Replimune®

Igniting a Systemic Immune Response to Cancer

Corporate Presentation
May 2024

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 global pandemics and related public health issues, the ongoing military conflicts between Russia-Ukraine and Israel-Hamas 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.

Industry Leader in Oncolytic Immunotherapy

Establishing a Broad Skin Cancer Franchise

Clinical activity demonstrated across multiple skin cancers and settings

- ✓ IGNYTE primary analysis and BLA submission in anti-PD1 failed melanoma on track for RP1 in 2H 2024
- ✓ IGNYTE-3 confirmatory phase 3 study design in anti-PD1 failed melanoma agreed on with FDA; planned to start prior to BLA submission
- ✓ ARTACUS clinical trial of RP1 as monotherapy in solid organ transplant patients shows strong response rates
- ✓ CERPASS study continuing to allow time-based endpoints to mature

Focused on Rare Cancers

Powerful activity both as monotherapy and in combination with nivolumab

- ✓ Compelling data in uveal melanoma
- ✓ Pivotal study in metastatic uveal melanoma being planned
- ✓ Clinical activity seen in other rare tumors, including:
  - ✓ Sarcomas (e.g., chordoma)
  - ✓ Rare head & neck (e.g., mucoepidermoid)
- ✓ On path to build rare cancer franchise

Positioned to Bring our Oncolytic Immunotherapies to Market

Industry leading experience and pipeline in oncolytic immunotherapy

- ✓ All programs wholly owned
- ✓ Potential to deliver substantial commercial revenues beginning in late 2025
- ✓ Strong financial position with cash of $466.4M as of 31 December 2023
- ✓ Cash runway into 2H 2026

Oncolytic Immunotherapy is Intended to Activate a Powerful and Durable Systemic Anti-Tumor Response

Replimune®

Injected tumor

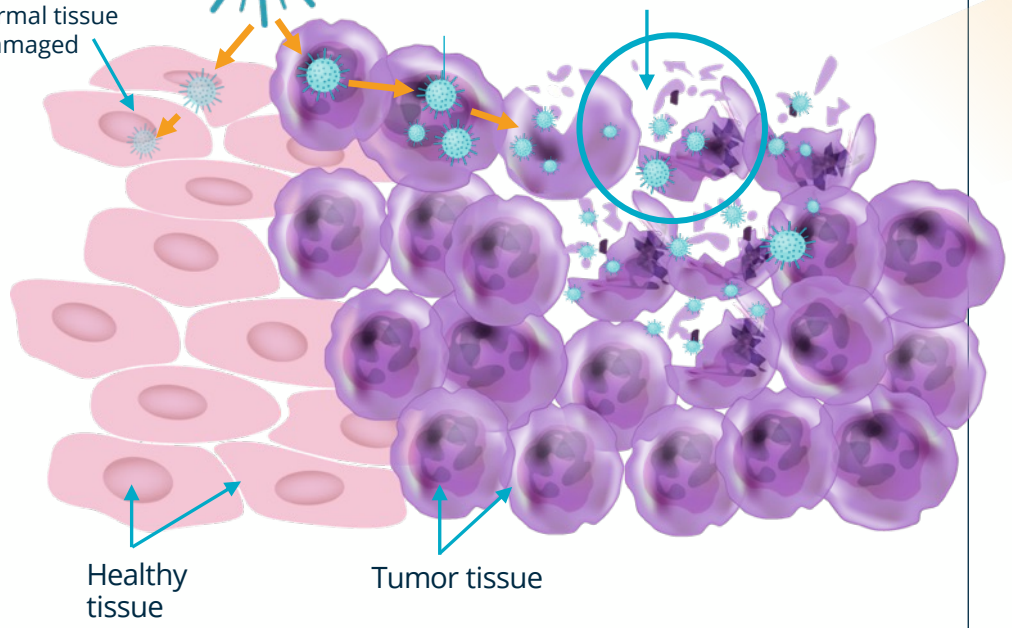
MECHANISM 1

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

Oncolytic immunotherapy

Dysregulated host antiviral response allows robust virus replication and tumor lysis

Intact host antiviral response: Normal tissue remains undamaged



Healthy tissue

Tumor tissue

Immune response

MECHANISM 2

Release of virus progeny

Infection of more tumor cells

Tumor cell death and release of tumor antigens

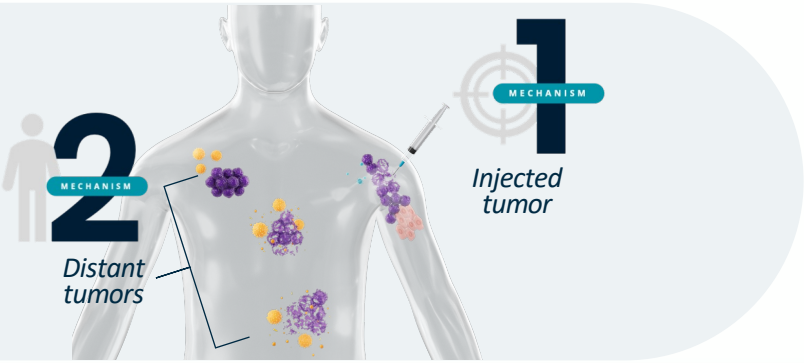
Local Inflammation

Altering of tumor microenvironment

Enhanced T cell priming and activation

T cell infiltration and killing of distant, uninjected tumors

Generating a strong and durable systemic anti-tumor immune response



Bommareddy PK et al AJCD. 2016

RPx Platform Addresses a Range of Tumor Types Intending to Optimize Clinical Outcomes

	RP1	RP2
Payloads	GALV-GP R-, GM-CSF	GALV-GP R-, anti-CTLA-4, GM-CSF
Target	Immunologically responsive tumor types, including anti-PD1 failed	Less immunologically responsive tumor types
Intended indication(s)	Skin cancers (CSCC inc. SOT*, anti-PD1 failed melanoma, anti-PD1 failed CSCC, other NMSCs, etc)	Rare cancers and neo adjuvant ; uveal melanoma registration study planned
Clinical activity in anti-PD1 failed patients demonstrated	✓	✓
Good tolerability and Safety profile demonstrated	✓	✓
Injection location	Superficial, nodal & visceral	Superficial, nodal & visceral
Systemic activity	***Clear systemic effects seen in responding patients (un-injected tumor responses, responses are generally highly durable)***	
Other design considerations	Designed for more I-O sensitive tumor types with excellent safety profile alone & in combination	Increased I-O systemic activity, also with excellent safety profile alone & in combination

*SOT=solid organ transplant

Pipeline

* Under a clinical trial collaboration & supply agreement with BMS for the supply of nivolumab – full commercial rights retained by Replimune
# Under a clinical trial collaboration agreement with Regeneron, includes certain sharing of clinical trial costs – full commercial rights retained by Replimune
^ Under clinical trial collaboration & supply agreement with Roche for atezolizumab & bevacizumab supply – full commercial rights retained by Replimune

RP1: Establishing a Broad Skin Cancer Franchise

IGNYTE Clinical Trial

High Unmet Need in Anti-PD1 Failed Melanoma Creates a Significant Potential RP1 Opportunity

5TH
Most common cancer in the US[1]

~98,000
Incidence in the US[1]

~8,000
Annual deaths in the US[1]

Unmet needs remain for anti-PD1 failed patients

40-65% *of all metastatic melanoma are refractory to initial anti-PD1 therapy*[2]

6-7% *expected response to anti-PD1 therapy following confirmed progression on single agent anti-PD1*[3,4]

~30% *response with lifileucel (Amtagvi™); AE profile and logistical hurdles potentially limit broad utility*

Other options for patients who have not already received anti-CTLA-4:

ipilimumab, ipi +nivo or Opdualag

~12% *expected response for Opdualag*[5*]

10%-30% *response for ipilimumab or ipi+nivo* ***with high toxicity***[6-8]

Other options for patients who have received anti-CTLA-4:

~12% *expected response for Opdualag*[5*]

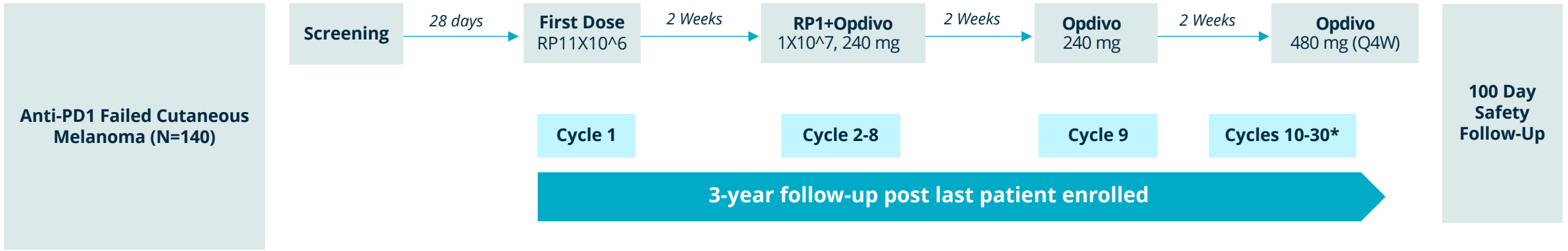
[1]National Cancer Institute Surveillance, Epidemiology and End Results (SEER) Program. 2023 Estimates. [2]Global Burden of Disease Cancer Collaboration JAMA Oncol 2019 (12; [3]Ribas et al Lancet Oncology 2018 (19); [4]Hodi et al JCO 2016 (34) ;[5]Ascierto P, JCO 2023 (RELATIVITY-020), [6]Pires da Silva I, et al. Lancet Oncol. 2021;22(6):836-847, [7]Olson DJ, et al. J Clin Oncol. 2021;39(24):2647-2655.; [8]Vanderwalde AM, et al. Presented at AACR 2022. New Orleans *Study (RELATIVITY-020) included multiple parts; presented data is from part D2, which allowed for failure of multiple lines of immunotherapy including ipi-nivo

IGNYTE: Phase 2 Study Design

Anti-PD1 Failed Cutaneous Melanoma Cohort; Registration-directed

IGNYTE

Tumor response assessment
Radiographic imaging (CT) at baseline and every 8 weeks from first dose and every 12 weeks after confirmation of response



Primary Objectives

- To assess the safety and tolerability of RP1 in combination with nivolumab
- To assess the efficacy of RP1 in combination with nivolumab as determined by ORR using modified RECIST 1.1 criteria

Secondary Objectives

To assess the efficacy of RP1 in combination with nivolumab as determined by DOR, CR rate, DCR, PFS, and 1-year and 2-year OS

Key Eligibility

Advanced or metastatic non-neurological solid tumors without treatment options; at least 1 measurable and injectable lesion (≥ 1cm LD); adequate organ function; no prior treatment with oncolytic therapy. ECOG performance status (PS) 0-1.

Criteria for CPI-failed:

At least 8 weeks of prior anti-PD1, confirmed progression while on anti-PD1, anti-PD1 must be the last therapy before the clinical trial. Patients on prior adjuvant therapy must have progressed while on prior adjuvant treatment (confirmed by biopsy).

Note: Dosing with Opdivo begins at Dose 2 of RP1 (C2D15)
*Option to reinitiate RP1 for 8 cycles if criteria are met
Data shown is a snapshot from the ongoing study, with a data cut off date of 6th Nov 2023

IGNYTE: RP1 + Nivolumab in Anti-PD1 Failed Melanoma

Promising ORR across all subgroups

BOR n (%)	Prior cohort (n=16)	Anti-PD1 failed cohort (n=140)	All patients (n=156)						
			All patients (n=156)	Prior single agent anti-PD1 (n=84)	Prior combination anti–PD-1 & anti–CTLA-4* (n=72)	Stage IIIb/IIIc/IVa (n=76)	Stage IVb/c/d (n=80)	Primary resistance to anti-PD1 (n=91)	Secondary resistance to anti-PD1 (n=63)
CR	2 (12.5)	17 (12.1)	19 (12.2)	14 (16.7)	5 (6.9)	15 (19.7)	4 (5.0)	12 (13.2)	6 (9.5)
PR	4 (25.0)	26 (18.6)	30 (19.2)	16 (19.0)	14 (19.4)	14 (18.4)	16 (20.0)	19 (20.9)	11 (17.5)
SD	2 (12.5)	29 (20.7)	31 (19.9)^	21 (25.0)	10 (13.9)	18 (23.7)^	13 (16.3)	15 (16.5)^	16 (25.4)
PD	8 (50.0)	68 (48.6)	76 (48.7)	33 (39.3)	43 (59.7)	29 (38.2)	47 (58.8)	45 (49.5)	30 (47.6)
ORR	6 (37.5)	43 (30.7)	49 (31.4)	30 (35.7)	19 (26.4)	29 (38.2)	20 (25.0)	31 (34.1)	17 (27.0)

