Replimune®

NEXT-GENERATION ONCOLYTIC IMMUNOTHERAPY

August 2022

Safe Harbor

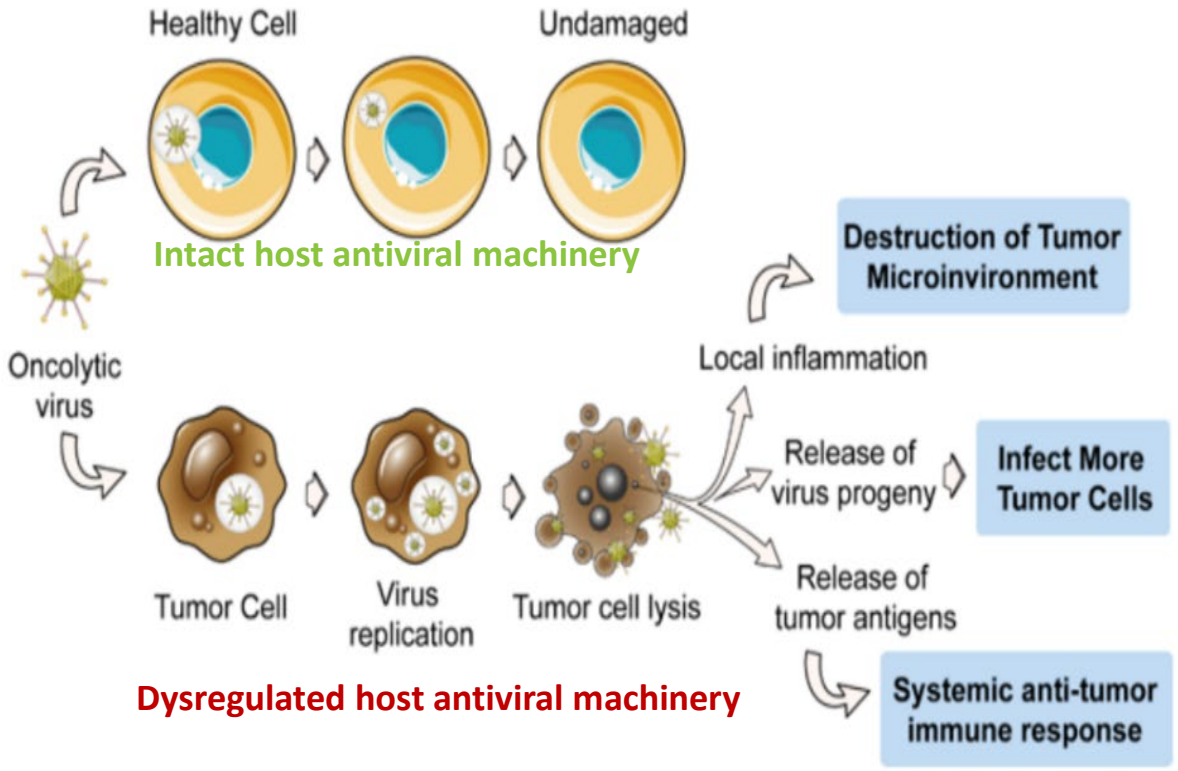
Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding the 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.

Certain information herein relates to or is based on publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable, we have not independently verified and makes no representation as to the adequacy, fairness, accuracy or completeness of any information obtained from third-party sources.

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)
- Major skin cancer franchise planned with RP1
  - Data from two RP1 registrational clinical trials in <12 months
    - CSCC randomized study primary analysis H1 2023
    - Snapshot data from first 75 patients of 125 patient study in anti-PD1 failed melanoma Q4 2022
- Broad mid-stage development planned with RP2/3
- Potential for the portfolio to deliver substantial commercial revenue in 2025-2030
- Capitalized to build a fully integrated global biotech company
  - US commercial infrastructure, in-house manufacturing
  - $395 million as of 30 June 2022

Tumor directed oncolytic immunotherapy provides a unique dual mechanism by which to kill tumors



1. Direct local killing of the tumor & altering the TME
2. Release of tumor antigens igniting a strong systemic anti-tumor immune response
3. Flexibility to combine with multiple modalities due to minimal additive side effects
4. Designed to deliver transformational results across tumor types

Bommareddy PK et al AJCD. 2016

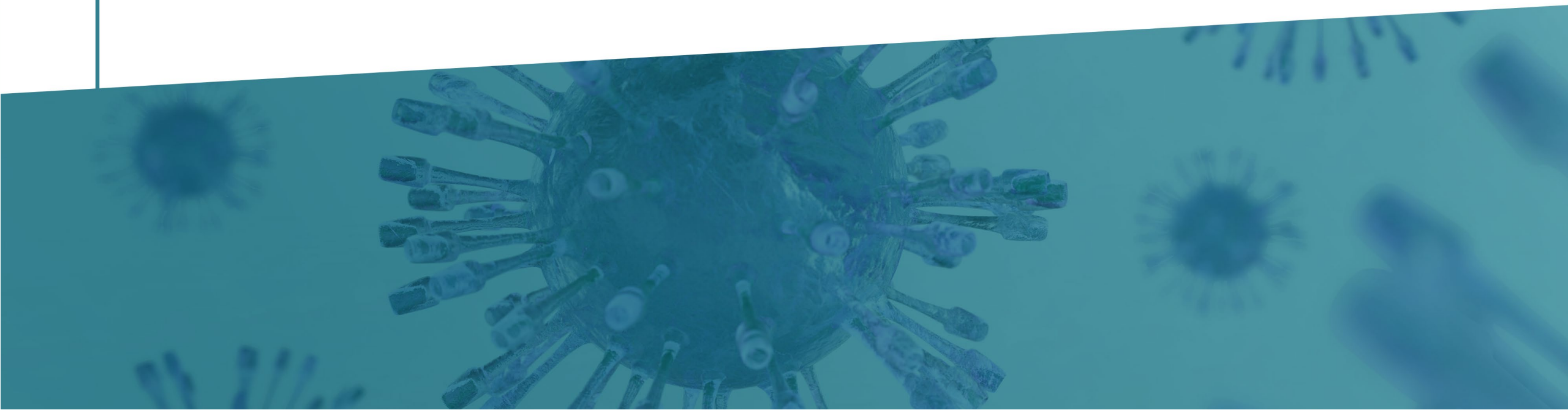
RPx positioning: Platform designed to address a range of tumor types with an optimal balance of potency & safety

Replimune®

CRITERIA	RP1	RP2	RP3
Payloads	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 compared to RP2)
Intended indication(s)	Skin cancers (CSCC, ant-PD1 failed melanoma, anti-PD1 failed CSCC, other NMSCs, etc)	Various solid tumor including primary liver cancers and/or those with a high prevalence of liver mets e.g. HCC, CRC Early disease (neoadjuvant/LA opportunities) e.g. SCCHN	
Clinical activity in anti-PD1 failed patients demonstrated	✓	✓	Ongoing
Safety & good tolerability demonstrated	✓	✓	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 systemic I-O activation & potency

Replimune®

RP1

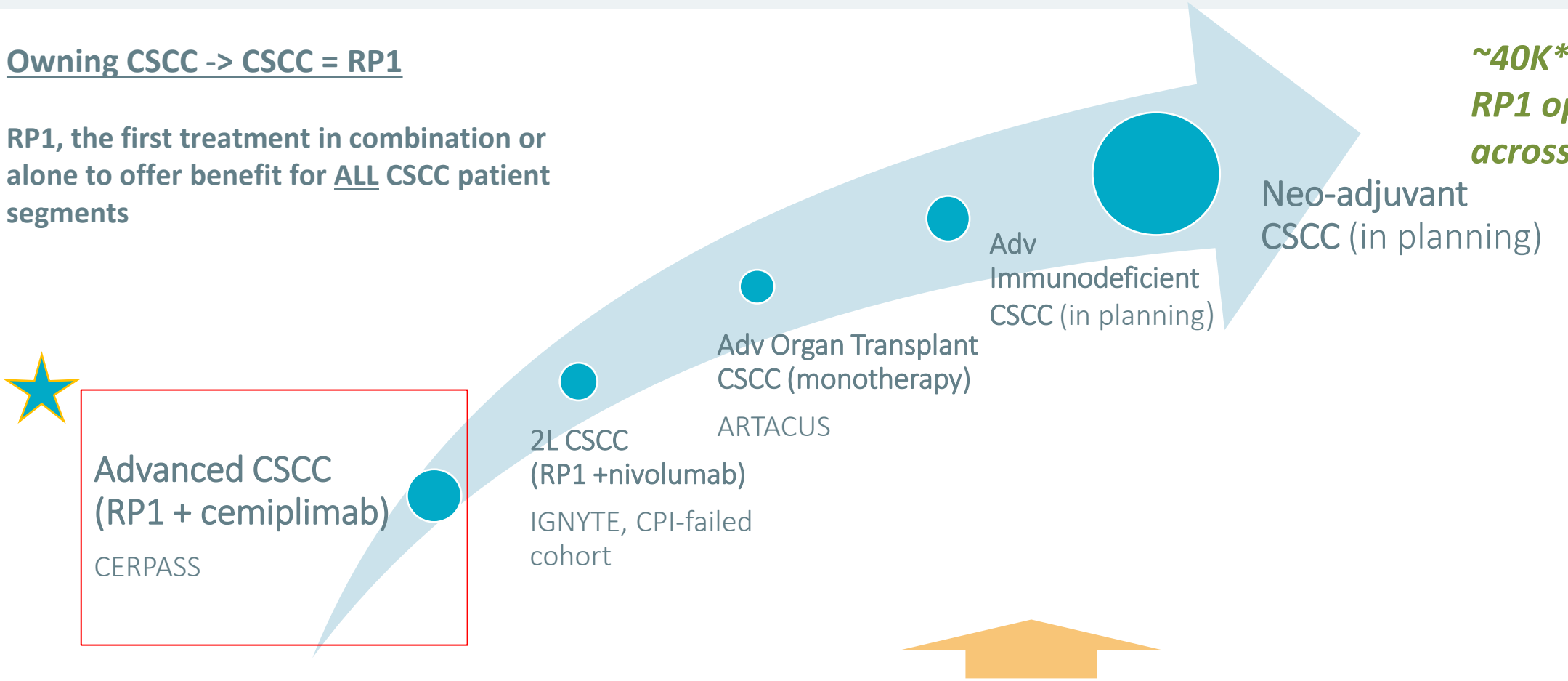


Building a skin cancer franchise starts with a successful RP1 launch in advanced CSCC

Owning CSCC -> CSCC = RP1

RP1, the first treatment in combination or alone to offer benefit for ALL CSCC patient segments

