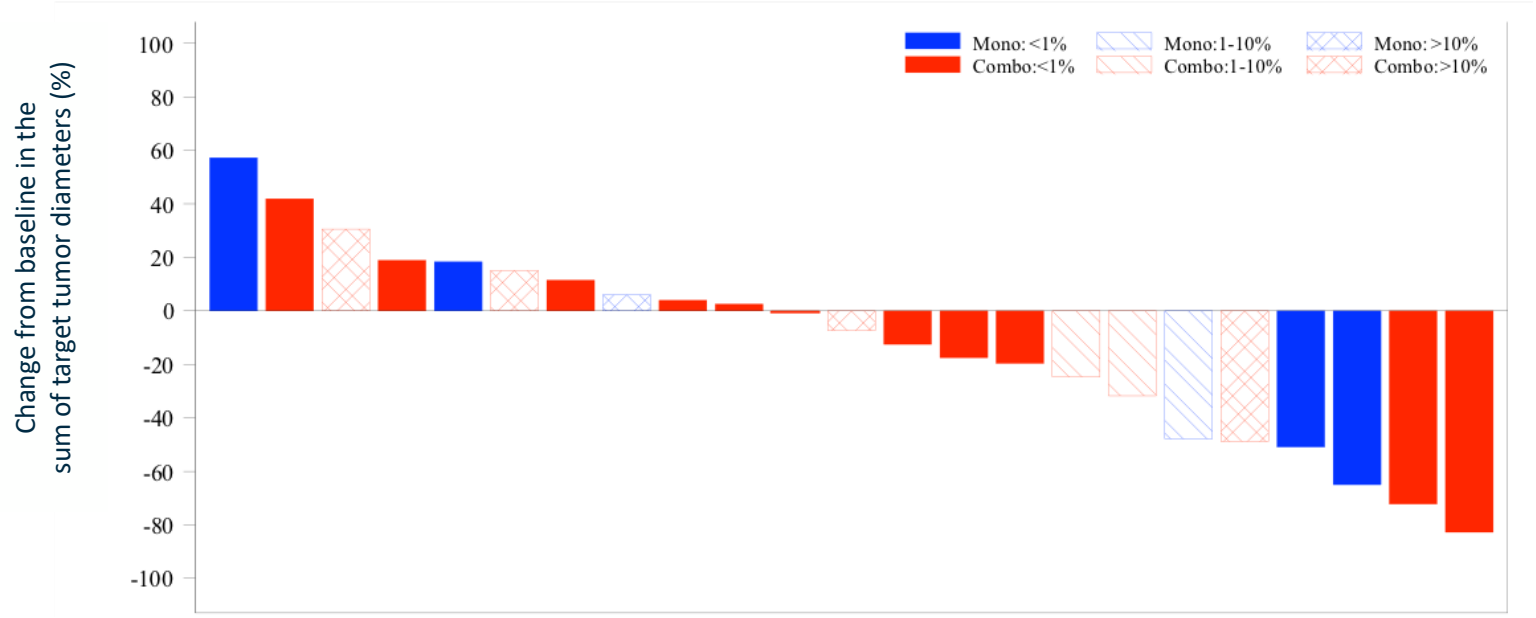
- Immunogenic tumor killing by RP2 releases tumor antigens to activate the immune system against the patient's cancer, including the expansion of pre-existing T cell clones and the induction of new T cell clones
  - Expected to include previously unrecognized epitopes
- Broad immune activation is intended to provide systemic immune-mediated activity, recognizing the patient's cancer throughout the body, and providing a long-lived response

RP2 aims to ignite a systemic & sustained immune response specific to each patient's cancer

RP2 activity is not dependent on PD-L1 status

Maximal change in tumor size

Patients with quantified PD-L1 expression



Supports the intended mechanism of action, with activity irrespective of PD-L1 status: Both immunologically 'hot' and 'cold' tumors respond

Beyond skin cancers – Background & rationale for development in patients with liver metastases

