Investor Day
June 24, 2025

Igniting a systemic immune response to cancer with oncolytic immunotherapy

Replimune®

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 or financial status, 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.

Agenda

10:00–10:10	**Delivering Oncolytic Immunotherapy to Patients** Sushil Patel, PhD, CEO
10:10-10:30	**Advanced Melanoma: Landscape & RP1 Opportunities** Nikhil Khushalani, MD, Moffit Cancer Center
10:30-10:50	**Interventional Radiology in Oncology Treatment** Rahul Sheth, MD, MD Anderson Cancer Center
10:50-11:10	**Poised for Commercial Success** Chris Sarchi, Chief Commercial Officer
11:15-Noon	**Fireside Chat and Q&A** Sherrif Ibrahim, MD, PhD, Rochester Dermatologic Surgery Nikhil Khushalani, MD, Moffit Cancer Center Kim Margolin, MD, PhD, Saint John's Cancer Institute Bhavesh Shah, RPh, Boston Medical Center Rahul Sheth, MD, MD Anderson Cancer Center
12:00–12:15	**RPx in Skin Cancer** Kostas Xynos, MD, Chief Medical Officer
12:10–12:30	**Treatment of Cutaneous Squamous Cell Carcinoma** Sherrif Ibrahim, MD, PhD, Rochester Dermatologic Surgery
12:30-12:45	**RPx: Following the Data** Kostas Xynos, Chief Medical Officer Nina Aragam, SVP, Portfolio Strategy & Program Management
	Q&A
	Lunch with Management and KOLs

Our Team

Sushil Patel, Ph.D.
CEO

Chris Sarchi
Chief Commercial Officer

Emily Hill
Chief Financial Officer

Kostas Xynos, MD, PhD, MBA
Chief Medical Officer

Nina Aragam
SVP, Portfolio Strategy & Program Management

Our Speakers and Panelists

Sherrif Ibrahim, MD, PhD
Dermatologist

Dermatologist, Mohs Surgeon and Owner, Rochester Dermatologic Surgery & Associate Professor, University of Rochester

Nikhil Khushalani, MD
Medical Oncologist

Vice Chair, Department of Cutaneous Oncology at Moffitt Cancer Center

Kim Margolin, MD
Medical Oncologist

Medical Director, Borstein Family Foundation Melanoma Program at Saint John's Cancer Institute

Bhavesh Shah, RPh
Pharmacist

Chief Pharmacy Officer, Hematology Oncology at Boston Medical Center

Rahul Sheth, MD
Interventional Radiologist

Associate Professor, Department of Interventional Radiology at MD Anderson Cancer Center