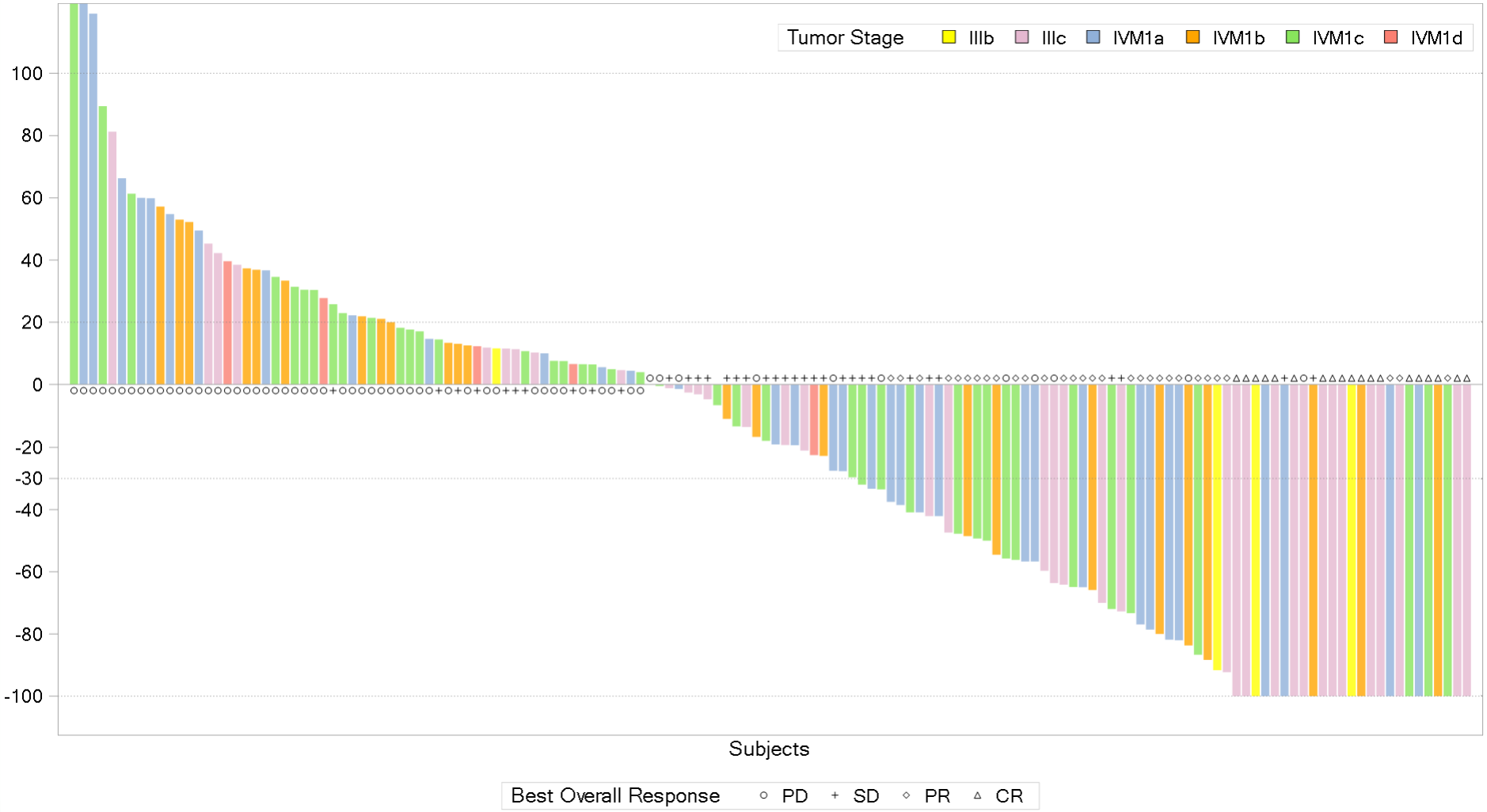
- Approximately 1 in 3 patients experienced a response
  - 26.4% ORR in particularly hard-to-treat Ipi+Nivo failed patients (approx. 50% of the study population)
  - 100% of responses lasted >6 months, with median DOR >24 months

BOR=best overall response

^Includes 1 patient with a unconfirmed PR (uPR). **There are 5 patients still on study with the opportunity for response.**
Response data as presented during Dec 5, 2023 investor event, data presented is by investigator assessment; the primary analysis from the study will be by blinded, independent central review.

IGNYTE: Depth of Response*

Target tumor reduction seen in greater than 50 percent of patients (n=156)



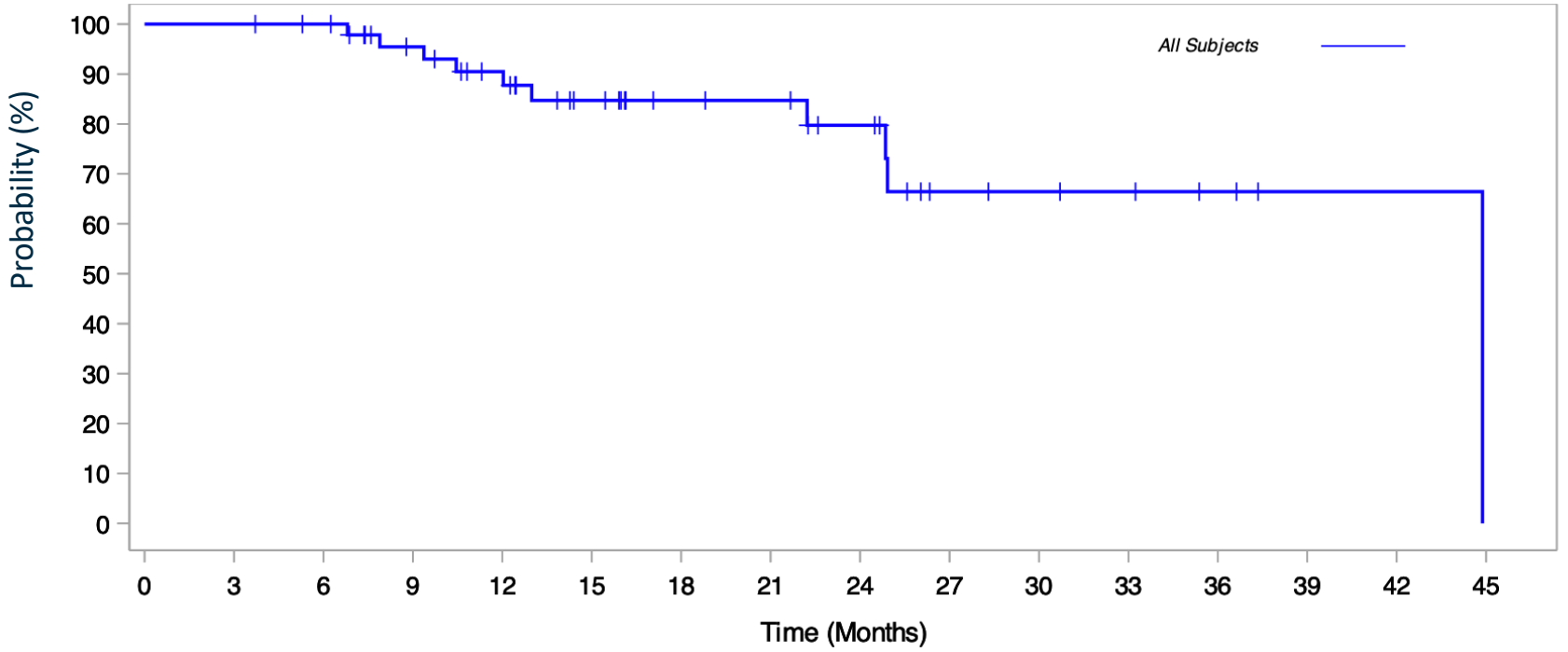
Key Takeaways

- Target tumor reduction is seen in >50% of patients
- Responses were seen across disease stages, including complete responses in patients with stage IVM1b/c disease

*Patients with at least one post baseline assessment – maximum change in target lesions; target lesion response for each patient; data presented during Dec 5, 2023 investor event

IGNYTE: Duration of Response

Durable responses with median DOR greater than 24 months



Key Takeaway

Responses are durable, with median DOR >24 months

>6 months	>12 months	>18 months	>24 months
100%	90.5%	84.7%	79.7%

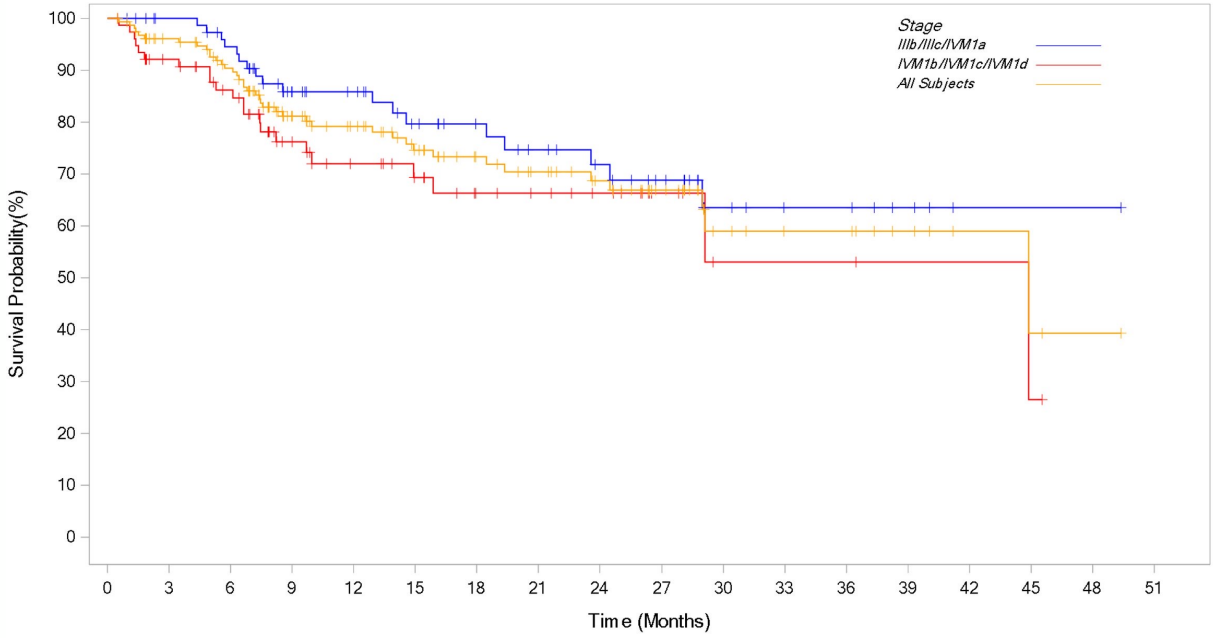
All patients have at least 6 months follow up, median follow up is 88.21 weeks
Data presented during Dec 5, 2023 investor event

IGNYTE: Overall Survival (OS)

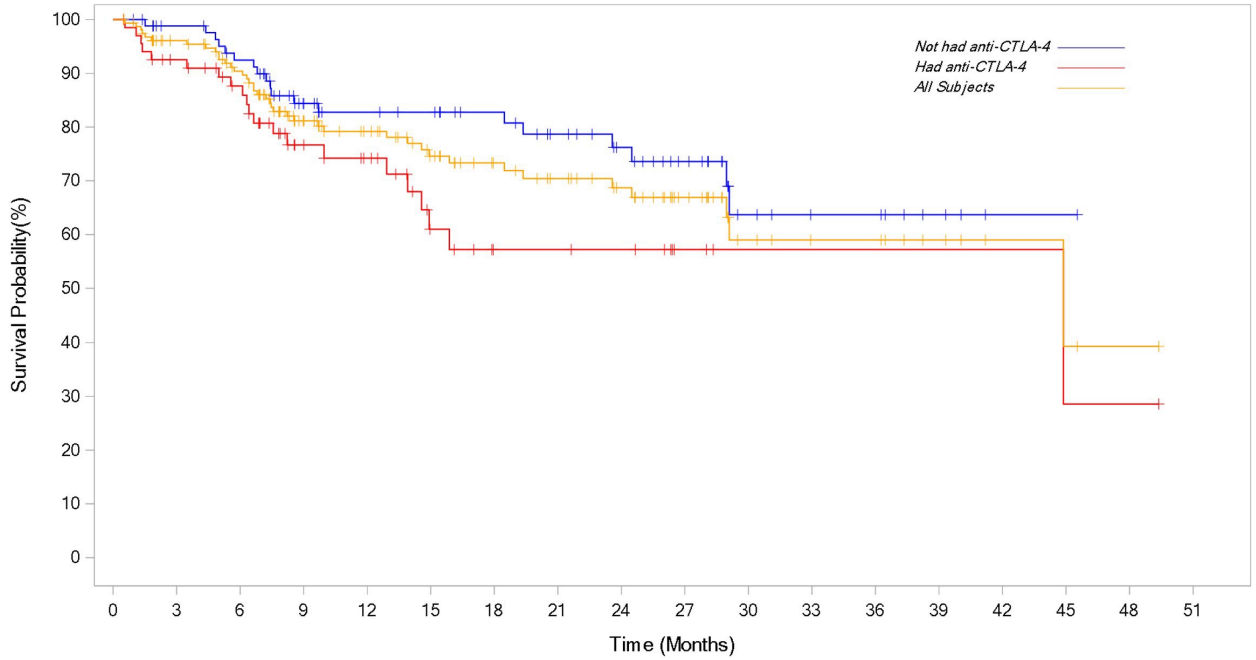
Promising OS seen across disease subsets, including those with greatest unmet need