~40K* US patient RP1 opportunity across segments



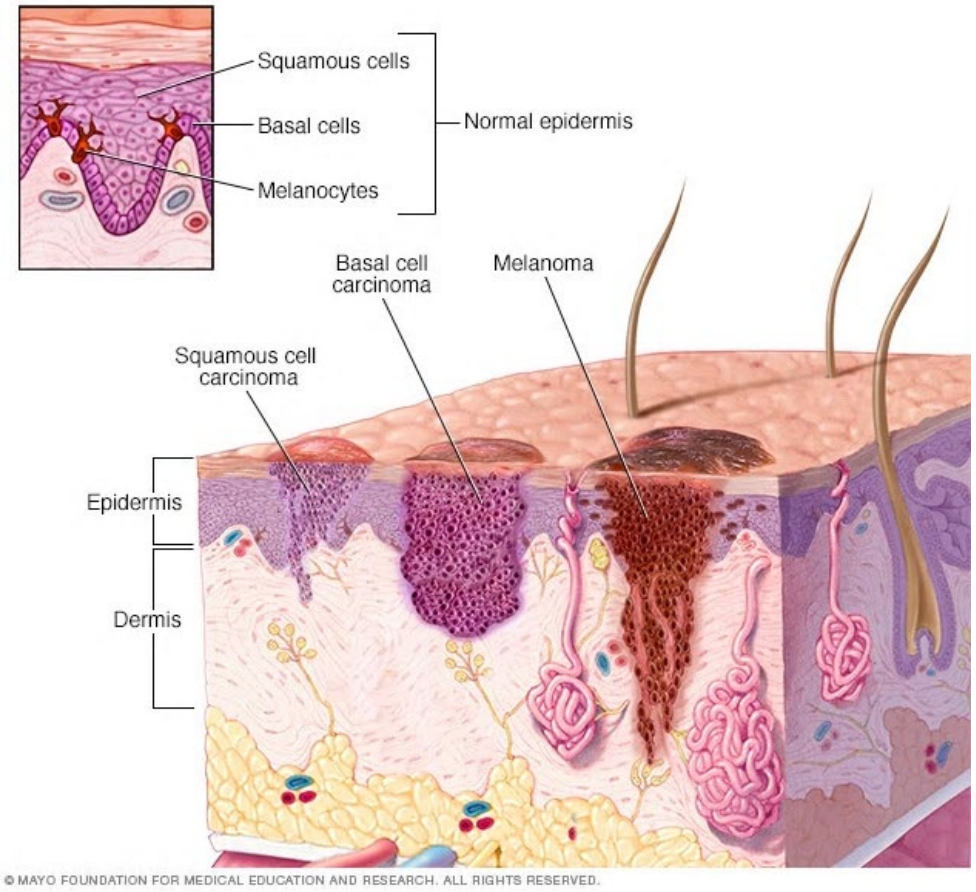
Unmet needs addressed by RP1

- **Better 1L/neoadjuvant therapy : higher/faster CR rates and improved durability**
- **Better 2L therapy post-CPI**
- **Immunodeficient pts who can't get a CPI and/or don't benefit from them**

*Est. US treated population (based on multiple sources including IQVIA claims, primary market research, and company data)

CSCC disease characteristics, largely superficial/local issue

- Second most common skin cancer with ≈700,000 patients annually in the U.S.[1,] 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[1-3]
  - **80% of patients die from locoregional progression**, not metastatic disease[4,5]
- **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%)



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

High rates of CR in CSCC in completed study

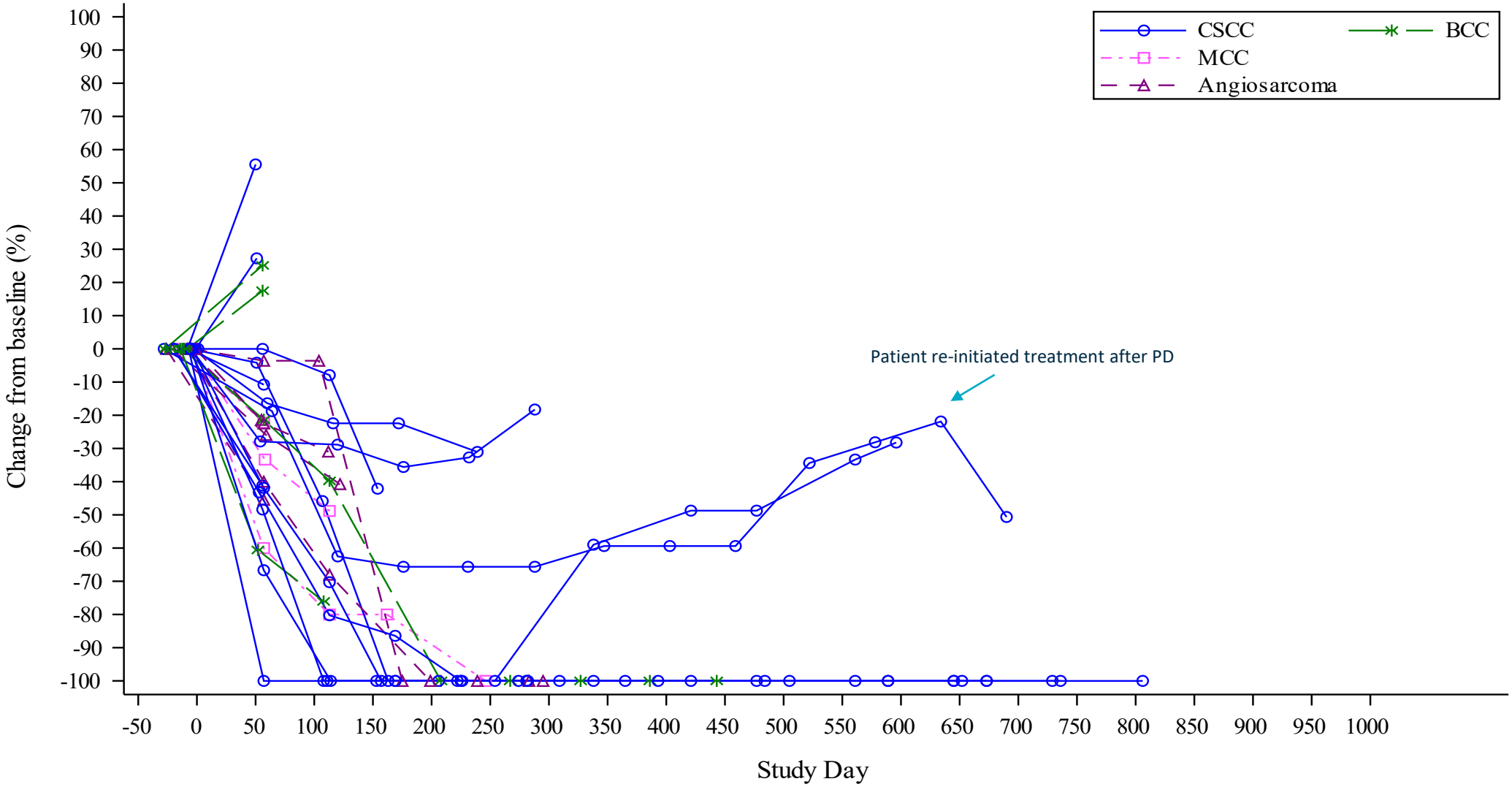
	CSCC June	CSCC now	BCC June	BCC now	MCC June	MCC now	Angiosarcoma June	Angio now
# of patients*	15	17	4	4	4	4	5	6
Best overall response n (%)								
CR	7 (46.6)	8 (47.1)	0	1 (25.0)	0	2 (50.0)	0	1 (16.7)
PR	2 (13.2)	3 (17.6)	1 (25)	0	3 (75)	1 (25.0)	3 (60)	3 (50.0)
SD	1 (6.7)	1 (5.9)	2 (50)	2 (50.0)	0	0	1 (20)	1 (16.7)
PD	4(26.7)	4 (23.5)	1 (25)	1 (25.0)	1(25)	1 (25.0)	1 (20)	1 (16.7)
OR	9 (60)	11 (64.7)	1 (25)	1 (25.0)	3 (75)	3 (75.0)	3 (60)	4 (66.7)
CR+PR+SD	10 (66.7)	12 (70.6)	3 (75)	3 (75.0)	3 (75)	3 (75.0)	4 (80)	5 (83.3)

- Incremental improvement in each of CSCC, BCC, MCC & angiosarcoma

* Patients with follow up assessments (n=31), on study with no follow up currently for the other patient (MCC)

Data snapshot date: 11th March 2022

Anti-PD1 naïve NMSC: Deep & durable responses in CSCC



Data snapshot date: 11th March 2022

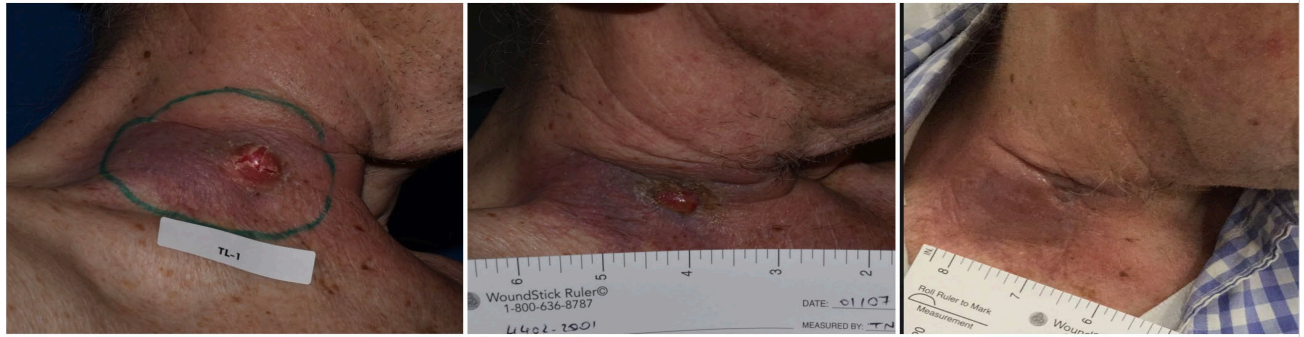
- A high frequency of durable responses continues to be observed

Robust abscopal 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)

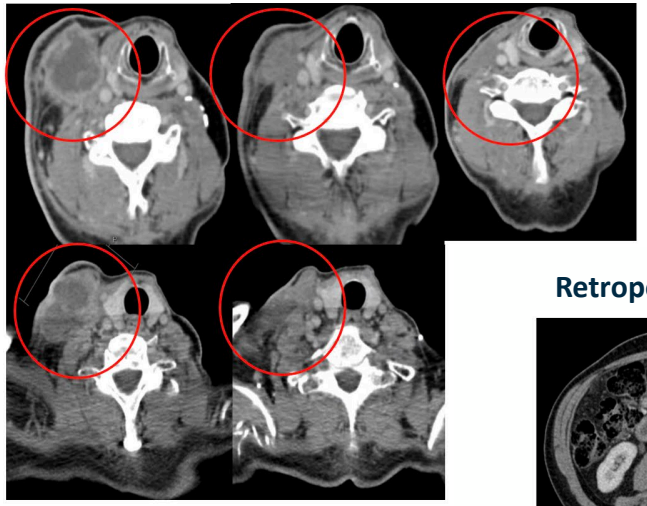


Pt 4402-2001 - CR

- 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

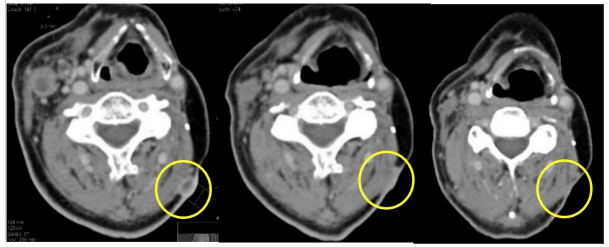
Right neck (injected)