- The liver is one of the most common sites of metastasis across tumors (including lung, breast, and colon cancer)
- The prognosis for patients with liver metastases is poor, with limited effective treatment options
  - Liver metastases across tumor types are associated with systemic resistance to immune checkpoint blockade
- Liver metastases are associated with antigen-specific elimination of T cells from the circulation by macrophages resident in the liver metastases
  - Leads to systemic loss of T cells and diminished immunotherapy efficacy
- The oncolytic immunotherapy MOA is intended to
  - Directly kill tumors
  - Induce systemic T cell mediated (& other) immune responses to the antigens released
- Intratumoral RP1 & RP2 alone & combined with anti-PD1 is well tolerated & has demonstrated compelling evidence of efficacy, including in liver metastases

Riihimaki et al Cancer Med 2018; Yu et al Nat Med Jan 2021

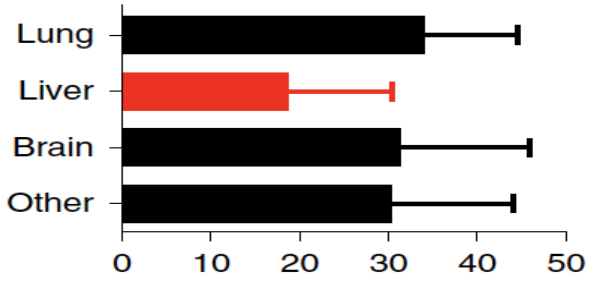
There is a significant unmet need for patients with liver metastases

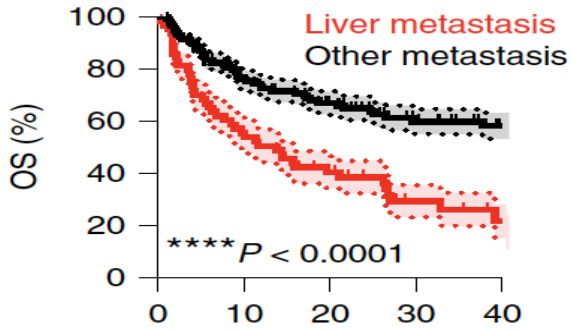
The presence of liver metastasis correlates with **poor outcomes** to immunotherapy

- Reduced objective response rates
- Survival gaps and long term outcomes significantly lower

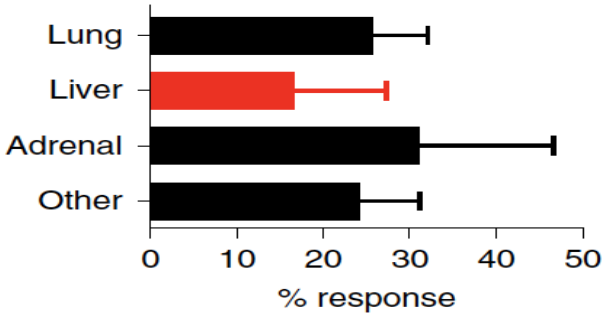
Two illustrative tumor types show a substantial outcome gap