Delivering Oncolytic Immunotherapy to Patients

Sushil Patel, PhD
CEO, Replimune

Poised to Deliver on the Promise of Oncolytic Immunotherapy

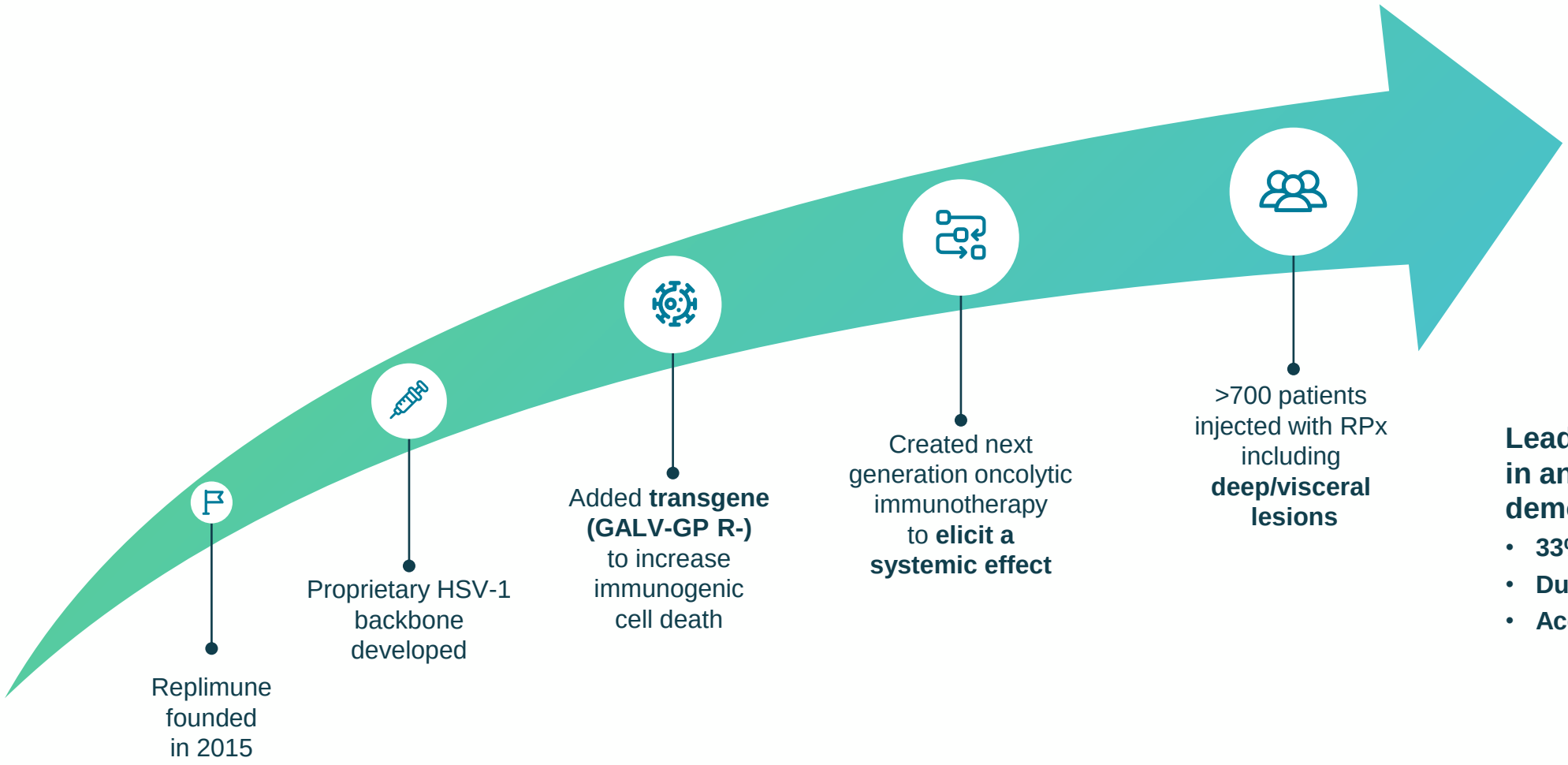
- **RP1 granted Breakthrough Therapy Designation with BLA for advanced melanoma under priority review;** July 22nd PDUFA
- **US manufacturing facility anticipated to support commercial supply** with capacity for RPx platform expansion
- **Commercial buildout complete and launch ready**
- **7 ongoing clinical trials** leveraging RPx platform assets
- **Strong financial position** with cash of $483.8 million as of March 31, 2025
- **Wholly owned, unincumbered** assets / RPx platform

U.S. Based Manufacturing for Commercialization

RPx end-to-end production and commercial benefits

- 63,000 square foot state-of-the-art facility for GMP manufacturing, packaging, and labeling in Framingham, MA
- Capacity to support global commercialization of RP1 and RP2
- Commercially attractive cost of goods & ‘off the shelf’ product