Baseline 8 weeks 24 weeks

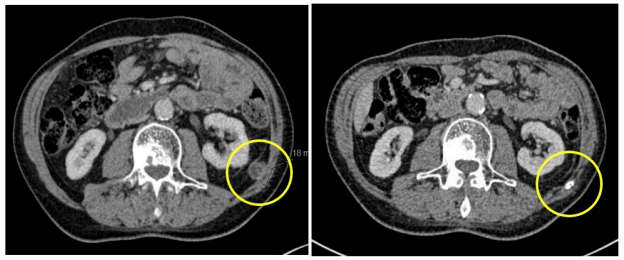


Left neck (un-injected)

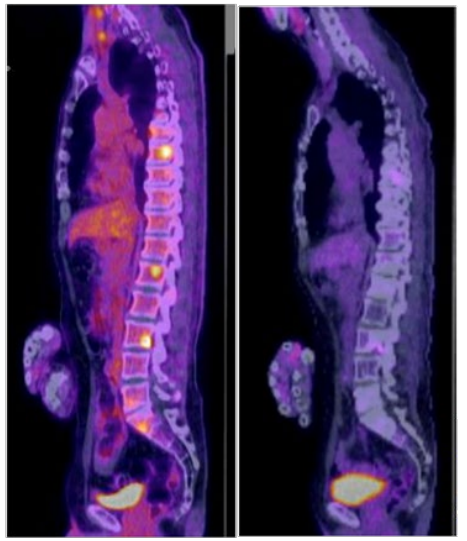
Baseline 8 weeks 16 weeks



Retroperitoneal lymph nodes (un-injected)



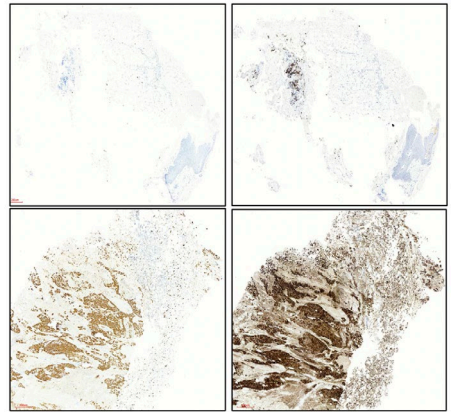
June 2018 **Feb 2020**



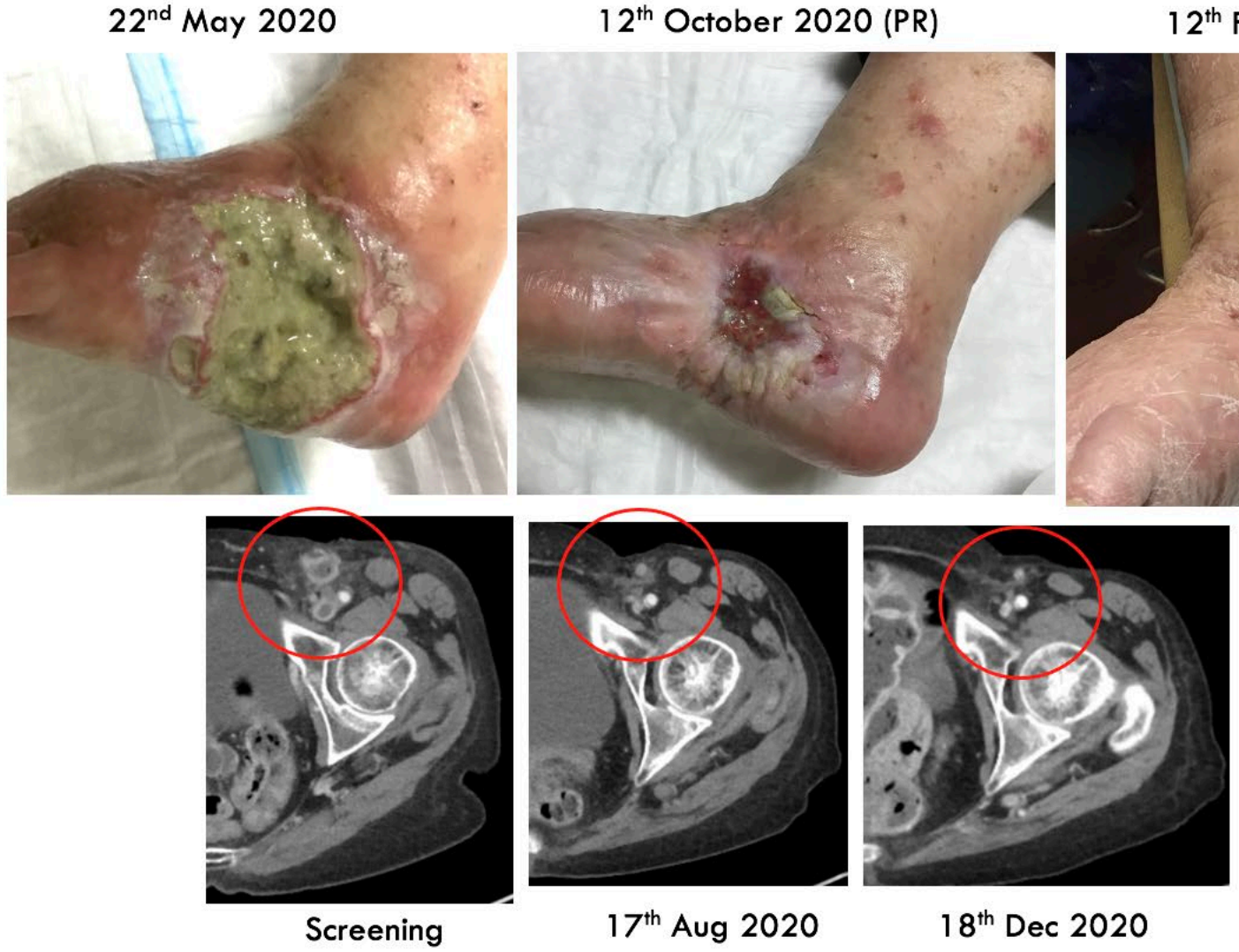
CD8 PD-L1

Baseline

Day 43



Complete 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

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

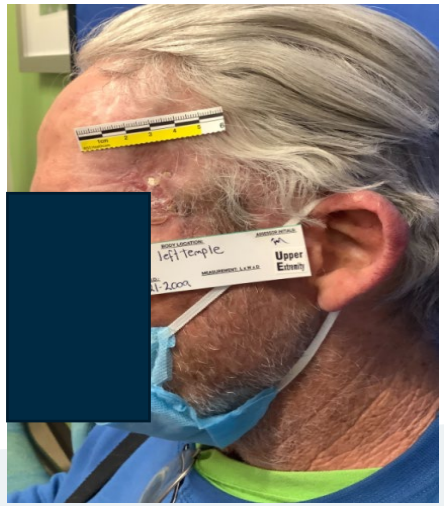
"CRs are very important in this setting, as they usually lead to long-term survival and also have a huge impact on the patient's quality of life"

KOL in market research

Future Market Impact

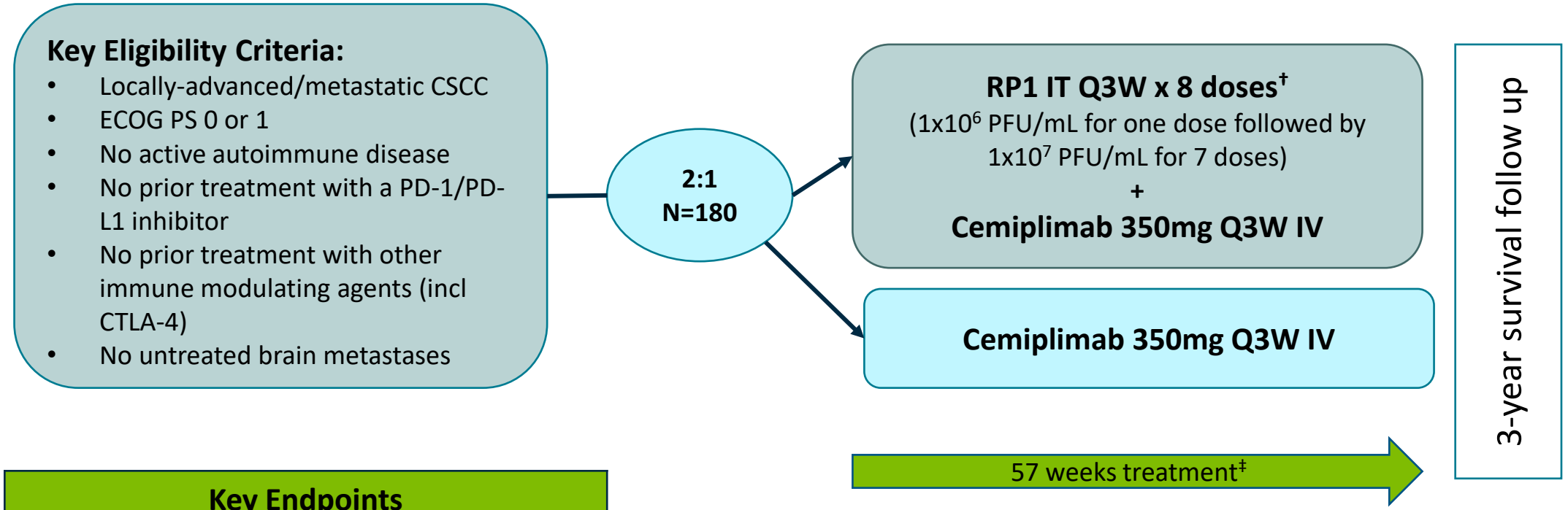
- Potential to change existing mindset and treatment approach -> opportunity to treat more patients
- Early disease -> driving CRs key to success in neoadjuvant allowing many more patients to be treated and cured

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

Randomized controlled Phase 2 study in CSCC (CERPASS)



Key Endpoints

Dual primary *independent* 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

†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

- Top level primary analysis data expected in H1 2023

Response to treatment: RP1 monotherapy in solid organ transplant recipients (ARTACUS) – First Look

	Total (#/%)
Tumor type	CSCC
# of patients	6
CR	1 (16.6)
PR	1 (16.6)
SD	0
NE	1 (16.6)
PD	3 (50)
ORR	2 (33.3)

All enrolled patients have CSCC & kidney transplants so far

- Three patients had PD & one patient died of COVID-19 before the first response assessment