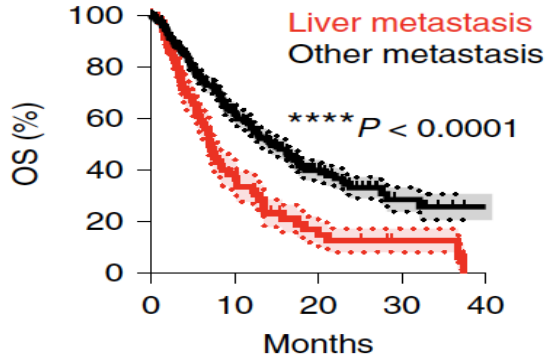
Melanoma





NSCLC





Response rates by metastatic site

Survival curves by metastatic site

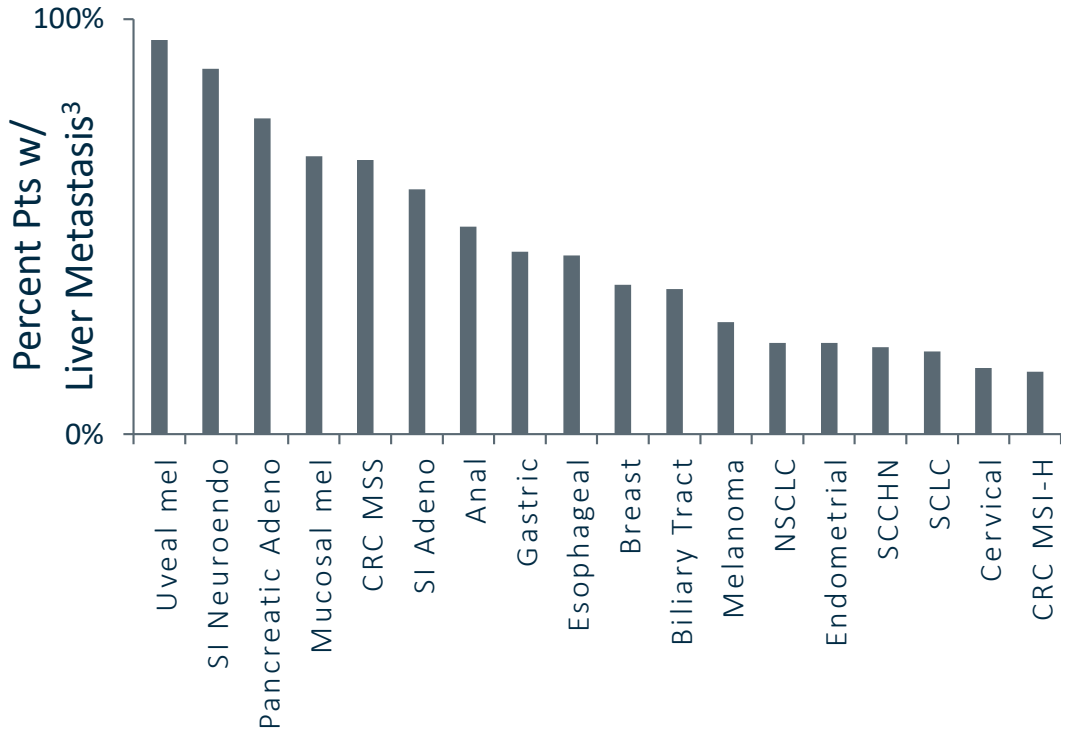
Yu et al Nat Med Jan 2021

There is a large unmet need in patients with liver metastases

In three major indications, large numbers of patients with liver metastases could benefit from improved treatment

	Breast	Colon	Lung
Estimated Annual US Deaths[1]	43,600	52,980	131,880
Autopsy Liver Met. Rate[2]	36%	69%	23%
Rough Estimate of Amenable Patients	~16k	~37k	~30k

Numerous other cancer types also have a high frequency of liver metastases



1) SEER 2021 Estimated Deaths. From SEER Cancer Stat Facts by indication

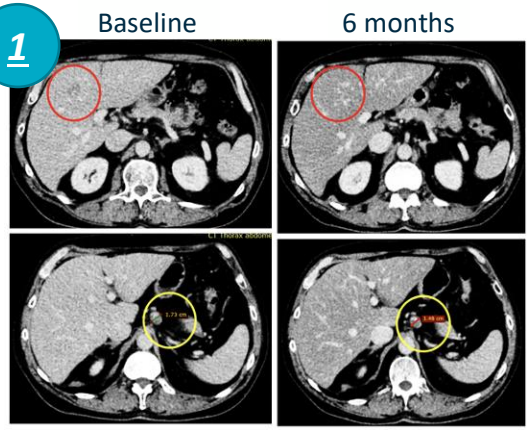
2) Riihimaki et al Cancer Med 2018

3) Data displays % of liver metastases at initial diagnosis or death Source: Independent analysis conducted on behalf of Replimune

Six example patients with liver metastases across tumor types responding to RP1 or RP2