Replimune®

Stage IIIb/IIIc/IVM1a vs Stage IV M1b/c/d



Prior anti-CTLA-4+anti-PD1 vs prior anti-PD1 alone



All patients have at least 6 months follow up, median follow up is 88.21 weeks
Data presented during Dec 5, 2023 investor event

Risk:Benefit of Therapies after Anti-PD1
RP1 + Nivolumab (n=156)*

Preferred Term (n) (%)	TRAEs which occurred in >5% of patients				
	Grade 1-2 (all) (%)	**Grade 3 (all) (%)**	**Grade 4 (all) (%)**	**Grade 5 (all) (%)**	**Total (N=156) (%)**
Chills	52 (33.3)	0	0	0	52 (33.3)
Fatigue	50 (32.1)	2 (1.3)	0	0	51 (32.7)
Pyrexia	47 (30.1)	0	0	0	47 (30.1)
Nausea	33 (21.2)	0	0	0	33 (21.2)
Influenza like illness	28 (17.9)	0	0	0	28 (17.9)
Injection site pain	21 (13.5)	0	0	0	21 (13.5)
Vomiting	20 (12.8)	0	0	0	20 (12.8)
Diarrhoea	19 (12.2)	1 (0.6)	0	0	19 (12.2)
Headache	19 (12.2)	0	0	0	19 (12.2)
Pruritus	19 (12.2)	0	0	0	19 (12.2)
Asthenia	12 (7.7)	1 (0.6)	0	0	13 (8.3)
Myalgia	11 (7.1)	0	0	0	11 (7.1)
Arthralgia	9 (5.8)	1 (0.6)	0	0	9 (5.8)
Decreased appetite	8 (5.1)	1 (0.6)	0	0	9 (5.8)
Rash	8 (5.1)	1 (0.6)	0	0	9 (5.8)

RP1 in combination with nivolumab

- Treatment-related adverse events associated (in >5% of patients) were predominantly Grade 1-2 constitutional type events, with a low incidence of Grade 3-5 events.

Other treatments used in this setting

- **Lifileucel** requires complex administration and lymphodepletion; in studies, 78% experienced more than 1 grade 3-4 TEAE with 12 grade 5 AEs recorded.[1]
- **Ipilimumab-nivolumab**, 57% of patients receiving experienced grade 3+ TRAEs.[2,3]

TRAE: Treatment-related adverse event
TEAE: Treatment-emergent adverse event

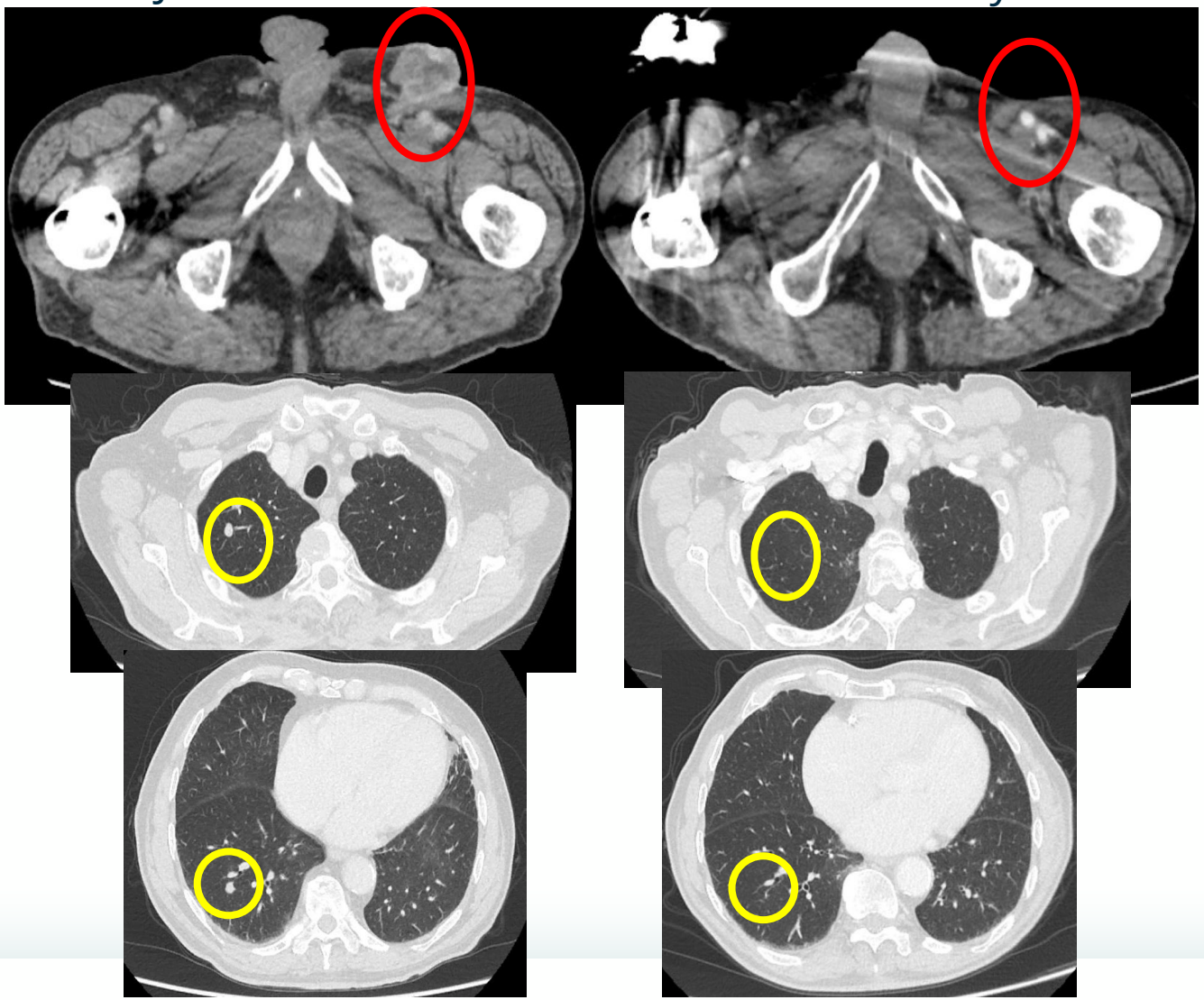
[1]Amtagvi (lifileucel) prescription information [2]Vanderwalde AM, Nature Medicine 2022 (SWOG S1616), [3]Vanderwalde AM, presented at AACR 2022 (CT103), *AE rates based on available literature, not head-to-head studies

Patient 4401-2021:

Prior Tafinlar/Mekinist, progressed on Keytruda, anti-PD1, Stage IVM1c

12JAN2021/Baseline

15FEB2022/Day 368

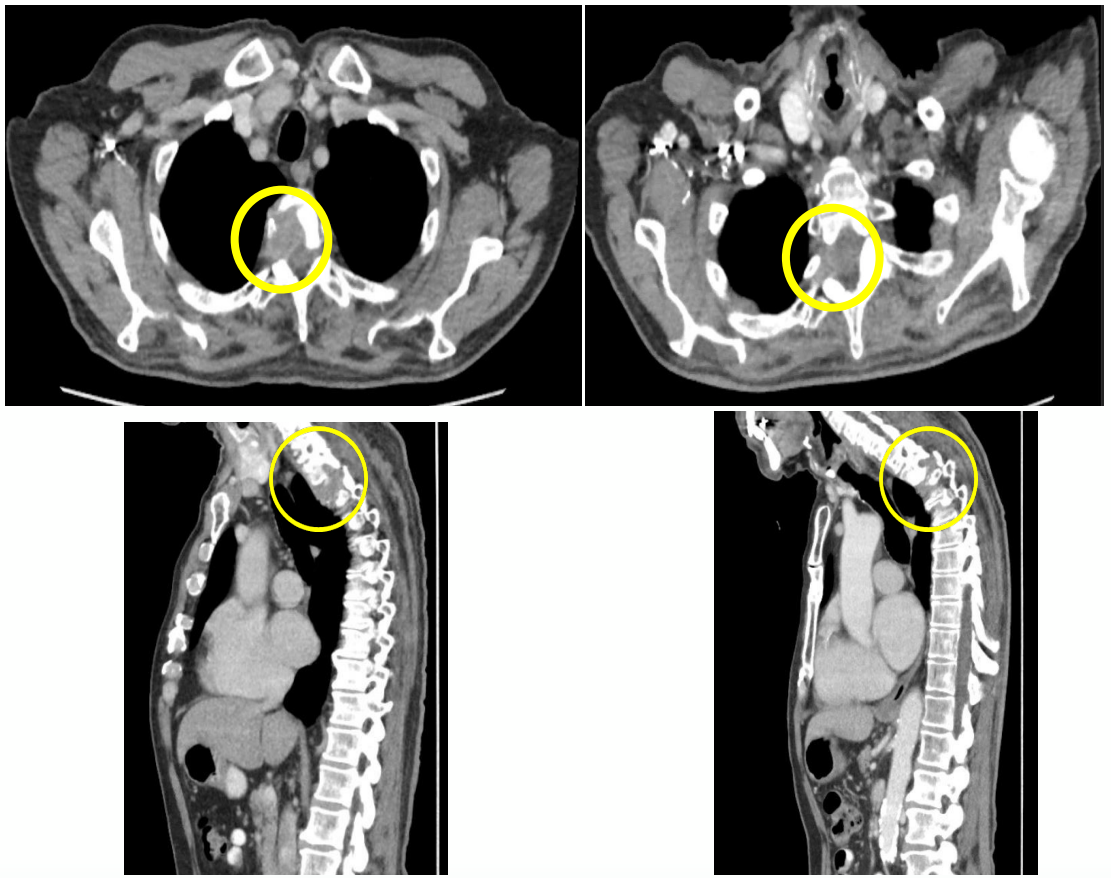


Injected

Un-injected

12JAN2021/Baseline

15FEB2022/Day 368

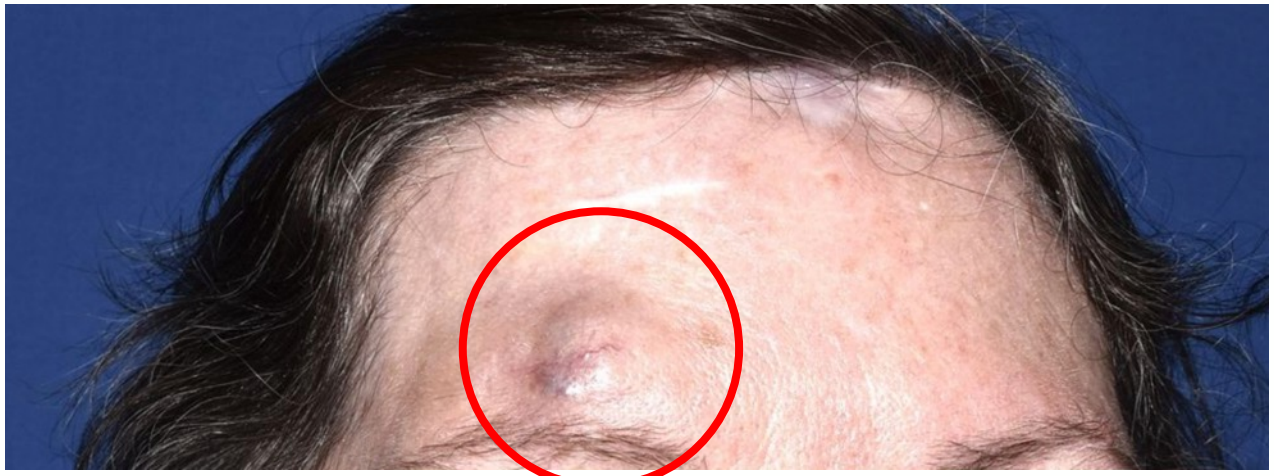


Data snapshot date: 3 Nov 2022

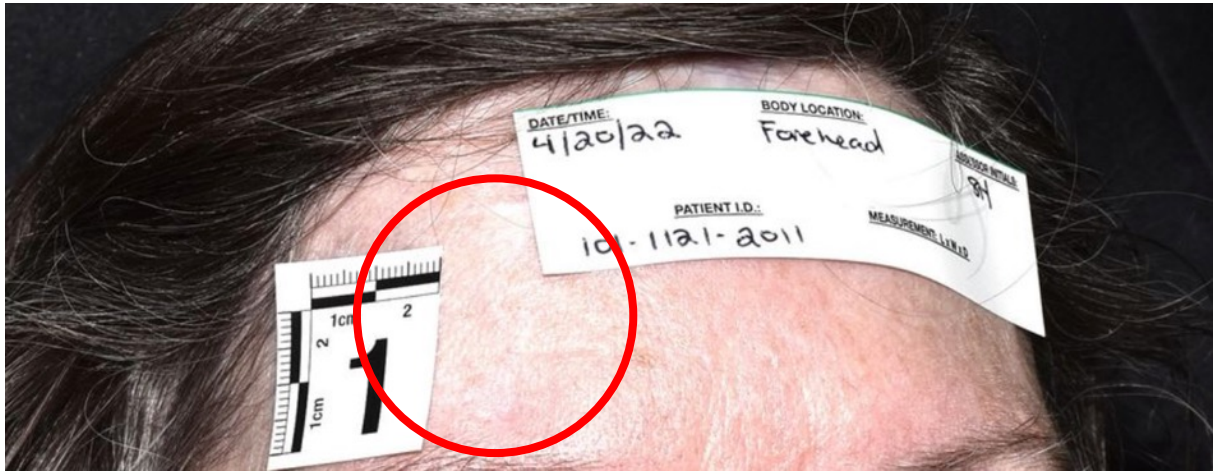
Patient 1121-2011:

Prior Opdivo (adjuvant) and Keytruda (first line for metastatic disease), Stage IVM1c

29 JUL 2021 / Screening



20 APRIL 2022



Injected Un-injected

Patient 1121-2011 Cont'd:

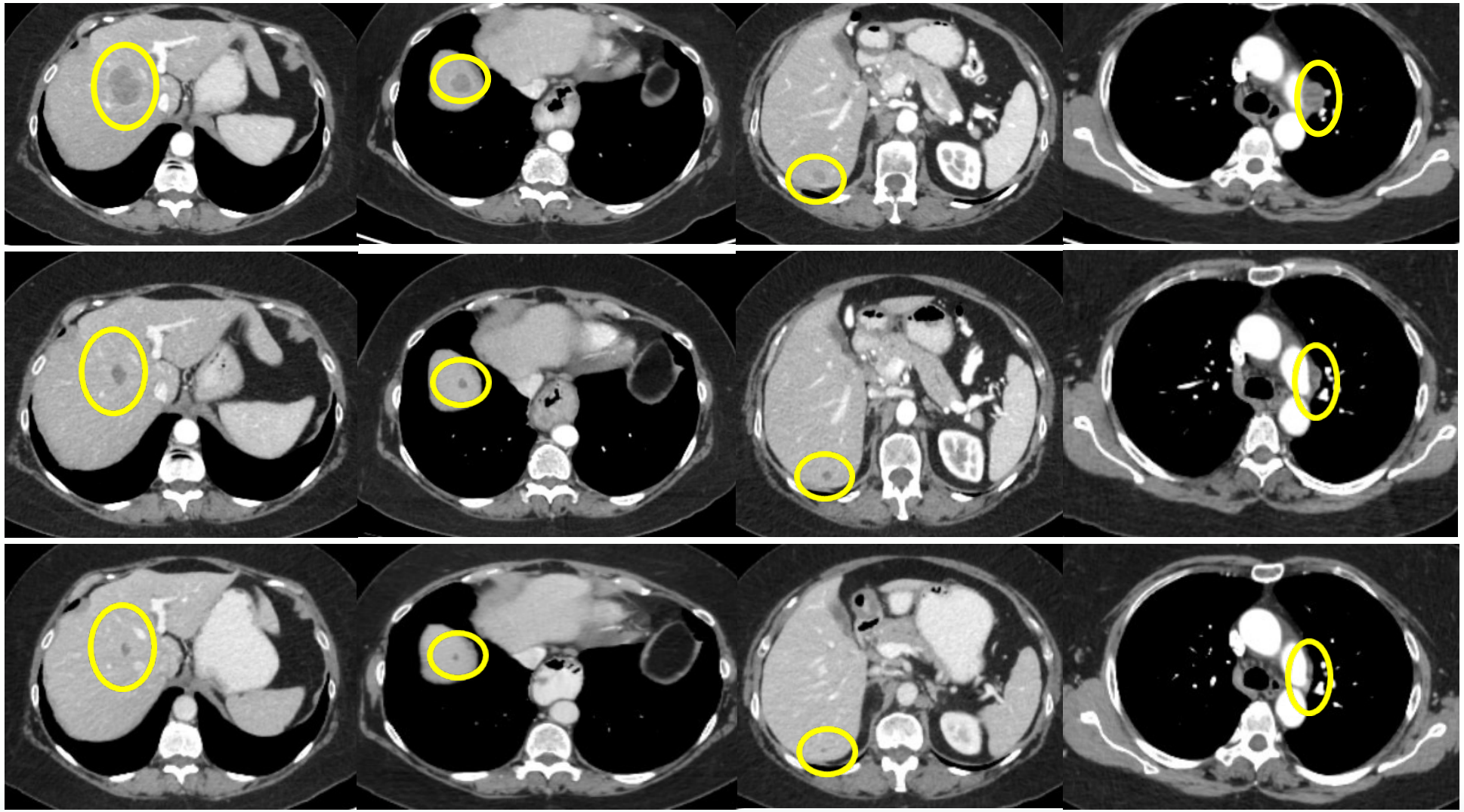
Prior Opdivo (adjuvant) and Keytruda (first line for metastatic disease), Stage IVM1c

Replimune®

22 Jul 2021/
Baseline

22 Sep 2021/
Day 57

29 Dec 2021/
Day 155



Injected Un-injected

IGNYTE: Regulatory Summary and Next Steps

IGNYTE FDA Type C meeting on anti-PD1 failed melanoma

- FDA acknowledged that IGNYTE population represents one of unmet need
- FDA agreed on confirmatory study concept with a 2-arm randomized trial design in anti-PD1 failed melanoma with physician's choice as a comparator arm in the study population
  - Planning underway; will be initiated at time of BLA submission
- BLA submission for anti-PD1 failed melanoma is planned for 2H 2024 pending
  - Centrally reviewed data by RECIST v1.1 and mRECIST
  - All patients followed for at least 12 months (which is the per protocol primary analysis timepoint)
  - All responding patients followed for at least 6 months from response initiation

IGNYTE-3: Confirmatory Phase 3 Trial Design*

RP1 and Nivolumab in Ipi-Nivo pretreated patients

Unresectable stage IIIB/IV cutaneous melanoma

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

Up to 2 prior lines of systemic therapy for advanced disease allowed

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

N=~400

Randomized 1:1

RP1 + Nivolumab

Treatment of Physician's Choice (TPC)

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

Primary Endpoint
Overall Survival

Key Secondary Endpoints
Progression Free Survival and Objective Response Rate

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

CERPASS Clinical Trial

CERPASS 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 untreated brain metastases

2:1
N=211

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 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

**Note $p \leq 0.05$ was required if both dual primary endpoints hit for statistical success, if only one of the dual endpoints hits, a $p \leq 0.025$ was needed*

†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

CERPASS: Confirmed ORR & CRR (ITT population)

Number of patients achieving CR substantially increased with RP1; CR rate more than doubled for RP1 in locally advanced CSCC

BOR (confirmed response)	All N=211	
n/%	Cemiplimab n=72	RP1+ cemiplimab n=139
PR	19 (26.4)	20 (14.4)
SD	14 (19.4)	18* (12.9)
PD	12 (16.7)	27 (19.4)
OR	**37 (51.4%)**	**73 (52.5%)**
	P=0.692[1]	
CR	**18 (25.0%)**	**53 (38.1%)**
	P=0.040[1]	

BOR (confirmed response)	Locally advanced CSCC n=83		Metastatic CSCC n=128	
n/%	Cemiplimab n=31	RP1+ cemiplimab n=52	Cemiplimab n=41	RP1+ cemiplimab n=87
OR	18 (**58.1%**)	33 (**63.3%**)	19 (46.3%)	40 (46.0%)
CR	7 (**22.6%**)	25 (**48.1%**)	11 (26.6%)	28 (32.2%)

*One patient shown as SD was a CR due to the confirmatory assessment happening 21 days rather than later 28 days as required per protocol (CRR if included = 38.8%; p=0.031); **&Nominal p value 0.013

[1]Per the protocol p≤0.025 is required for formal statistical success in CERPASS for CRR or ORR alone and p≤0.05 if both endpoints were met

BOR=best overall response

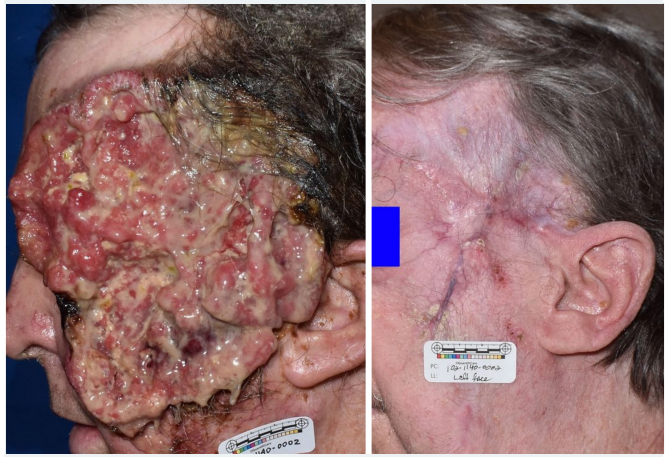
Key Takeaways / Next Step

- Study missed its primary endpoints (ORR/CRR)
- Study continuing to allow time-based endpoints to mature (DOR, PFS and OS)
- In locally advanced CSCC, CR rate more than doubled for RP1+cemiplimab vs cemiplimab alone (48.1% vs 22.6%)