- Initial data shows that one third of the patients enrolled to date have responded to treatment, with all responses maintained to date
- May provide a potential new treatment option for these patients

Data snapshot date: 11th March 2022

RP1: anti-PD1-failed* Non Melanoma Skin Cancers (NMSC) response table – first look

	All	CSCC	BCC	MCC	Angio-sarcoma
# of patients**	12	7	1	2	2
CR	1 (8.3)	0	0	1 (50.0)	0
PR	3 (25.0)	1 (14.3)	0	1 (50.0)	1 (50.0)
SD	5 (41.6)	4 (57.1)	1 (100)	0	0
PD	3 (25.)	2 (28.6)	0	0	1 (50.0)
OR	4 (33.3)	1 (14.3)	0	2 (100)	1 (50.0)
CR+PR+SD	9 (75.0)	5 (71.4)	1 (100)	2 (100)	1 (50.0)

- Initial data shows responses across each anti-PD1-failed tumor type
- Other SD patients, including with CSCC, with only short follow up are also responding to treatment

* Progressed while on anti-PD1 therapy as the patients last treatment before the clinical trial

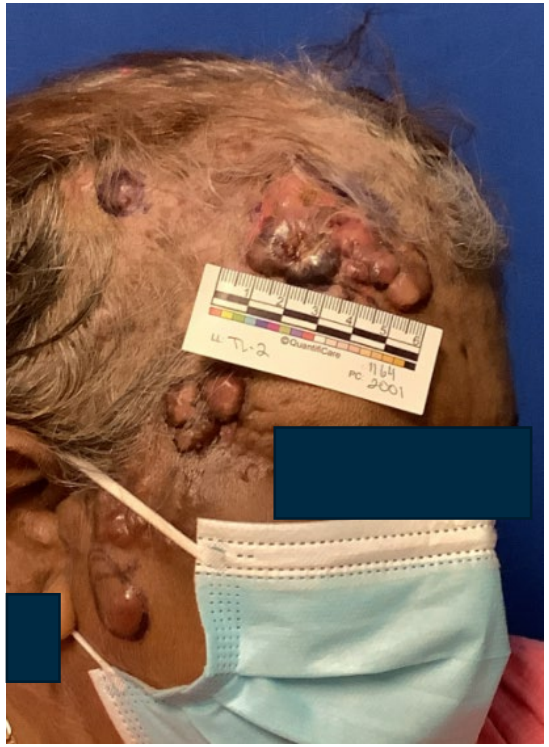
** Patients with follow up assessments (n=12), on study with no follow up as yet for the other two patients enrolled

Data snapshot date: 11th March 2022

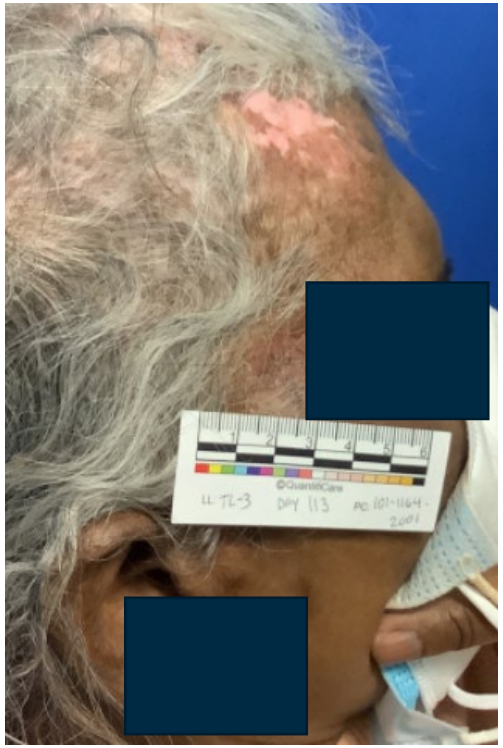
Patient example: anti-PD1-failed angiosarcoma (ongoing PR)

Pt. 101-1164-2001 - Anti-PD1-failed angiosarcoma (ongoing PR)

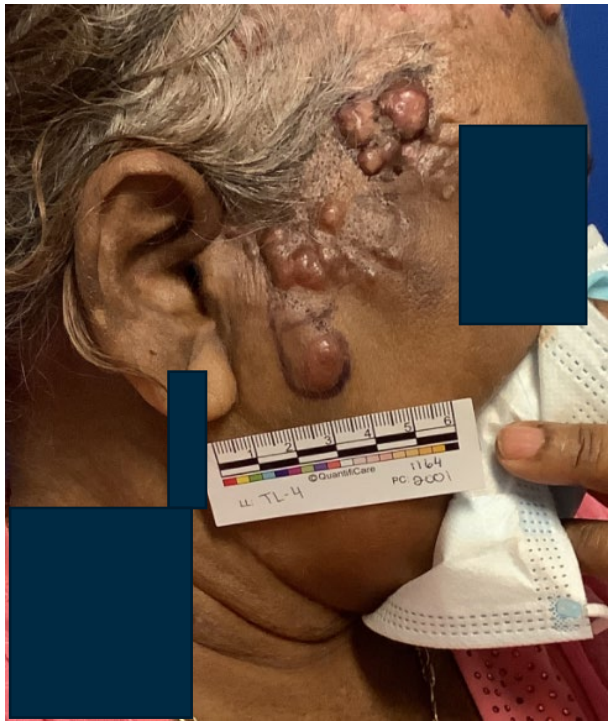
Baseline



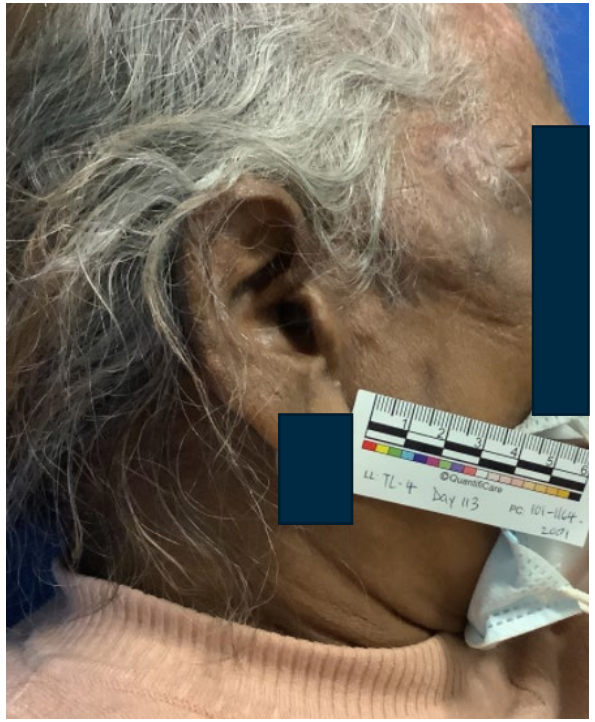
4 months



Baseline



4 months



Anti-PD1 failed melanoma registration directed study
Directional data in < 6 months

- The overall melanoma WW market is large and growing, estimated at ~$8B[1] USD in 2022
  - While new treatment options have transformed melanoma, significant unmet needs remain in specific patient segments especially for CPI-failed patients with no approved options to date
    - Approximately half of advanced melanoma patients still die of their disease
  - 40-65% of all metastatic melanoma are refractory to initial anti-PD1 therapy[2]
- Expected response to anti-PD1 therapy following confirmed progression on single agent anti-PD1 is 6-7%[3,4]
- Ongoing registration-directed single arm 125 patient Phase 2 cohort of RP1 combined with Opdivo
  - Confirmed disease progression required while on prior anti-PD1 therapy
  - Primary endpoint: ORR by independent central review

[1]Evaluate pharma; [2]Global Burden of Disease Cancer Collaboration *JAMA Oncol* 2019 (12)
[3]Ribas et al *Lancet Oncology* 2018 (19); [4]Hodi et al *JCO* 2016 (34)

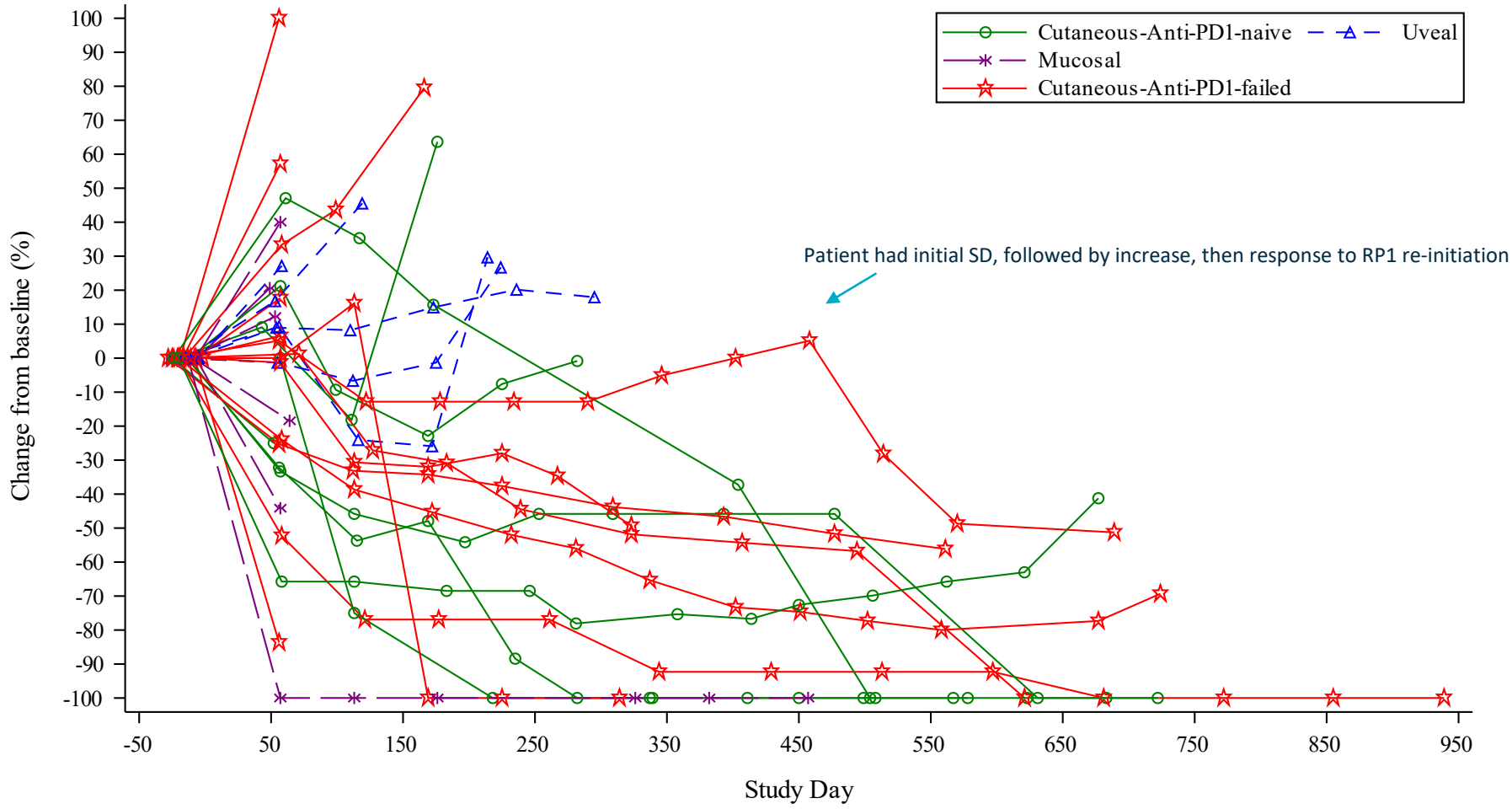
Strong anti-PD1 failed melanoma signal in prior study