Single Agent RP2

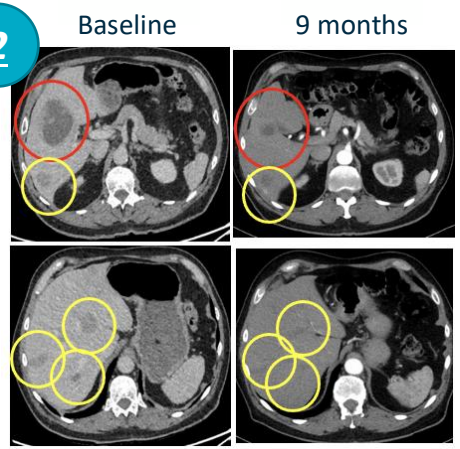
1



- Esophageal cancer, ongoing PR at 18 mos
- Previously treated w/ aPD-L1 and CTx

Single Agent RP2

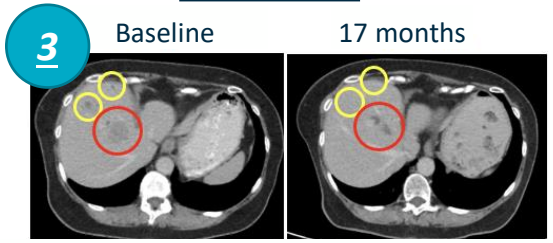
2



- Uveal melanoma, PR until 14 mos
- Previously treated w/ ipi-nivo

RP1 + nivo

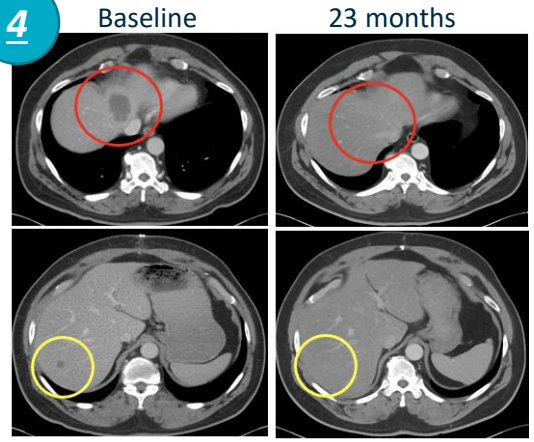
3



- Cutaneous melanoma, ongoing metabolic CR at 19 mos
- Previously failed ipi-nivo

RP1 + nivo

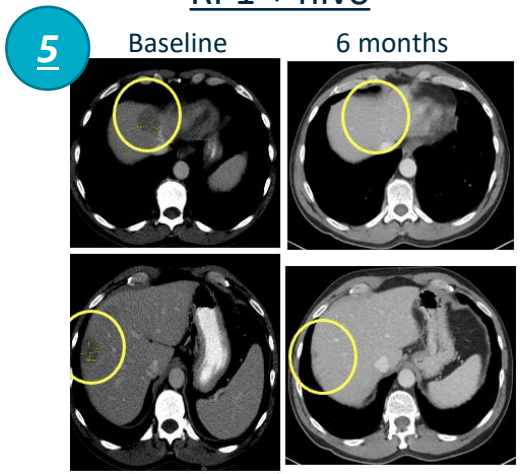
4



- MSI-H CRC, ongoing PR at 23 mos
- Previously treated w/ CTx + aVEGF

RP1 + nivo

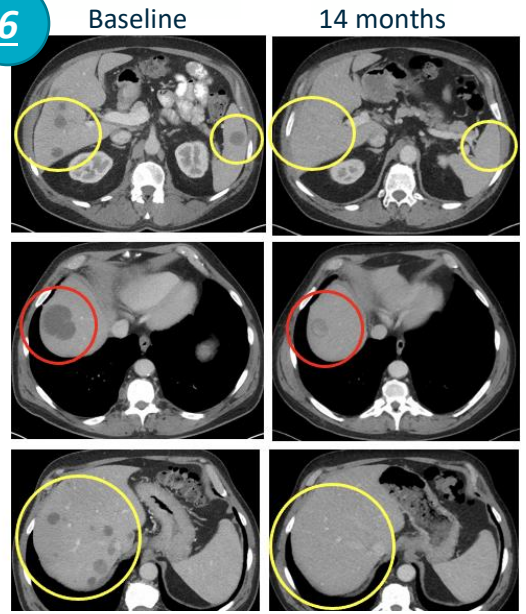
5



- Cutaneous melanoma (regression in lung and liver lesions post-injection to thigh lesion), ongoing CR at 15 mos
- aPD-1 naive