Five of the Most Visually Impactful CRs with RP1+cemiplimab

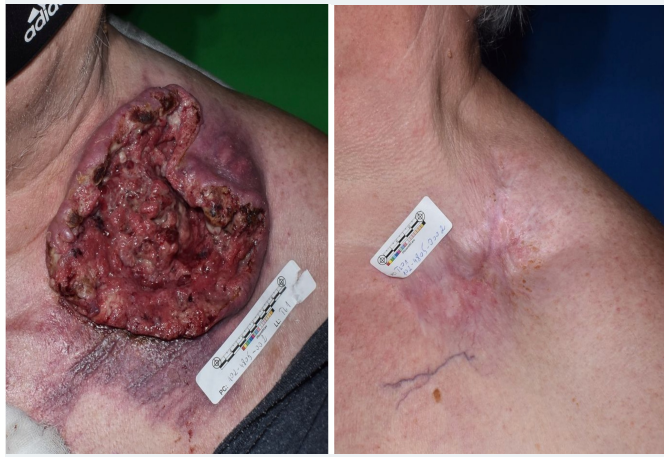
Replimune®

Baseline | 81 weeks



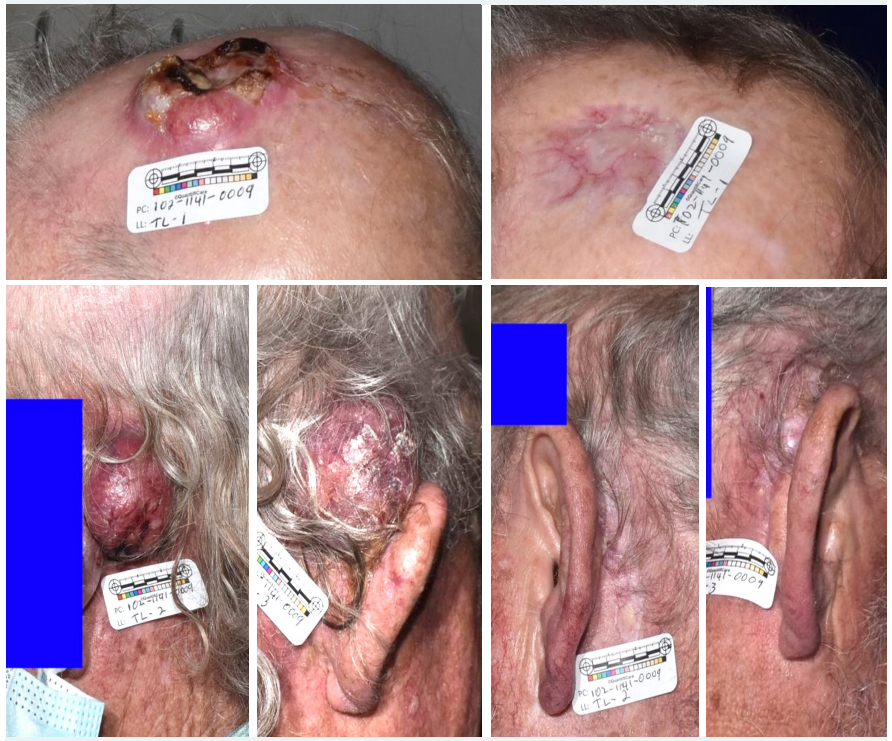
1140-0002

Baseline | 81 weeks



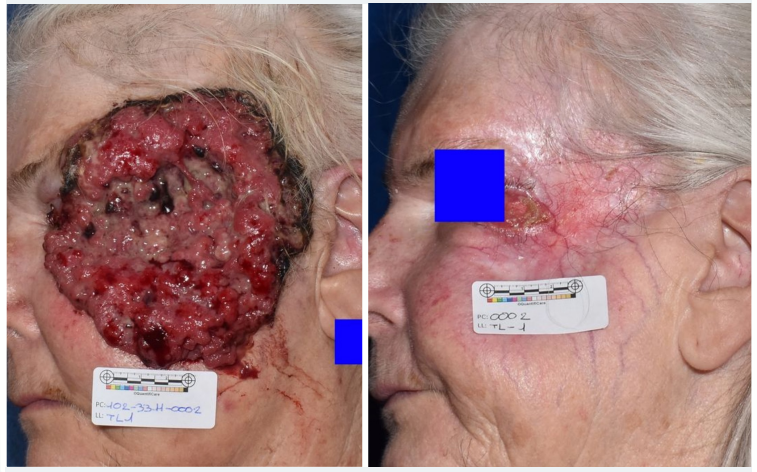
4805-0002

Baseline | 54 weeks



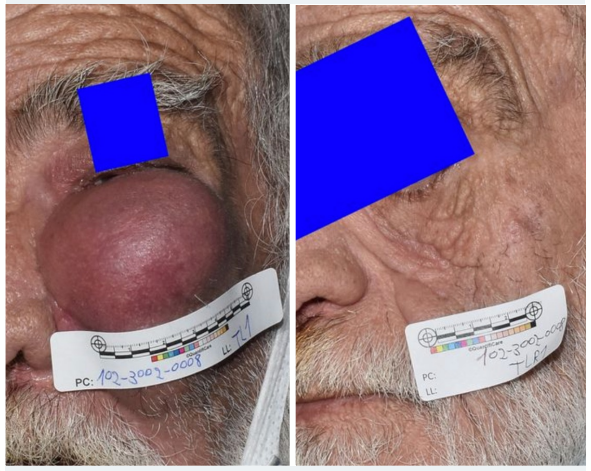
1141-0009

Baseline | 63 weeks



3311-0002

Baseline | 63 weeks



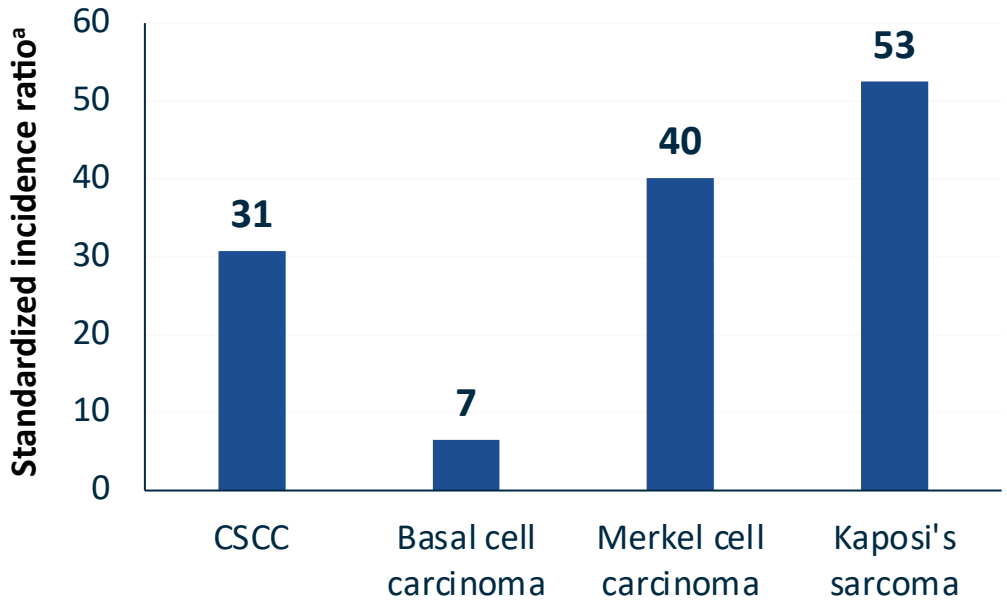
3002-0008

ARTACUS Clinical Trial

Solid Organ Transplantation and Non-Melanoma Skin Cancer (NMSC)

- Non-melanoma skin cancer (NMSC) is the most common post-transplant malignancy in solid organ transplant (SOT) recipients and occurs at a 7-53x higher incidence vs the general population[1]
  - Cutaneous squamous cell carcinoma (CSCC) and basal cell carcinoma account for >90% of all cases of NMSC in SOT recipients[1,2]
  - Systemic immune checkpoint blockade is contra-indicated in the setting of SOT-associated NMSC given the documented risk of allograft rejection[3,4]

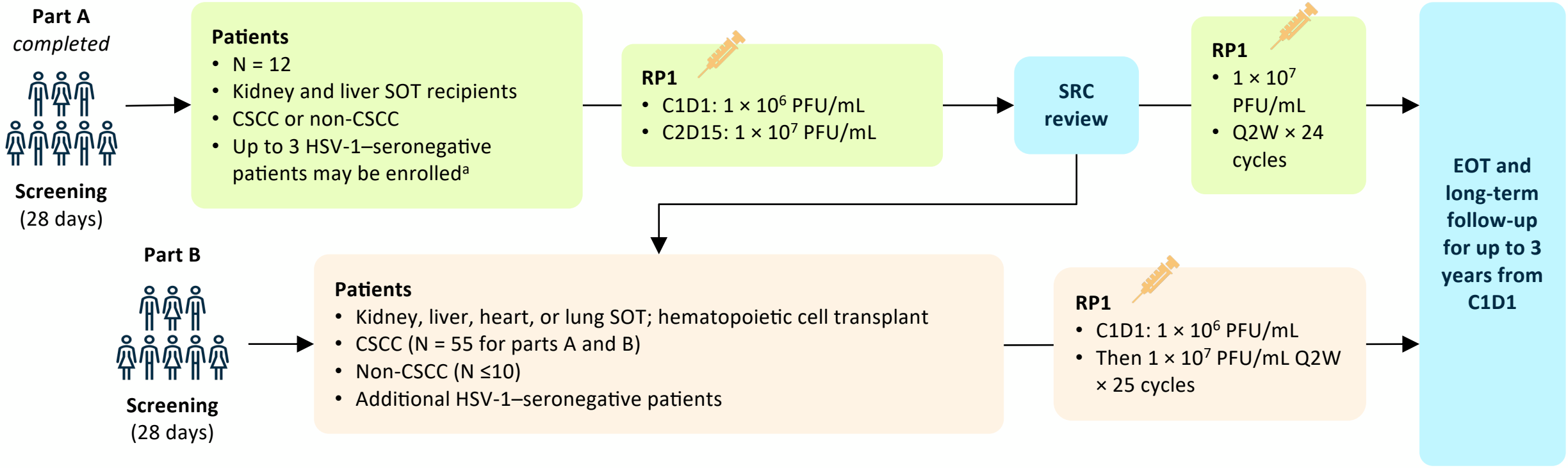
- Management of locally advanced and metastatic CSCC that has spread to other areas of the skin, soft tissue, or lymph nodes in SOT patients is not well established[3,4]
  - Withdrawal of immunosuppressive therapy may be required for the management of CSCC but may increase the risk of organ transplant rejection



[a]Standardized incidence ratios were calculated by dividing the observed number of NMSC cases by the expected number of cases based on the general population.
CSCC, cutaneous squamous cell carcinoma; NMSC, non-melanoma skin cancer; SOT, solid organ transplantation.

1. Friman T, et al. *Int J Cancer*. 2022;150(11):1779-91. 2. Garrett G, et al. *JAMA Dermatol*. 2017;153(3):296-303. 3. Mittal A and Colegio O. *Am J Transplant*. 2017;17(10):2509-30.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Squamous Cell Skin Cancer. Version 1. 2023.

ARTACUS: Study Design



RP1 is administered via direct or ultrasound-guided IT injection into superficial, cutaneous, subcutaneous, or nodal solid tumors. Deep visceral organ or nonsolid tumors (eg, malignant pleural effusions, malignant ascites, cerebral spinal fluid, etc); tumors in the brain, bone, or spinal cord; or tumors in transplanted organs are not eligible for RP1 injection

[a]After 3 seronegative patients were enrolled, safety in this population was assessed by the SRC, who approved continued enrollment of seronegative patients. One cycle = 2 weeks. The treatment period is up to 52 weeks (one year). C, cycle; CSCC, cutaneous squamous cell carcinoma; D, day; EOT, end of treatment; HSV-1, herpes simplex virus type 1; IT, intratumoral; PFU, plaque-forming unit; Q2W, every 2 weeks; SOT, solid organ transplant; SRC, safety review committee. Migden et al, AACR 2024, Presentation CT003

ARTACUS: Baseline Demographics, Characteristics, Activity

RP1 as monotherapy shows clear clinical activity with promising ORR/CRR

Characteristic	All patients (N = 27)
Age, years, median (range)	68.0 (48–86)
Male, n (%)	21 (77.8)
Race, n (%)	
White	26 (96.3)
Native Hawaiian/Pacific Islander	1 (3.7)
Allograft type, n (%)	
Kidney	22 (81.5)
Liver	4 (14.8)
Lung	1 (3.7)
Heart	0
Cutaneous malignancies, n (%)	
CSCC	24 (88.9)
MCC	3 (11.1)
Stage at study baseline, n (%)	
Locally advanced	15 (55.6)
Metastatic[a]	12 (44.4)
Primary tumor location, n (%)	
Skin	26 (96.3)
Lymph node	1 (3.7)

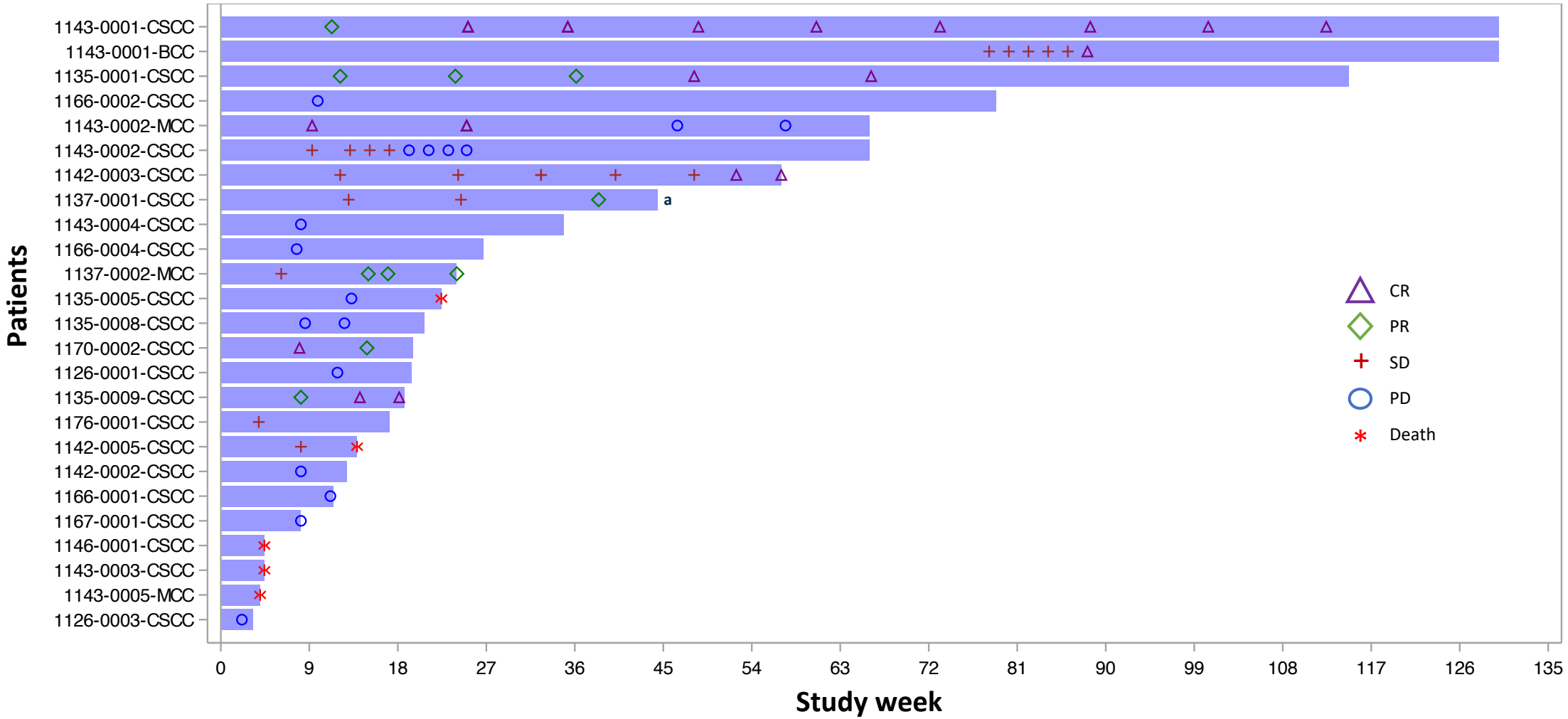
	Evaluable patients[a] (N = 23)
Best overall response (modified RECIST 1.1)	n (%)
CR	5 (21.7)[b]
PR	3 (13.0)[c]
SD	1 (4.3)
PD	14 (60.9)
ORR (CR + PR)	8 (34.8)
DCR (CR + PR + SD)	9 (39.1)

	Responders (n = 8)
Characteristics of responders	n
Tumor type	
CSCC	6
MCC	2
Stage at study baseline	
Locally advanced	6
Metastatic	2

[a]Per protocol, metastatic to skin, soft tissue, or lymph nodes.
CSCC, cutaneous squamous cell carcinoma; MCC, Merkel cell carcinoma
Migden et al, AACR 2024, Presentation CT003.