	Cutaneous: Anti-PD1 naïve	Cutaneous: PD1-failed	Mucosal: Anti-PD1 naïve	Mucosal: Anti-PD1-failed	Uveal: Anti-PD1 naïve	Uveal: Anti-PD1-failed
# of pts	8	16	1	5	3	3
Best overall response # (%)						
CR	3 (37.5)	2 (12.5)	1 (100)	1 (20.0)	0	0
PR	2 (25)	4 (25.0)	0	0	0	0
SD	2 (25)	1 (6.3)	0	0	1 (33.3)	3 (100.0)
PD	1 (12.5)	8 (50.0)	0	4 (80.0)	2 (66.7)	0
ORR	5 (62.5)	6 (37.5)*	1 (100)	1 (20.0)	0	0
CR+PR+SD	7 (87.5)	7 (43.8)	1 (100)	1 (20.0)	1 (33.3)	3 (100.0)

* 5/6 responders were primary refractory to prior immune checkpoint blockade (single agent anti-PD1 or ipi/nivo) - i.e. did not respond before progression

Data snapshot date: 11th March 2022

Strong anti-PD1 failed melanoma signal in prior study



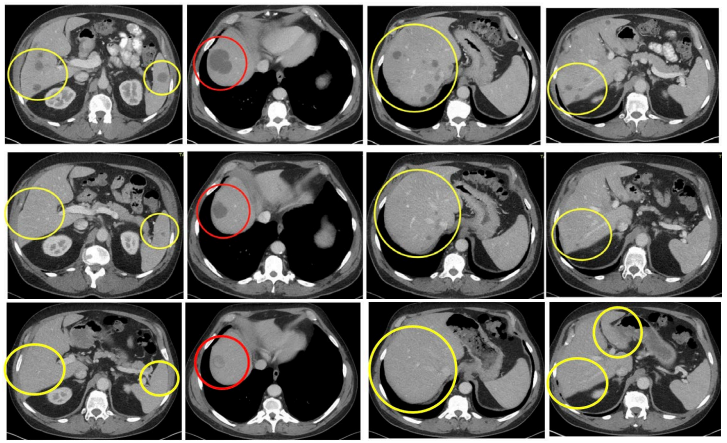
- Durability maintained, with general deepening of response over time

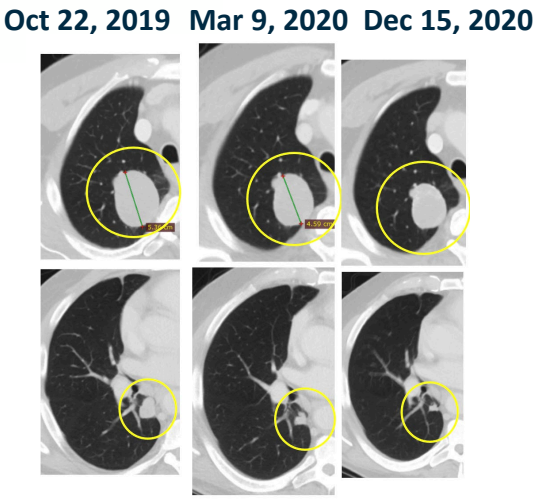
Data snapshot date: 11th March 2022

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





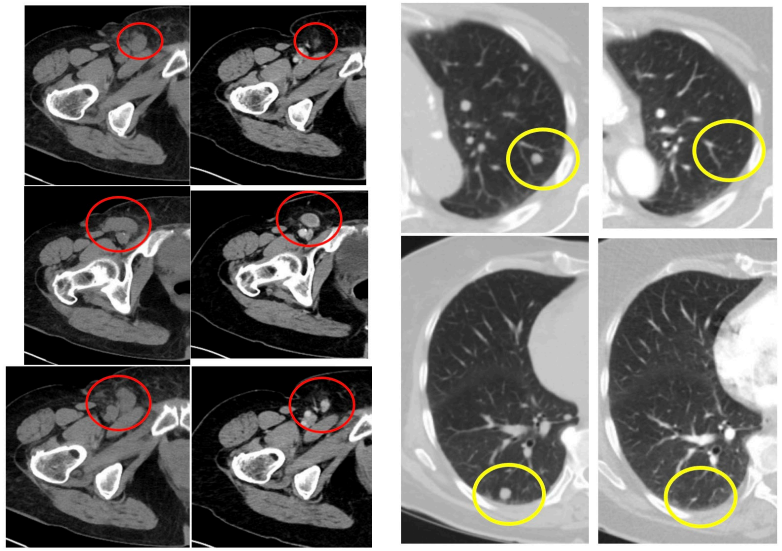
Injected

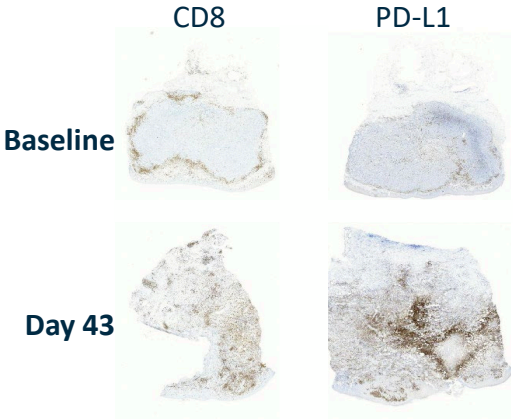
Un-injected

All lesions now PET neg

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

- Ipi/nivo failed cutaneous melanoma





Reversal of T cell exclusion

RP1 well positioned for both near-term (and growing) CPI-failed populations across treatment lines and future shifts in the melanoma landscape

Replimune®

"IGNYTE opportunity"

Advanced Melanoma (unresectable)
Current SOC: PD-1 mono and doublets for CPI naïve patients + TKIs for BRAF MT pts

1a Adj CPI refractory

Opportunity for I-O "refractory" patients i.e. those who progress on or within 12 months of adj I-O therapy

1b 2L/3L CPI-failures

Opportunity for patients post progression on I-O for metastatic disease

- 2/3L post I-O doublets and/or mono CPI in BRAF WT patients
- 2/3L for BRAF MT patients

Early-Stage Melanoma (stage II-III resectable)
Current SOC: PD-1 mono and TKIs for some BRAF MT pts

2 Neoadjuvant Tx

No approved options today but significant opportunity for RP1 in mono/combo in this setting given ability to drive RR/CRs, tolerability, and injection feasibility

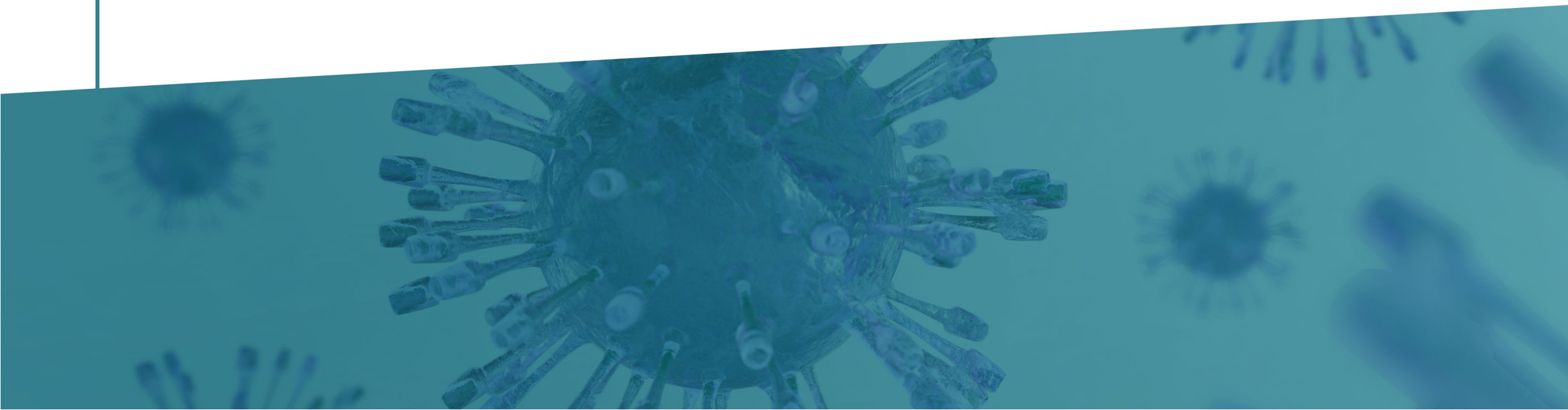
Objective to address unmet needs

- **Improved RR and DOR for CPI-failed patients (nearly all melanoma patients receive a CPI at some stage in their treatment journey hence could receive RP1 at progression)**
- **Improved tolerability vs Ipi+Nivo or TKI combos or TILs**