RP1 + nivo

6



- Cutaneous melanoma, ongoing PR at 15 mos
- Previously failed ipi-nivo

Development strategy for RP2/3, with focus on liver metastases

1. Expanded Phase 1 for RP2/3

RP2 expanded Phase 1

- Additional patients with liver metastases from lung, GI, breast & UM

RP3 expanded Phase 1

Dose escalation (3-6 patients /cohort)	Expansion @ RP3 RP2D
Cohort 1 (10^6 PFU/mL RP3 → HSV-1 neg (10^7 PFU/mL RP3); Cohort 2 (10^7 PFU/ mL RP3)	RP3+nivo combo & translational cohorts with focus on SCCHN, lung cancer, BC (inc chest wall), GI & UM and pts with liver mets

2. Follow on signal finding cohorts/studies in defined tumor types with RP2 or RP3 (n= 20-40pts each)

RP2/3 RP2D + anti-PD1 and/or other combo (example tumor types)

- Colorectal Cancer (MSS)
- Breast Cancer
- Lung cancer
- SCCHN
- Other GI cancers

Success criteria → Go/ No-Go

3. Registrational path

Indication specific OR Tumor agnostic OR Combination of the two

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 technology transfer from CMO successfully completed; RP2 underway

Complete manufacturing control to cover all clinical development and commercial needs

- Scale sufficient to cover global commercialization of Replimune's products at full capacity
- Avoids reliance on contract manufacturers

Attractive practicality & cost per dose

- Commercially attractive cost of goods & 'off the shelf' product practicality

Catalysts expected in 2021/22

2021

- RP2 + Opdivo updated data from combination cohort in all comers study

Q1 2022

- RP3 phase 1 initial single agent data in all comers
- RP1 + Opdivo anti-PD1 failed CSCC initial data
- RP1 ARTACUS single agent initial data in CSCC organ transplant patients
- Detail on RP2/3 development strategy

Q4 2022

- CERPASS (CSCC registration directed study) primary read out trigger
- IGNYTE (anti-PD1 failed melanoma registration directed study) interim read out
- RP1 + Opdivo anti-PD1 failed NSCLC initial data
- RP1 + Opdivo anti-PD1 failed CSCC updated data
- RP1 ARTACUS single agent data in CSCC organ transplant patients updated data
- RP2 combined with Opdivo liver metastases expansion initial data
- RP3 anti-PD1 combination initial data, with focus on liver metastases and prevalent tumor types

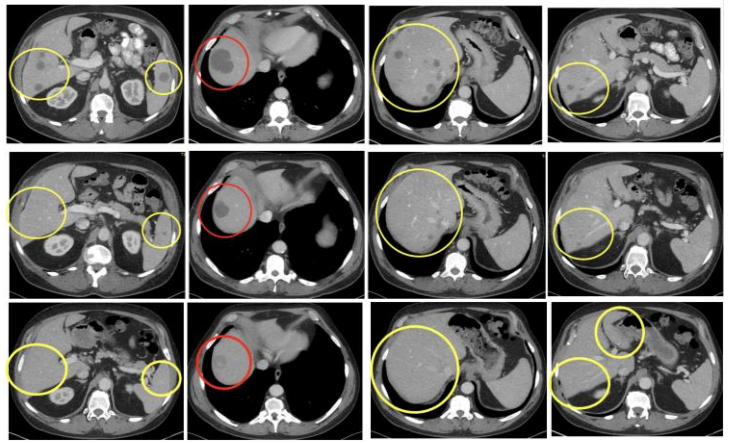
Well capitalized to deliver with cash into H2 2024