ARTACUS: Duration of Response

Robust antitumor activity with most responses ongoing



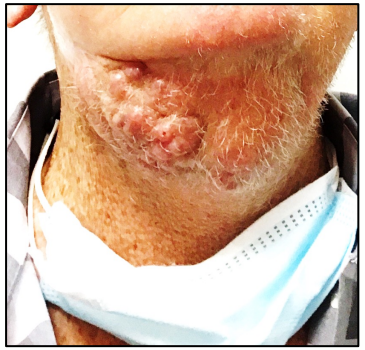
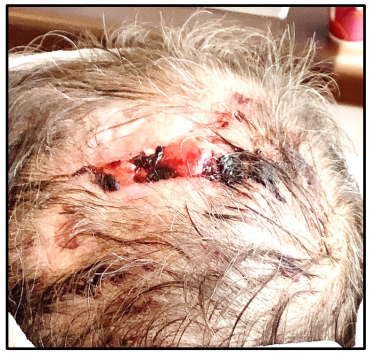
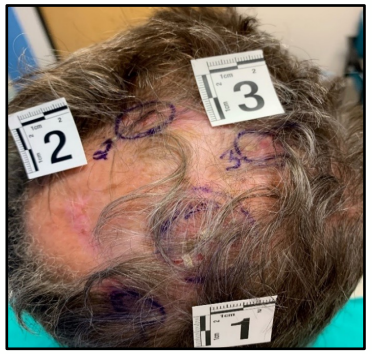
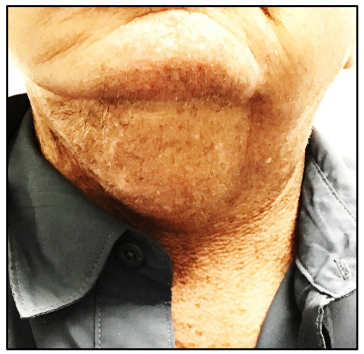
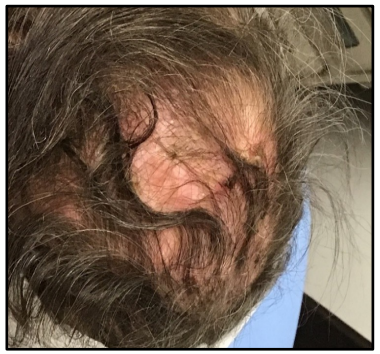
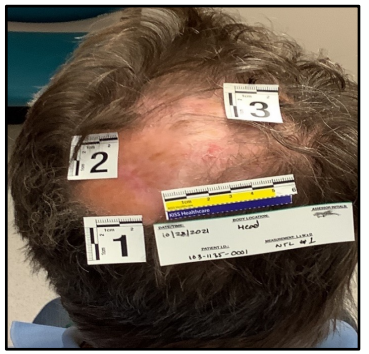
[a]Withdrew consent.

CR, complete response; BCC, basal cell carcinoma; CSCC, cutaneous squamous cell carcinoma; MCC, Merkel cell carcinoma; PD, progressive disease; PR, partial response; SD, stable disease.

Migden et al, AACR 2024, Presentation CT003

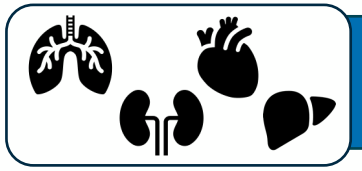
ARTACUS: Examples of Patients With Confirmed Response

Replimune®

	1143-0002	1143-0001	1135-0001
	May 2022	June 2021	July 2021
Baseline			
	August 2022 (3 months)	December 2021 (6 months)	October 2021 (3 months)
Best response			
	Complete response	Complete response	Complete response

Migden et al, AACR 2024, Presentation CT003

High Risk of Skin Cancer in Organ Transplant Patients Drives the RP1 ARTACUS Opportunity



~1.5K Addressable* Solid Organ Transplant Patients with skin cancer[6]

50%↑ Growth in transplants over the last 8 years[1]

Significant Unmet Need

UP TO 53x **Increased Risk of Cancer**
Increased risk of SoT patients developing skin cancer, with a high rate of metastasis[2]

35% **High Rate of Multiple Primary Lesions**
Percentage of patients developing multiple primary lessions[4,5]

30% **Treatment Options Risk Loss of Organ**
Rate of organ rejection, due to treatment with ICIs for skin cancer[3]

ARTACUS Data

RP1 showed an **35% ORR and a 22% CRR[7]** with safety similar to the profile seen in non-immunocompromised patients

RP1 has been **dosed up to 26 times to treat patients, with the potential for retreatment**

RP1 monotherapy has shown the ability to treat skin cancer with **no cases of allograft rejection[7]**

*Addressable defined as locally advanced or metastatic SoT (solid organ transplant) skin cancer patients
[a]Standardized incidence ratios were calculated by dividing the observed number of NMSC cases by the expected number of cases based on the general population.
CSCC, cutaneous squamous cell carcinoma; NMSC, non-melanoma skin cancer; SOT, solid organ transplantation.
1. OPTN, 2. Friman T, et al. *Int J Cancer*. 2022;150(11):1779-91, 3. Ji et al. Front Transplant 2023 4. Eggermont, et al JAAD 2023 5. Gilbert et al. Cureus. 2022 6. Replimune Analysis 7) Midgen et al AACR 2024 Pres CT-003

RP1 Commercial Opportunity

Significant Opportunity to Establish a Broad Skin Cancer Franchise Built Upon Strong Foundation in Melanoma

Replimune®

RP1 near-term opportunity

Anti-PD1-failed melanoma

~13K patients[1]

1L prior adjuvant

2L+ BRAF WT

2L+ BRAF MT

GOAL

Address high unmet need in anti-PD-1 failed settings

Potential NMSC* access via compendia+

~11K patients[2]

1L CSCC

SOT NMSC

Anti-PD1 failed

Immuno-compromised (other)

GOAL

Improve upon the SOC either as combo or as monotherapy

Future growth driver

Neoadjuvant skin cancers**

~45K patients

Neoadjuvant CSCC

Neoadjuvant melanoma

GOAL

Improve cure rates in early-stage patients

~70,000 treatable patients in the US

"Opportunity to change the treatment paradigm and ensure all appropriate patients can benefit from RP1"

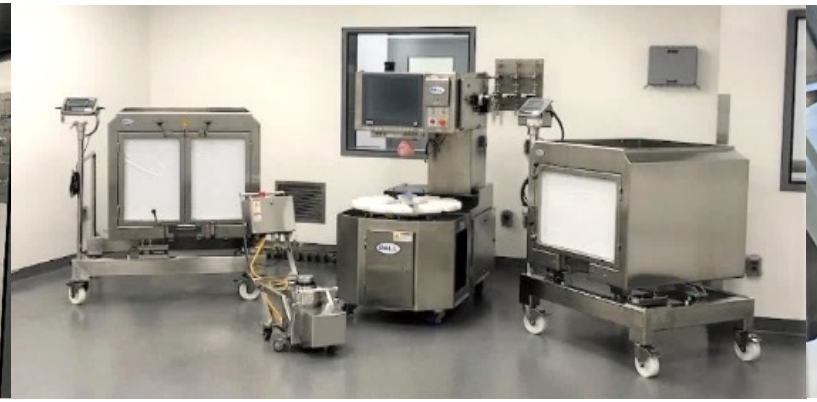
+Spontaneous use will not be promoted

Source: [1]Melanoma US treated patient population for 2030 based on CancerMPact® Patient Metrics, Cerner Enviza (available from www.cancermpact.com Accessed 15 Oct 2023), with adjustments to future 2L+ treatment rates based on primary market research. [2]CSCC US treated patient population for 2030 based IQVIA claims, primary market research, and company data.
*NMSC (non-melanoma skin cancers); RP1+cemiplimab or RP1+nivolumab or RP1 mono **Neoadjuvant CSCC (est. 30K patients) and melanoma (est. 15K patients). SOT=solid organ transplant

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
  - *RP1-2 technology transfer from CMO successfully completed*
  - *RP1-2 released to clinic for ongoing trials*
  - *RP1 BLA consistency lot runs complete*
- 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

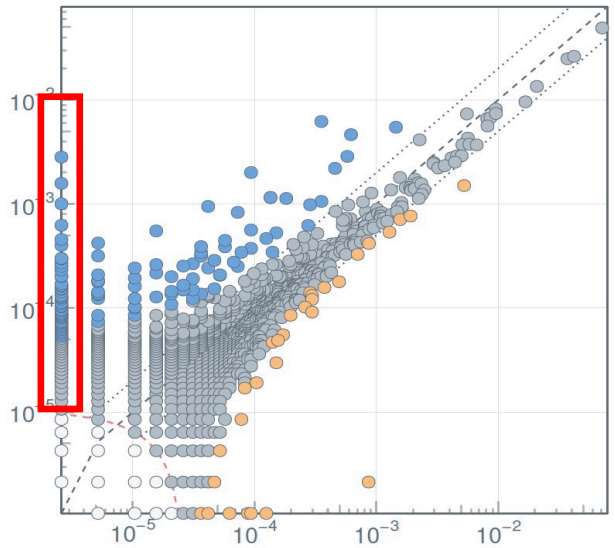


RP2: Focused on Rare Cancers

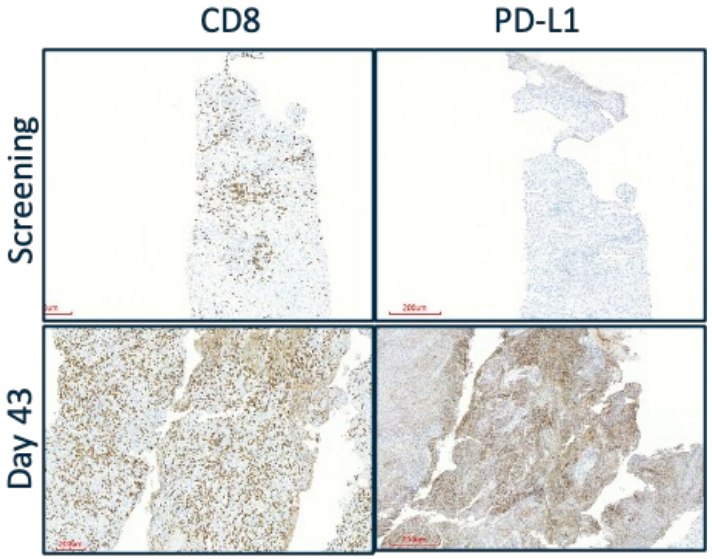
RP2: Fusion Enhanced Oncolytic HSV Expressing Anti-CTLA-4

Durable monotherapy and combination responses demonstrated in multiple immune insensitive tumor types

- Designed to focus on the delivery of molecules which function at the time and place of immune activation, i.e. in tumors & draining lymph nodes
- Anti-CTLA-4 antibody prevents immune blockade at the APC / T cell interface
  - Anti-CTLA-4 is clinically validated; Ipilimumab, tremelimumab[#]
  - RP2 intends to deliver anti-CTLA-4 where it is needed (at the tumor) without systemic toxicity of other therapies



TCR sequencing of PBMCs demonstrated expansion of pre-existing and generation of new T cell clones following treatment with RP2 with nivolumab (Example: pt 3412-0001, uveal melanoma, PR)*



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

*Bommareddy P et al AACR 2024, [#] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4400238/

Mucoepidermoid Carcinoma Monotherapy Patient Featured in BBC News

Prior carboplatin/paclitaxel, bicalutamide, ceralasertib - ongoing CR>2 years (RP2 mono)

BBC

Home News Sport Business Innovation Culture Travel Earth Video Live

Krzysztof's cancer is no longer detectable

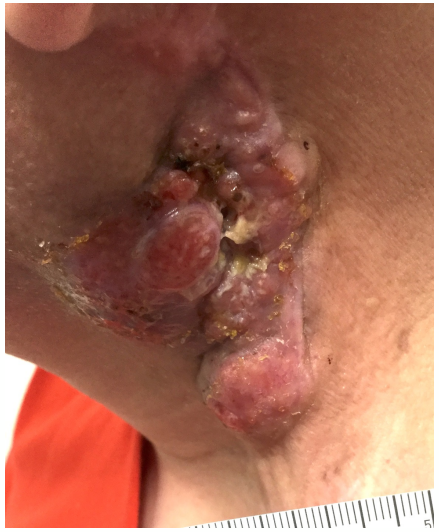
ICR The Institute of Cancer Research

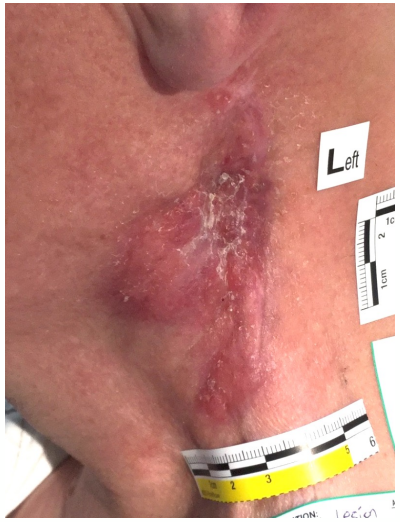
"My final lifeline"

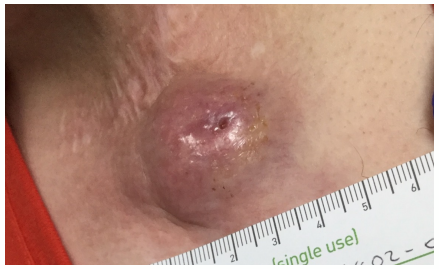
"I had injections every two weeks for five weeks which completely eradicated my cancer. I've been cancer-free for two years now."