= Future development opportunity

Replimune®

RP2/3



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

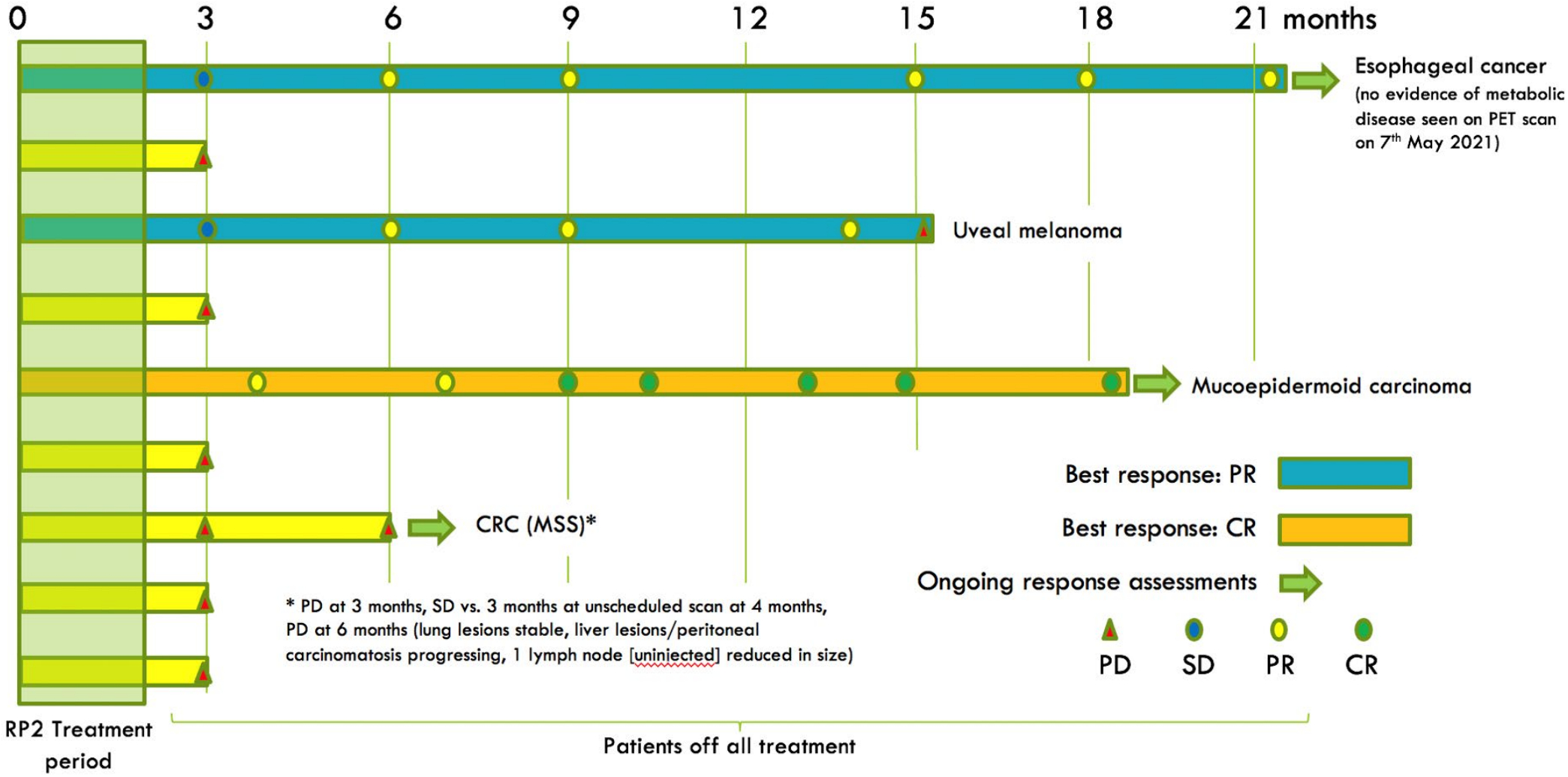
- Focus on the delivery of molecules which function at the time & place of immune activation, i.e. in tumors & draining lymph nodes
- Delivered mechanisms are clinically validated
  - Anti-CTLA-4 – ipilimumab, tremelimumab
  - CD40L, 4-1BBL – agonistic antibodies against CD40 & 4-1BB (CD137) have shown 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
    - 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



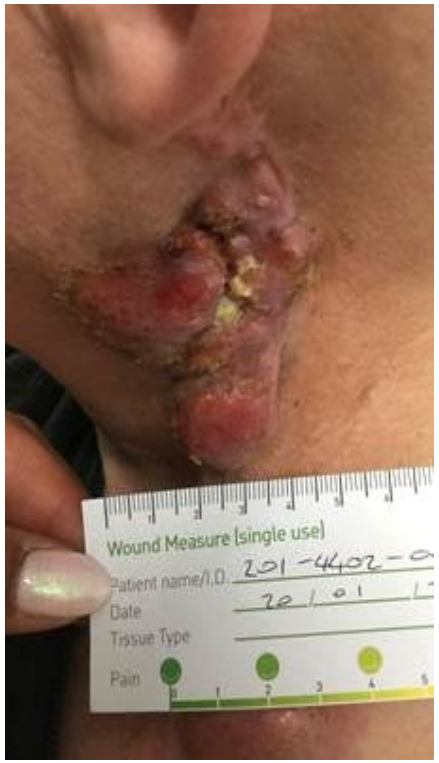
Data as of Oct 12th 2021

Ongoing CR in mucoepidermoid carcinoma following monotherapy RP2

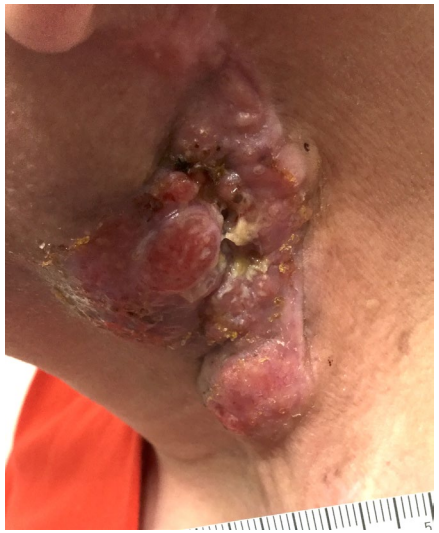
Pt 4402-0001 - ongoing CR

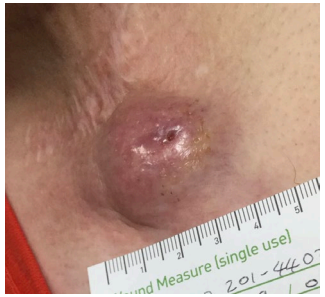
- Mucoepidermoid carcinoma of the parotid gland
- Prior therapies: carboplatin/ paclitaxel, bicalutamide, ceralasertib
- Cervical lymph node & supraclavicular fossa lesions injected

Baseline

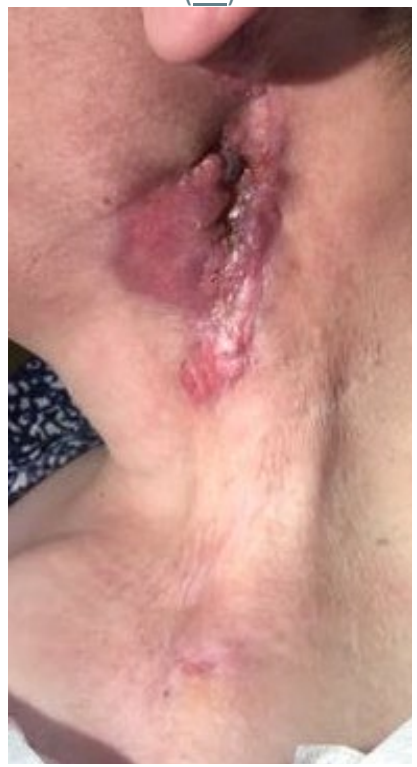


1 month

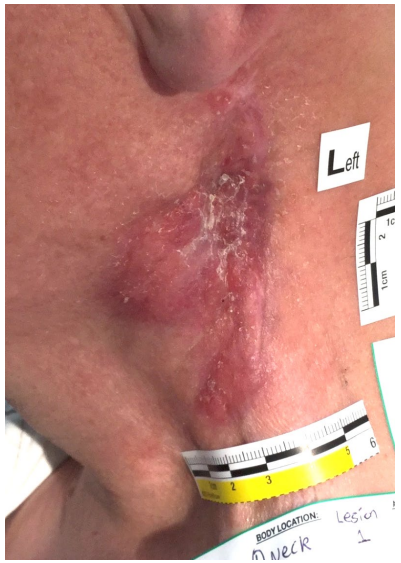


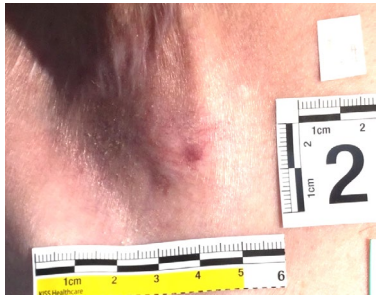


3 months
(PR)