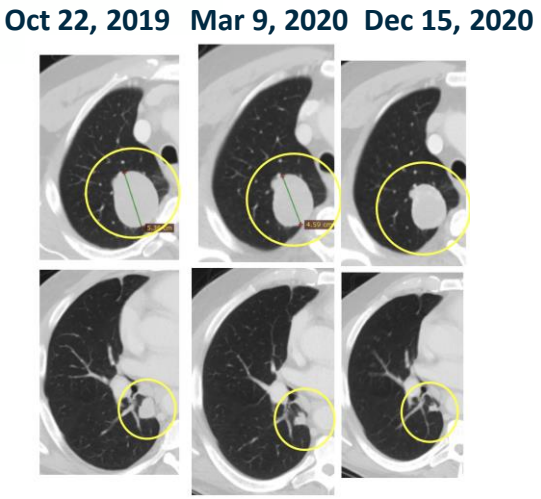

Replimune®
THANK YOU

Local & distant responses observed in ipilimumab/nivolumab failed melanoma

Pt 1122-2007 – PR (ongoing at 19 months from first RP1 dose)

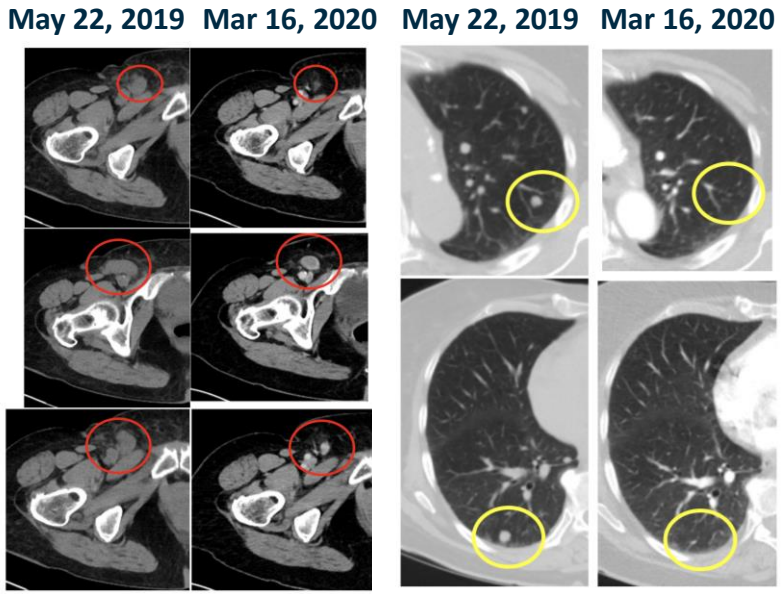
- Ipi/nivo failed cutaneous melanoma

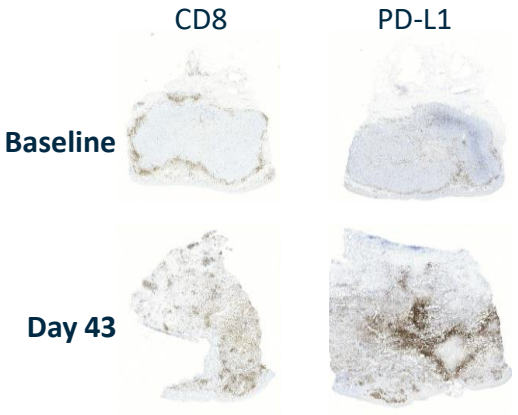




Pt 4403-1003 – PR (ongoing at 23 months from first RP1 dose)