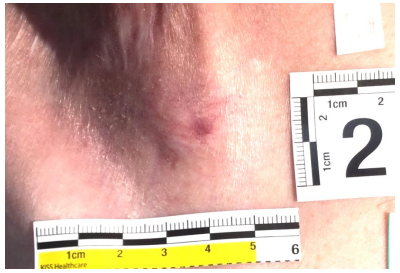
1 month

4 months







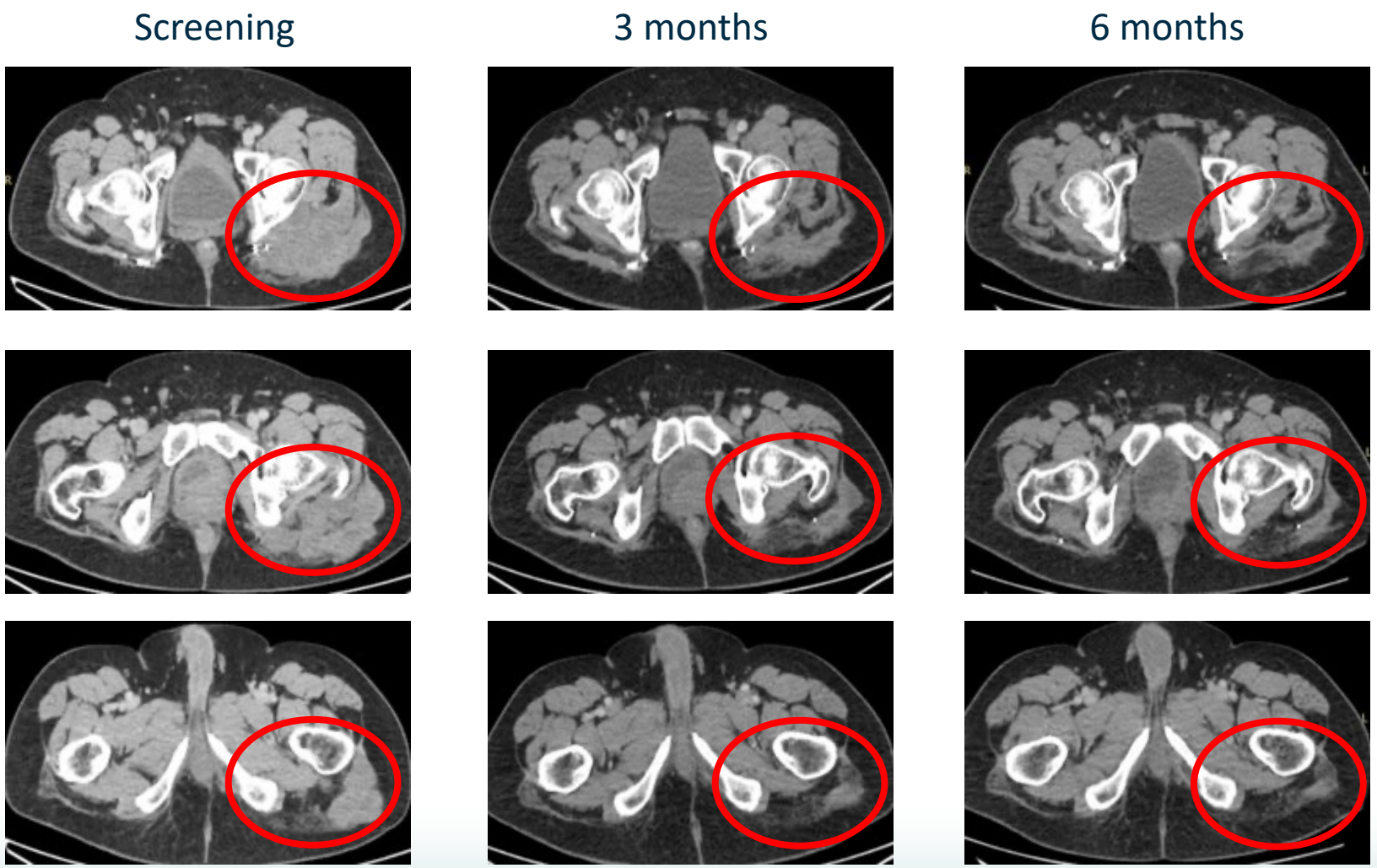


"It's a true miracle, there is no other word to describe it. I've been able to work as a builder again and spend time with my family, there's nothing I can't do."

RP2 Monotherapy Patient with Chordoma

Prior imatinib – ongoing PR at over 8 months (RP2 monotherapy)

Replimune®



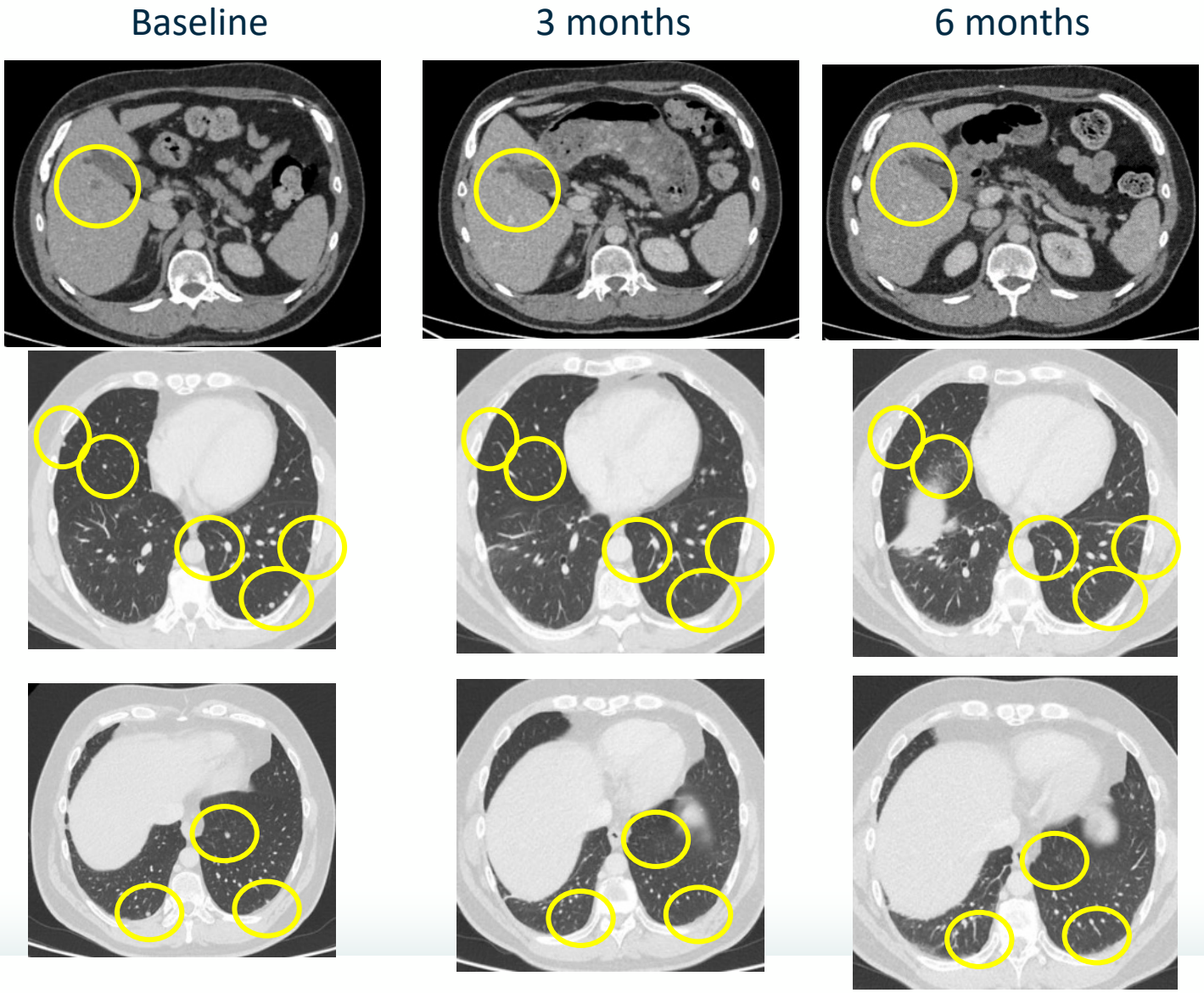
Pt 4401-0029 - ongoing PR

- Left gluteal muscle injected
- Liver & >50 small lung lesions also disappeared during treatment

Injected *Un-injected*

RP2 Monotherapy Patient with Chordoma

Prior imatinib – ongoing PR at over 8 months (RP2 monotherapy)



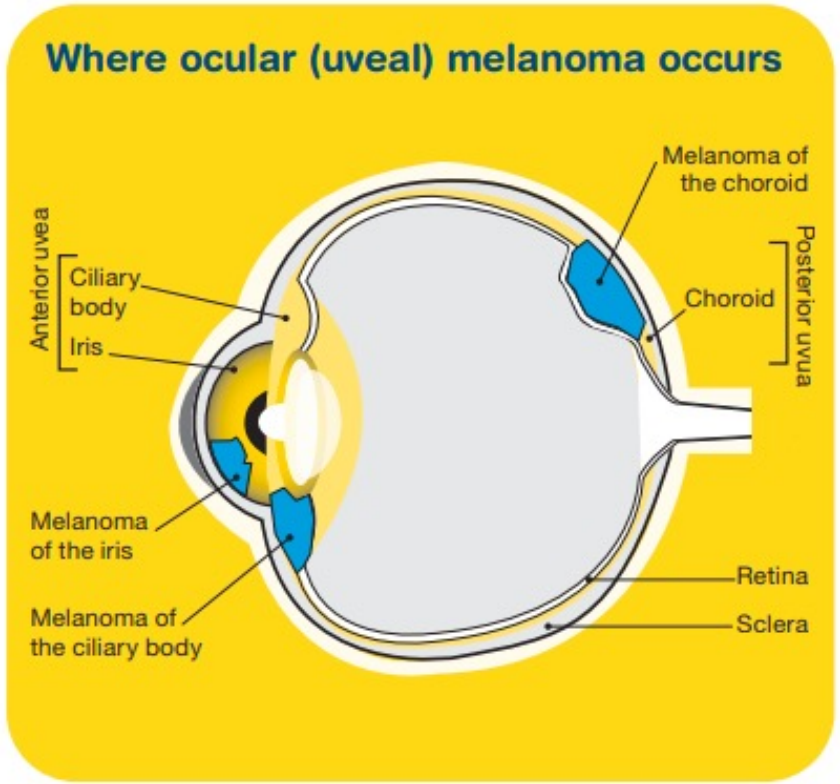
Pt 4401-0029 - ongoing PR

- Left gluteal muscle lesion injected
- Liver & >50 small lung lesions also disappeared during treatment

Injected Un-injected

RP2 in Uveal Melanoma

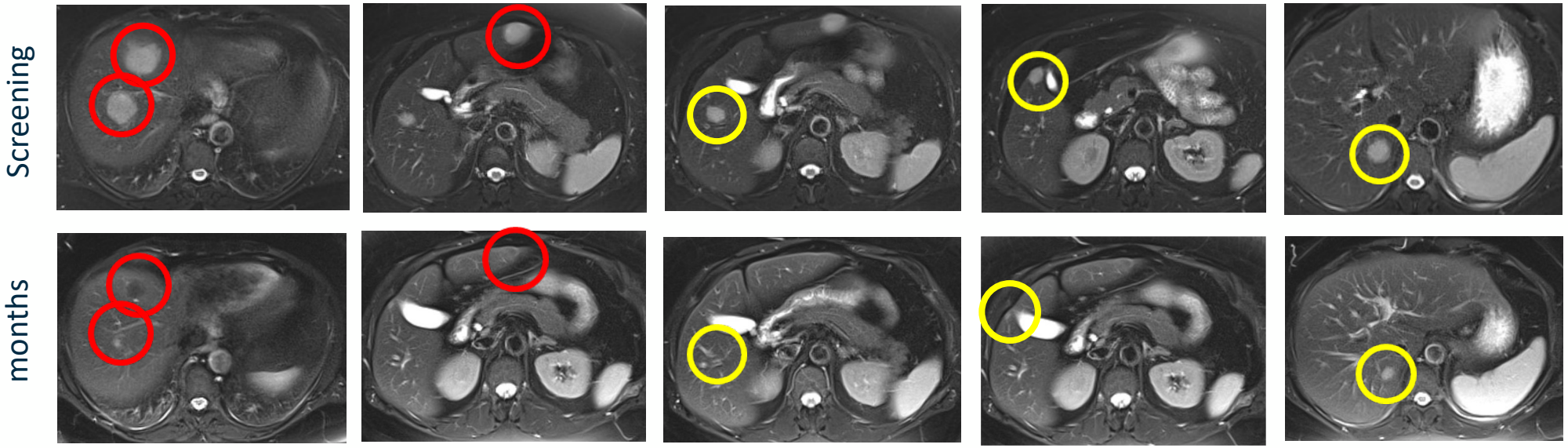
- Ocular or “uveal” melanoma is a rare cancer with approx. 1,000 cases in the US per year[1]
  - The historic median OS is approx. 12 months[1]
- Uveal melanoma behaves quite differently from skin melanoma
  - Mostly metastasizes to the liver (approx. 70-90% of cases) and once this occurs only about 10% of these patients survive beyond a year
  - Difficult to treat tumor where CPIs have demonstrated limited activity[2,3,4]
  - 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 remains high, including improved efficacy/tolerability, effective options for HLA negative patients, and those who have progressed on Kimmtrak (HLA positive) and/or I-O combinations regardless of HLA status
- **Approximately 30% ORR in those treated with RP2 monotherapy or combined with nivolumab in 2L uveal melanoma (n=17) with impressive duration; longest ongoing response over 24 months**[5]
- Planning underway for a registration-directed clinical trial