4 months

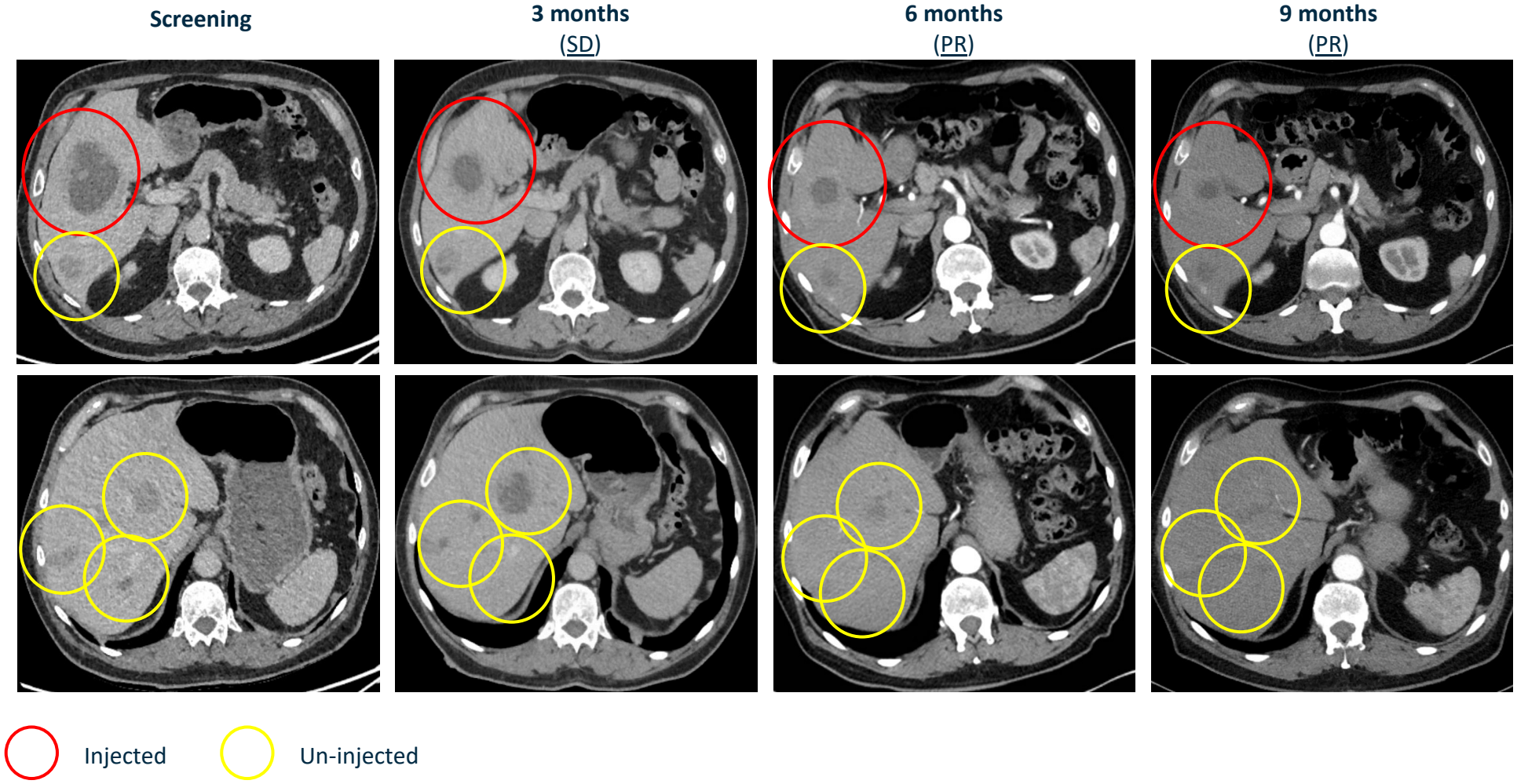




Example patient with liver metastases treated with RP2 monotherapy

Pt 4401-0003 – PR

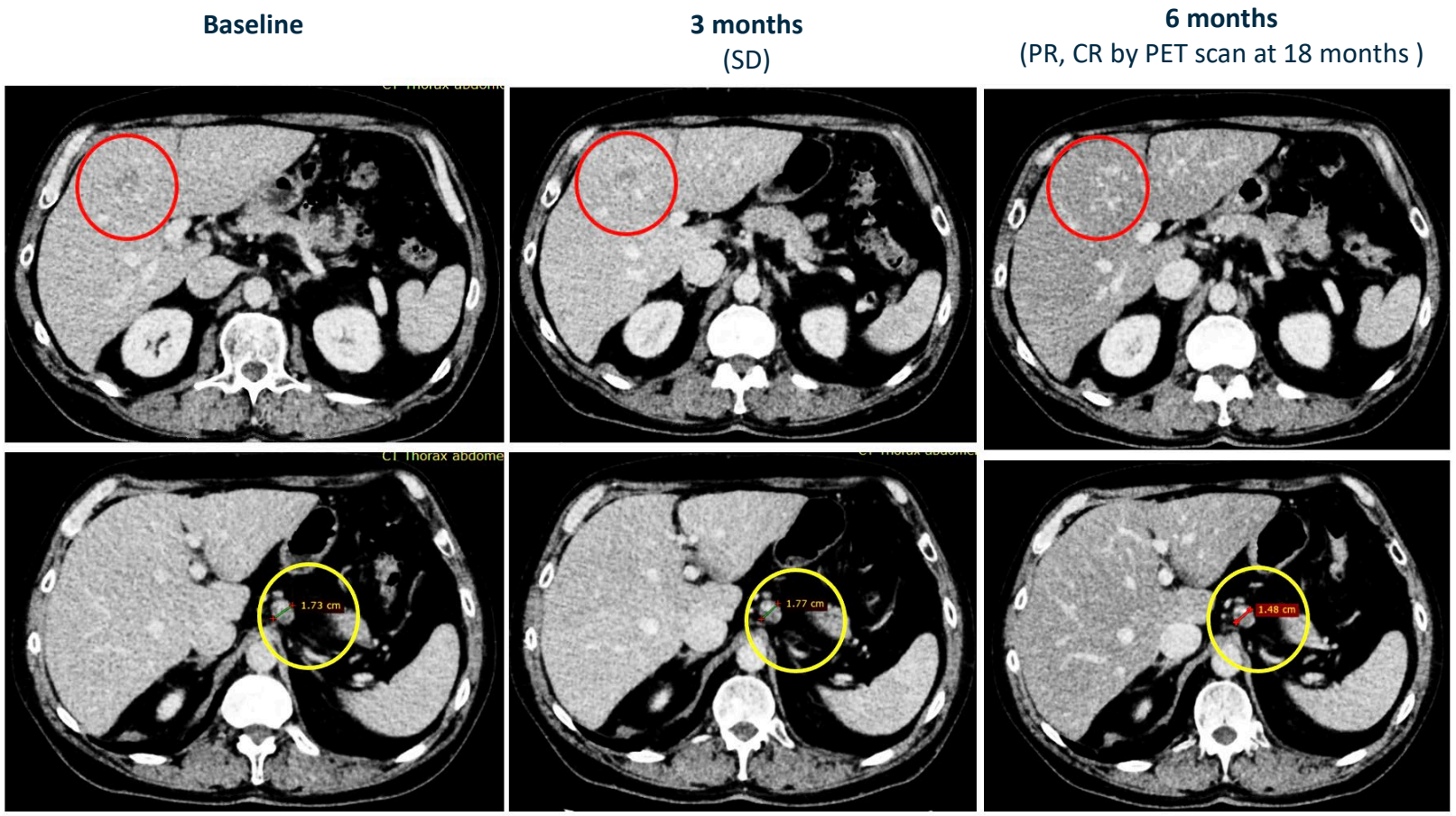
- Uveal melanoma
- Extensive liver metastases (others not shown)
- Prior therapies: Ipilimumab/ nivolumab
- Patient progressed at 15 months



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

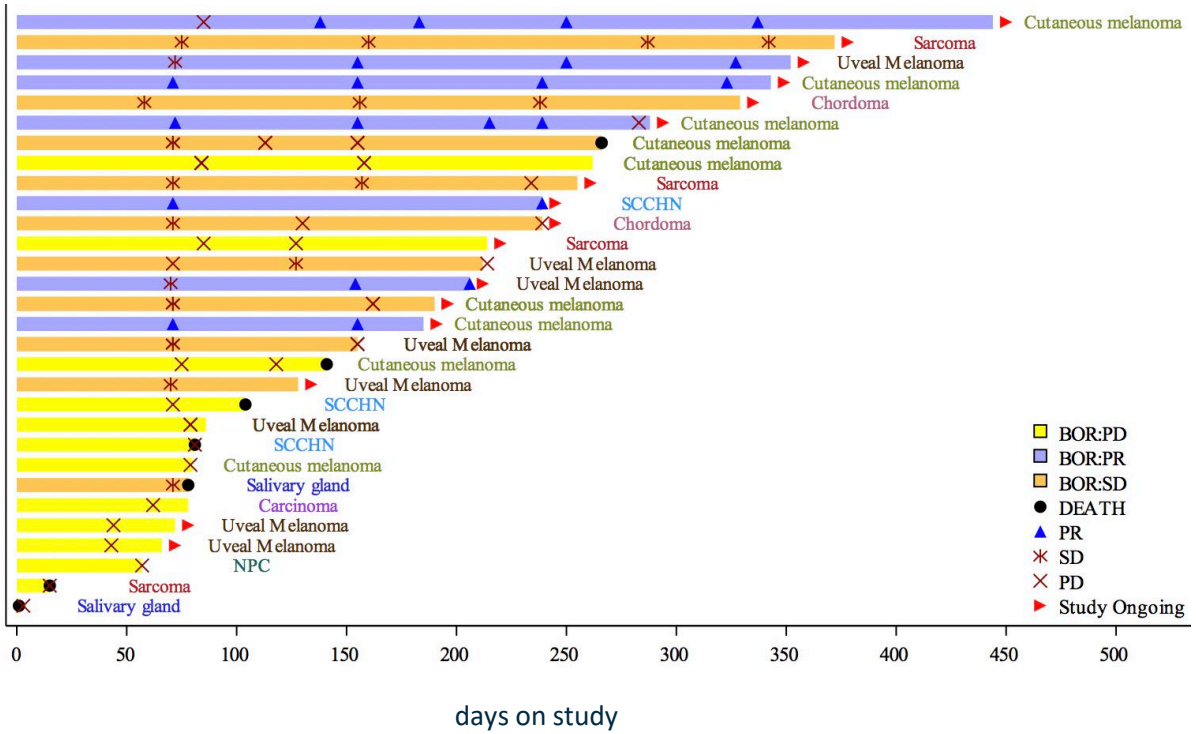


Injected Un-injected

RP2 + nivolumab shows deep and durable responses

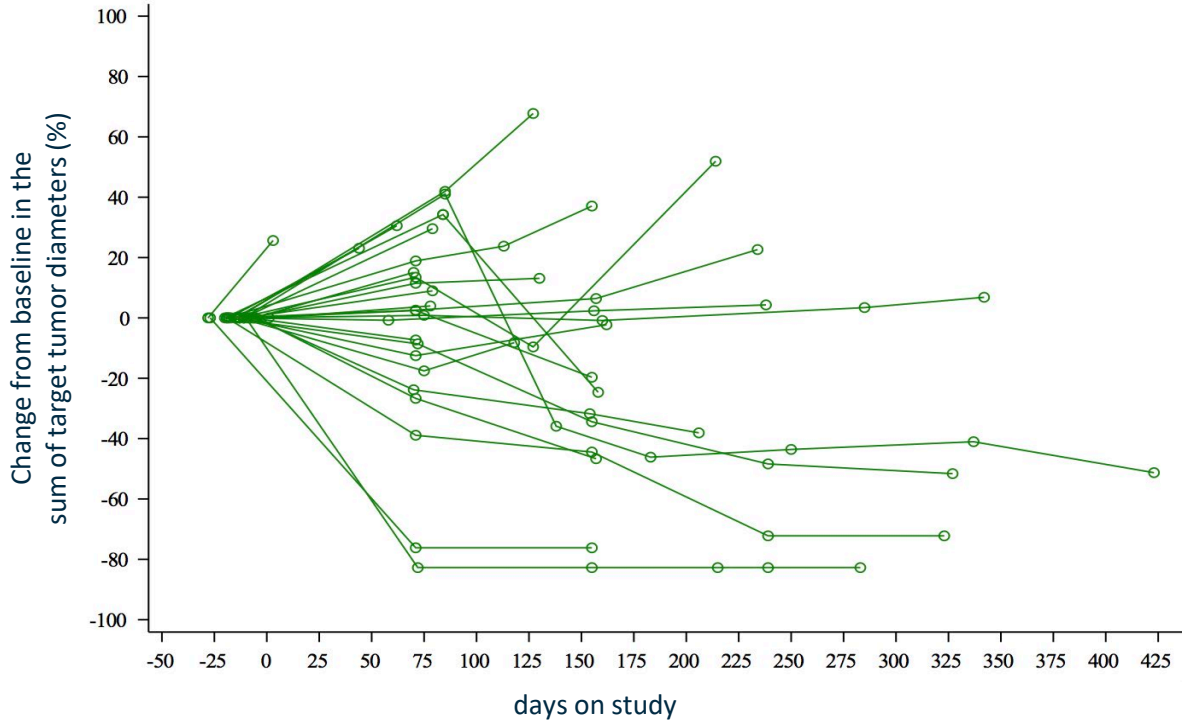
Duration of best response

Patients with a best response of at least SD



Change in tumor size

Patients with at least one follow up assessment

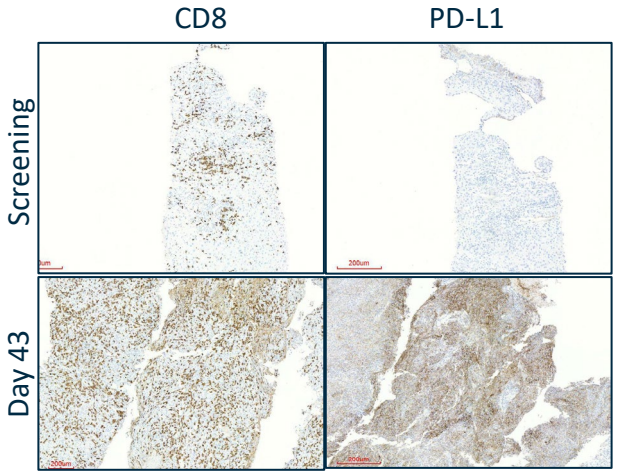


- 30 advanced, heavily-pretreated Phase 1 patients treated with RP2 combined with Opdivo
- Seven responses as of last data cut; all patients having failed prior anti-PD1
  - 2x uveal melanoma; 4x cutaneous melanoma; 1x SCCHN
- All but one response durable to date at out to >425 days