- Ipi/nivo failed cutaneous melanoma



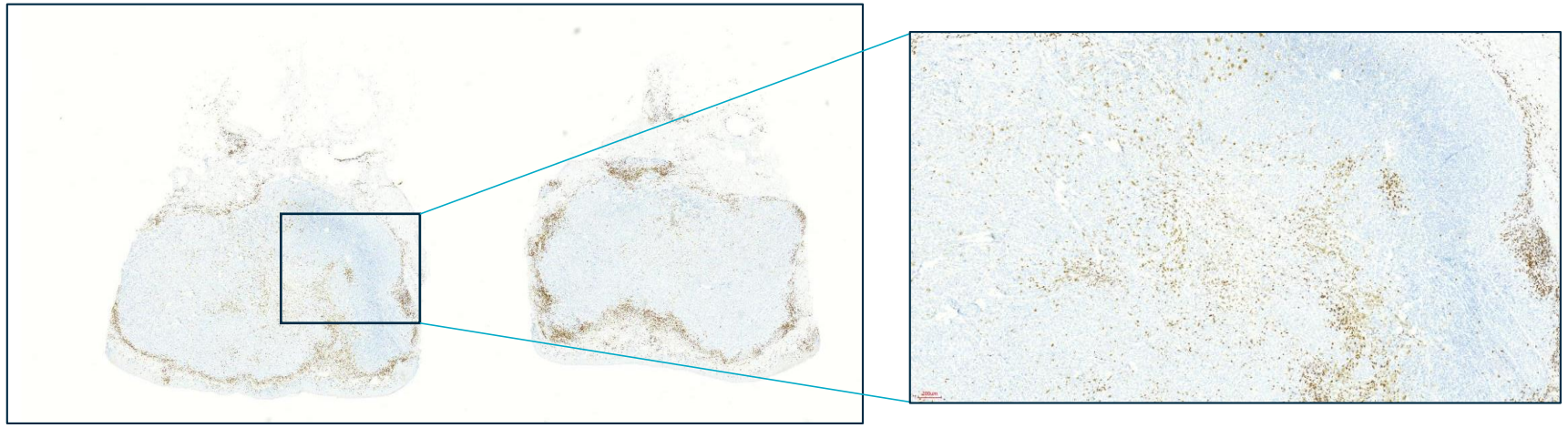


Reversal of T cell exclusion

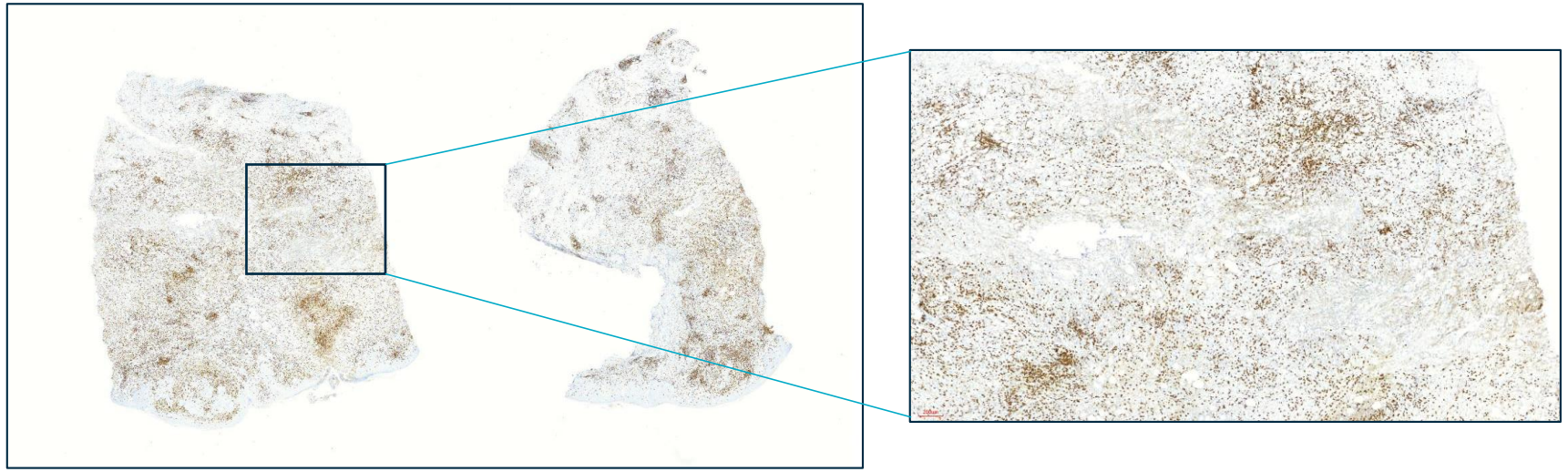
Reversal of T cell exclusion with RP1 combined with nivolumab