[1]Carvajal RD et al. Br J Ophthalmol 2017; [2]Nathan P et al. N Engl J Med. 2021;385(13):1196-1206; [3]PelsterMS et al. J Clin Oncol. 2021;39(6):599-607; [4]Lukzky J et al SMR 2022; [5]Sacco et al, 20th International Congress of the Society for Melanoma Research, November 2023
* Versus investigator’s choice, pembrolizumab, ipilimumab, or dacarbazine

Uveal Melanoma Patient Featured in ITV News

Prior nivolumab+ipilimumab – PR (RP2+nivolumab)



Pt 201-4403-0017 – ongoing PR

- Liver metastases
- Patient has ongoing PR at 19 months

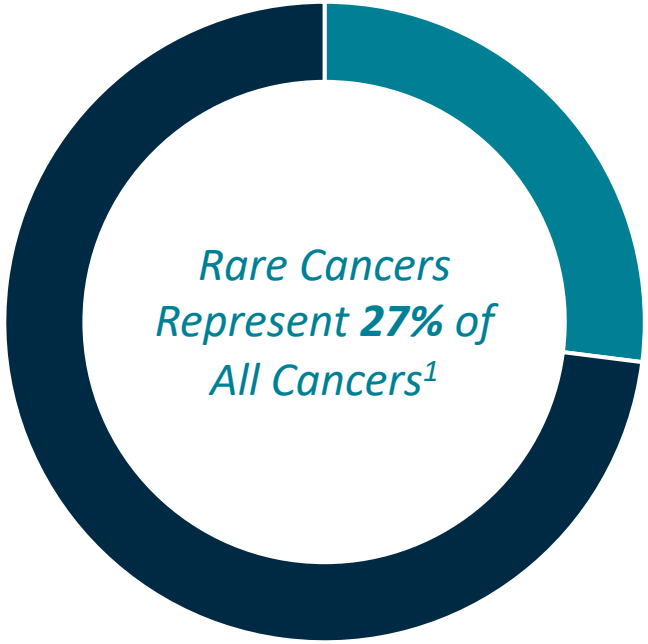
"This trial has given me hope in the treatment, the trial, my care, and I'm happy. I don't think about dying anymore at all"

ITV, 03 November 2023

Injected Un-injected

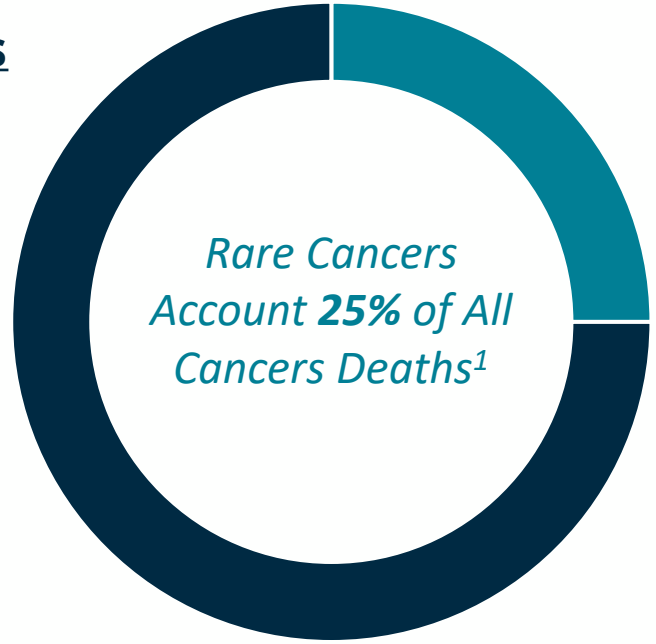
Rare Cancers Represent a Significant Unmet Need and Potential for Paths to Market for RP2

Treatment with RP2 has led to responses in multiple rare cancer settings[3]



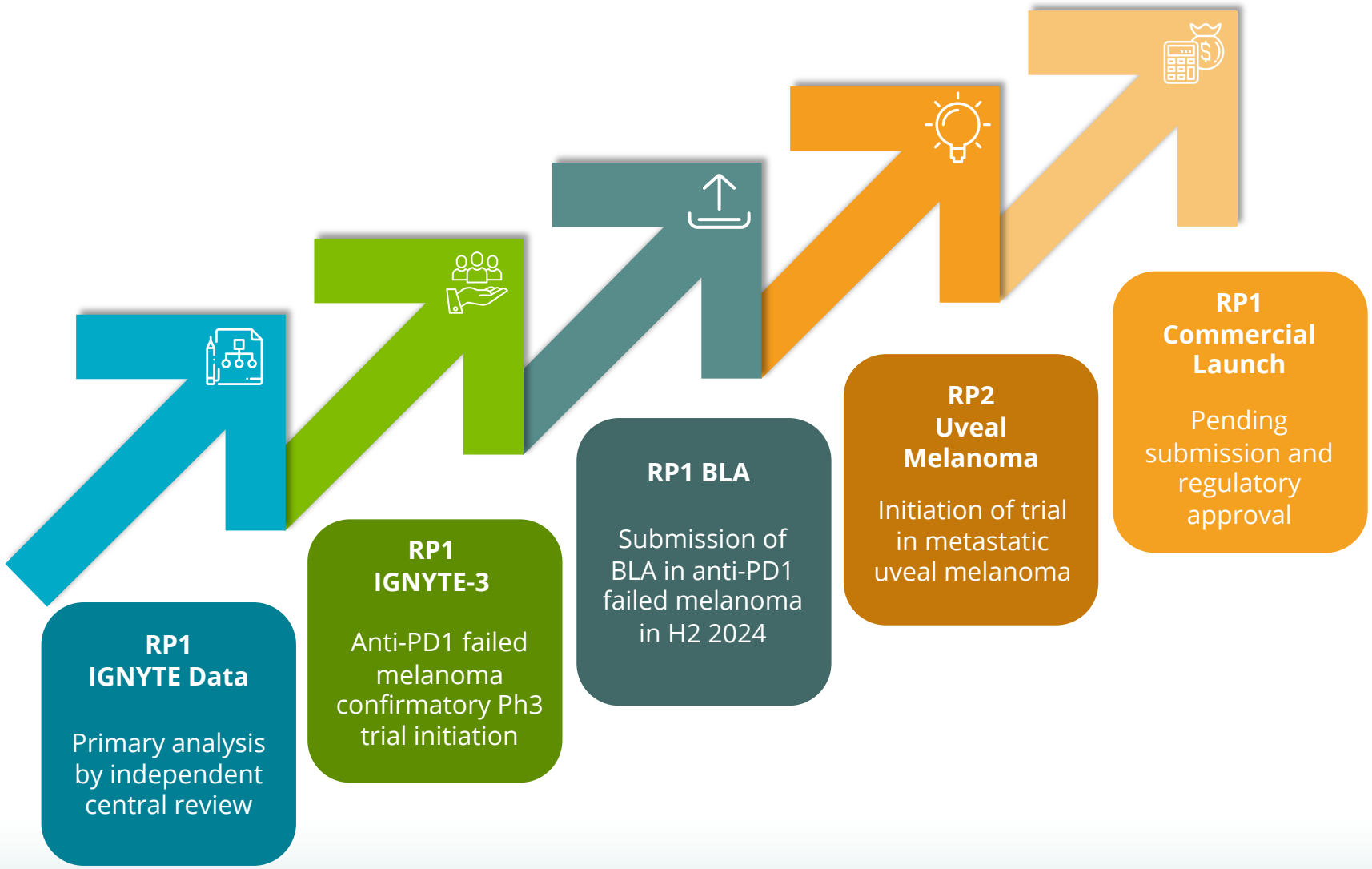
Rare Tumor Approximate Incidence Numbers

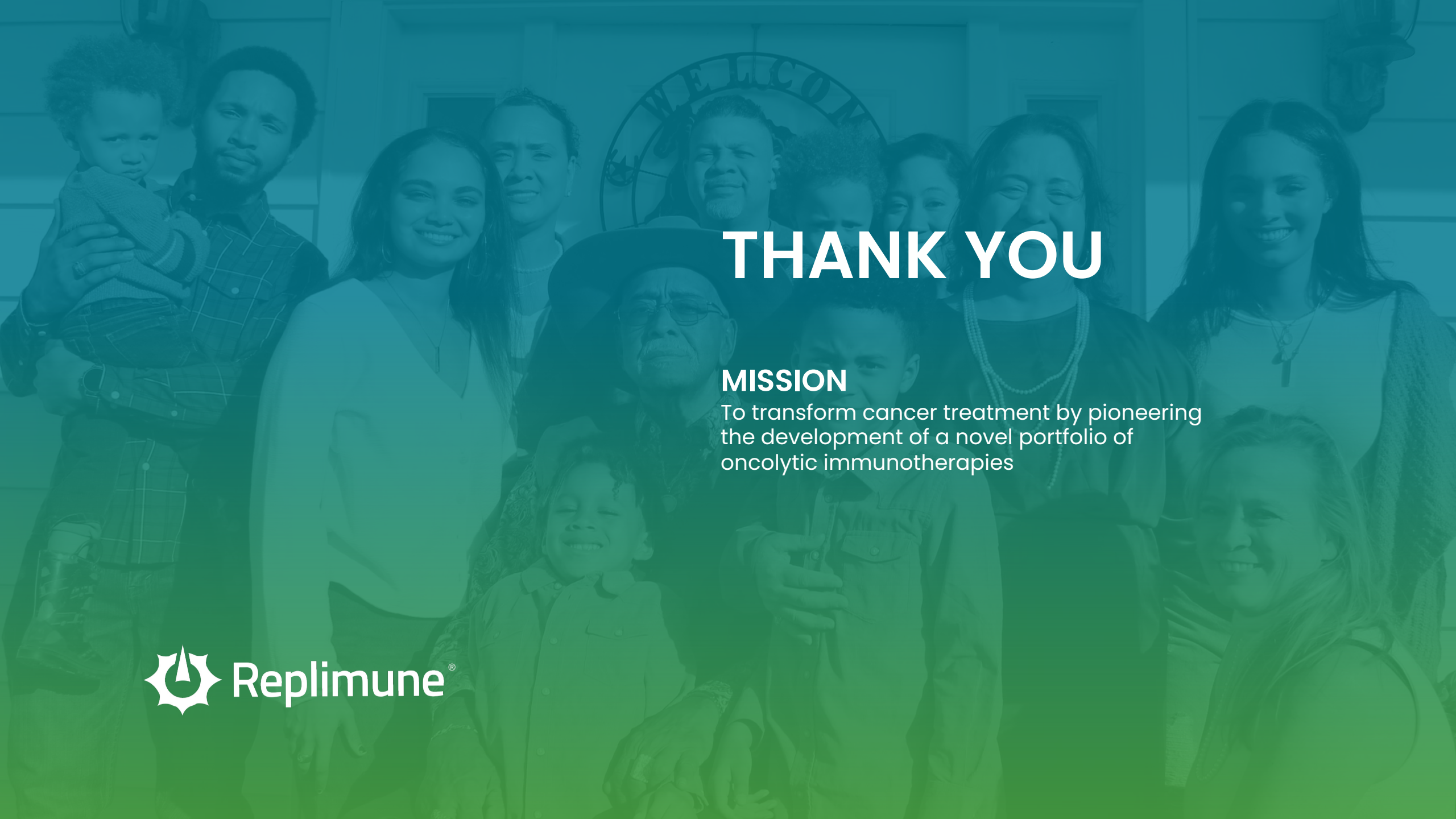
- Uveal Melanoma ~1,000 cases[2]
- Rare head and neck ~2,400 cases[2]
- Soft tissue sarcomas ~2,400 cases[2]



Source: 1) https://www.cancer.gov/pediatric-adult-rare-tumor/rare-tumors/about-rare-cancers
2) Replimune analysis based on literature review 3) Data on file

Upcoming Milestones to Drive Value





THANK YOU

MISSION

To transform cancer treatment by pioneering the development of a novel portfolio of oncolytic immunotherapies

Replimune®