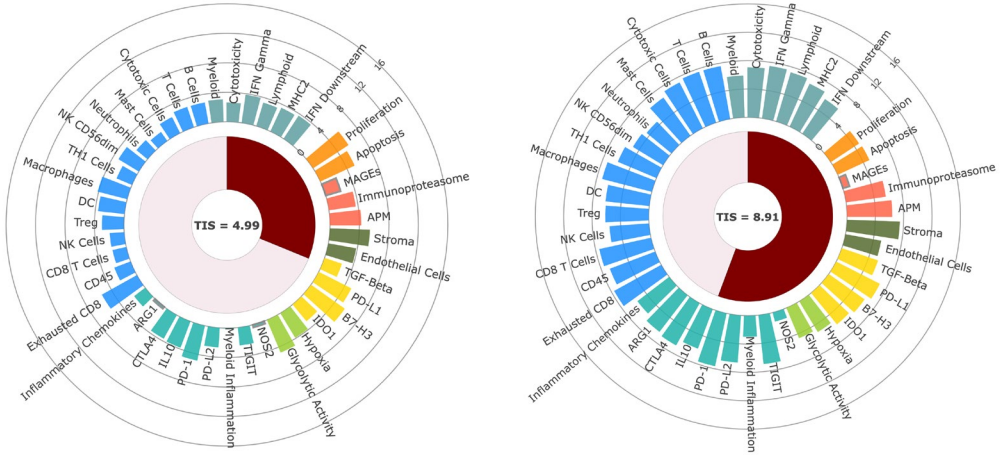
Data as of Oct 12th 2021

Broad immune activation with RP2: Response is independent of baseline PD-L1 status & CD8+ T cell density

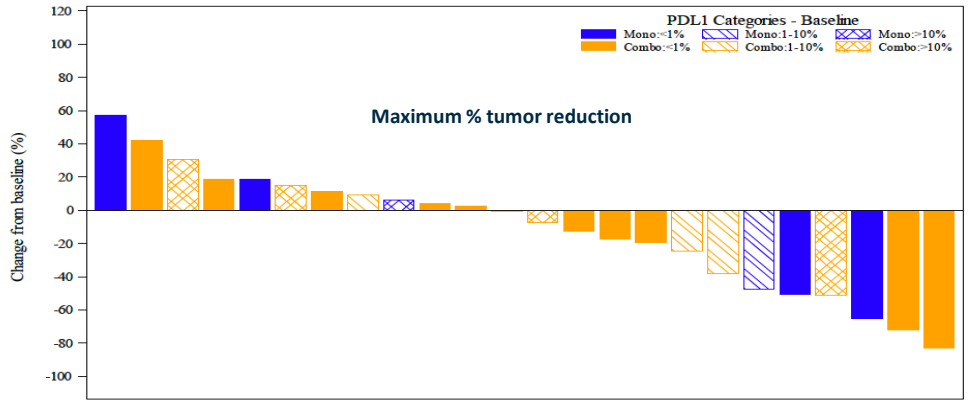
Substantial increases in in CD8+ T cell infiltration and PD-L1 expression are seen (Example: pt 4403-0015, uveal melanoma)



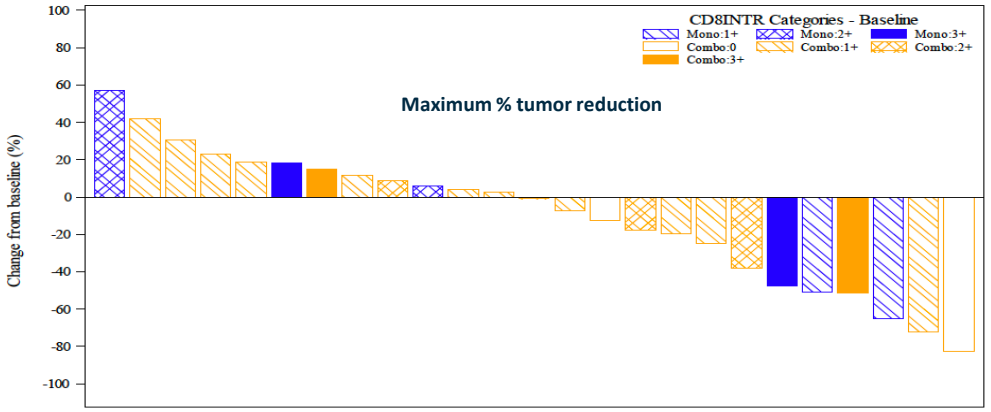
Changes in gene expression signature indicate broad immune activation (Example: pt 4401-0016 ipi/nivo-failed melanoma)



No correlation of clinical response with baseline tumor PD-L1 expression status



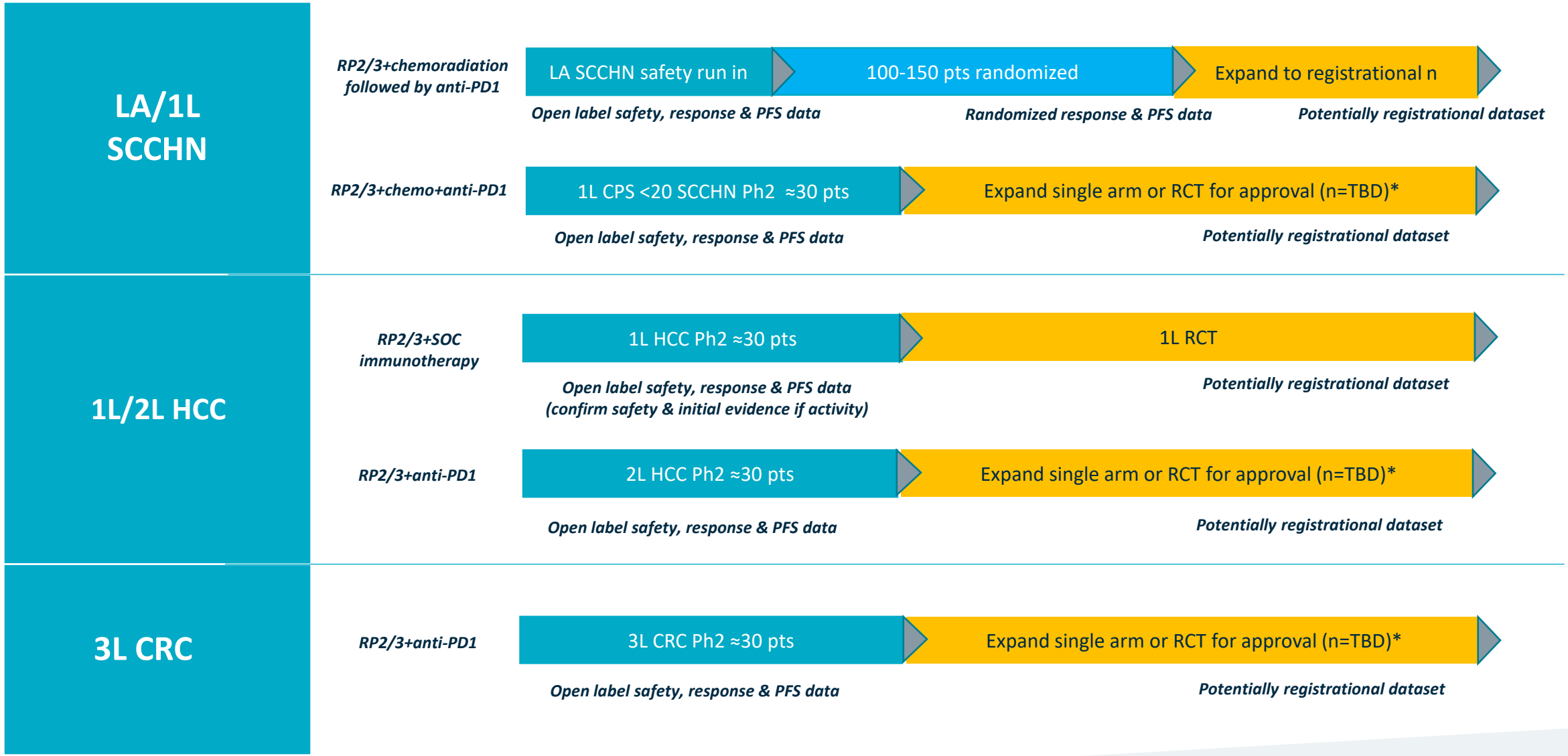
No correlation of clinical response with baseline intra-tumoral CD8+ T cell density



RP2/3 – Current Status

- **RP2 and RP3 are well tolerated (including injections into lung & liver)**
  - Vast majority of AEs are mild (90% grade 1-2)
    - Most commonly fever, chills, fatigue, influenza-like illness & injection site reaction
    - Quickly resolving: vast majority within 72 hours
  - Indicates the potential for combination across the spectrum of anti-cancer modalities
- **RP2 has shown durable clinical activity in difficult-to-treat & anti-PD1-failed all-comers Phase 1 patients**
  - Warrants progression into Phase 2 development - including in earlier patients in combination with the SOC
    - Clear signal in uveal melanoma (3/9 responses), in addition to activity in other tumor types including as single agent
    - Additional cohort of patients with GI, lung, breast cancer, SCCHN & uveal melanoma being enrolled
- **RP3 has shown good tolerability, & expected to provide enhanced efficacy as compared to RP1 and RP2, although based on the patients enrolled so far with RP3 it is too early to draw conclusions as to efficacy**
  - Focused cohort of patients with GI, lung, breast cancer & SCCHN being enrolled, together with further monotherapy patients to be enrolled
- **Appropriate to keep options open regarding which of RP2 or RP3 to develop in particular indications in Phase 2, i.e. as the data for RP3 catches up**

RP2/3 Phase 2 prioritized indications



*Pending FDA buy in

Replimune has a clinical trial collaboration & supply agreement with BMS for the supply of Opdivo in its clinical trial program with RP2/3

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; RP2/3 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

Summary

- Major skin cancer franchise planned with RP1
  - Strong data in multiple skin cancers in both the anti-PD1 naïve and anti-PD1 failed setting
  - Initial anti-PD1 failed melanoma registrational cohort data (first 75 patients) in late 2022; primary data from the registrational clinical trial in CSCC in H1 2023
  - At scale manufacturing in place
    - To serve worldwide market at attractive COGS
  - Commercial planning ramping up for US launch
- RP2/3 mid-stage pipeline
  - Focused on relatively easily injected tumor types with high commercial value
    - 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


Replimune®
THANK YOU