Biopsies Stained for CD8

Screening



Day 43



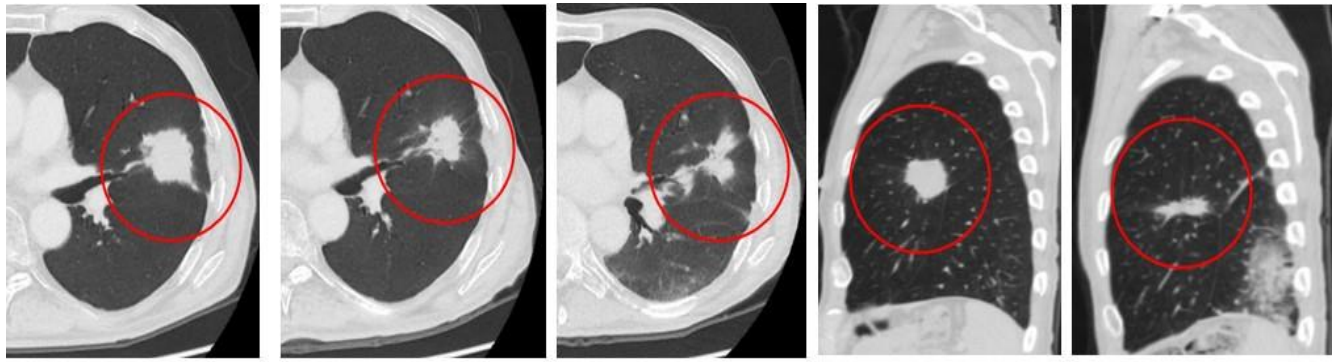
Example Patient 2
Cutaneous melanoma
(ipilimumab/nivolumab refractory)

PR achieved after RP1+nivolumab injection into lung

Pt 4401-1024 – PR

- Recurrent esophageal cancer

Injected



Dosing

C1D1: 23Apr2020; injected in Rt lower lobe(TL2), CT. Last dose C7D85, 16Jul2019.

Tumor response (RECIST)

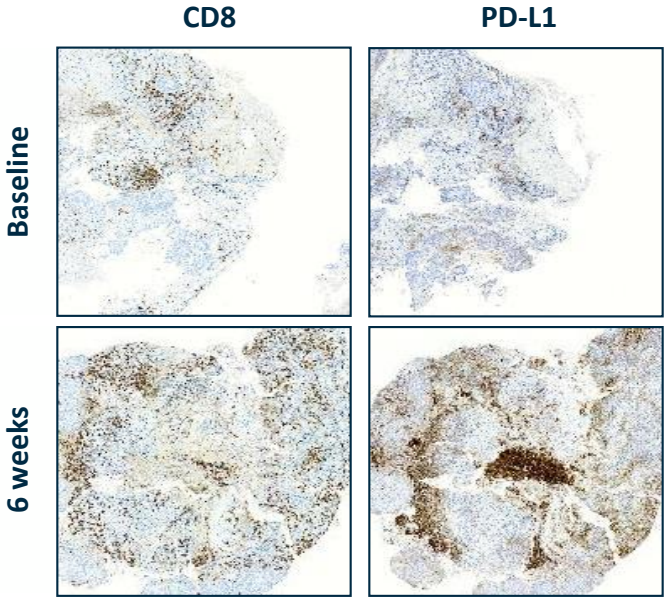
88 mm→89mm→68mm→52mm (-69%)
SD (C5D57 Jun 2019) SD→(C9D113 Aug 2019)
PR→(C11D169 08Oct2019)
PD (C12D197)

AEs (No G3/4 reported)

G2 pneumonitis (2 events, not related to RP1), G1 discomfort in the injection site

Status: Patient Completed study 05Mar2020

TME Analysis



Demographics

- Diagnosis: Esophageal carcinoma, squamous
- Initial Stage: III
- Current Stage: IV

Medical HX (ongoing)

- Arthrosis, shortness of breath, pruritus, abdominal cramps

Sites of metastases

- lung (RUL) and lymph nodes (retroperitoneal and mesenteric)

Prior Systemic therapy

- cisplatin/capecitabine (unk), Chemoradiotherapy (unk), epirubicin/cisplatin/capecitabine (PR), cyclin dependent kinase 7 inhibitor (SD), HDAC inhibitor (PD)

Prior Radiotherapy

- Esophagus (chemoradiotherapy)

Prior Surgery

- Lung Core Biopsies