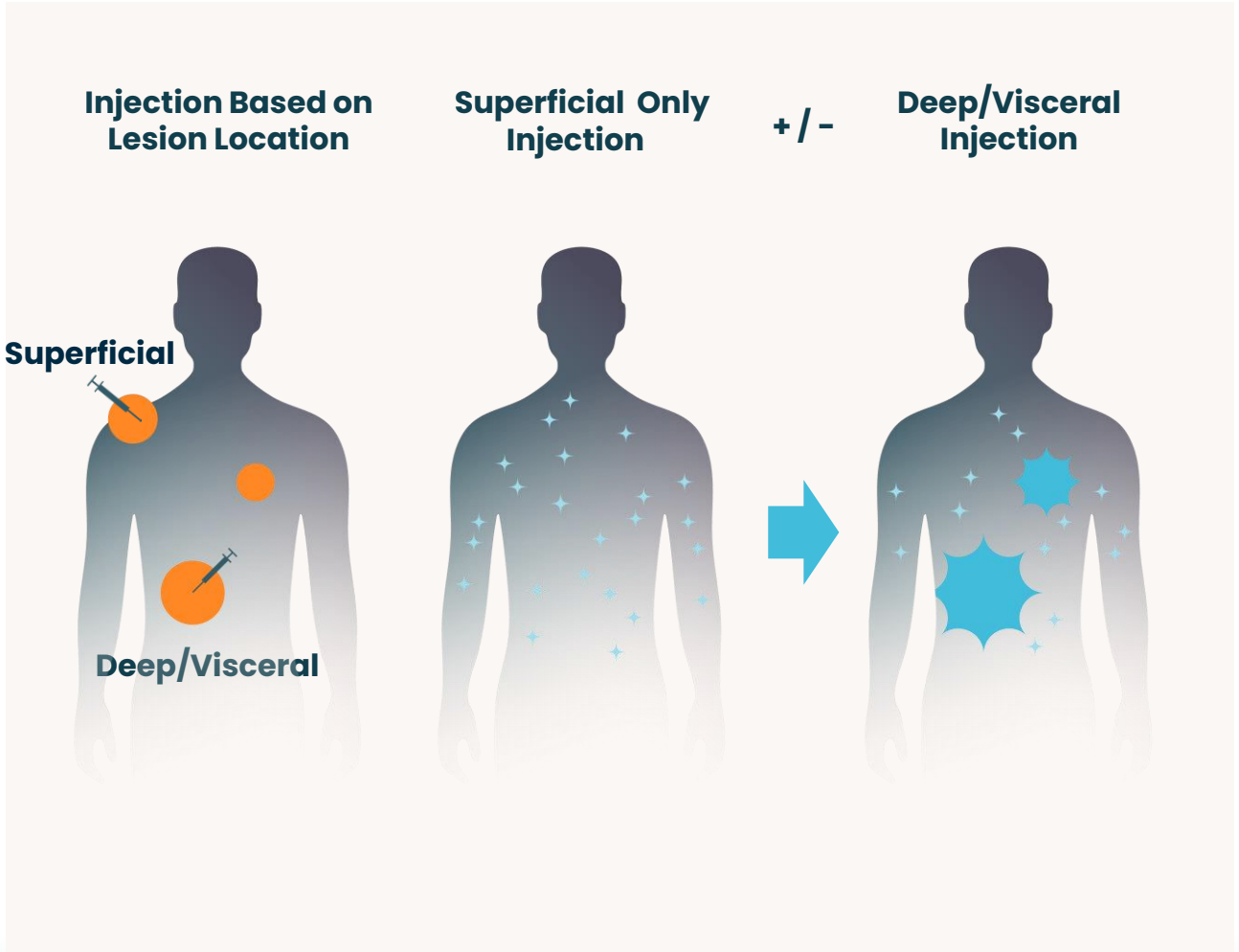
The Evolution of Oncolytic Immunotherapy



Lead asset, RP1 + nivolumab in anti-PD1 failed melanoma demonstrated:

- **33% ORR**
- **Durable response rates**
- **Acceptable safety profile**

Transforming the Cancer Treatment Paradigm: Oncolytic Immunotherapy



Therapeutic Objective

- Robust local and distant / systemic anti-tumor response
- Limit adverse events and toxicities
- Combinability and Rx synergy e.g., I-O, targeted therapies

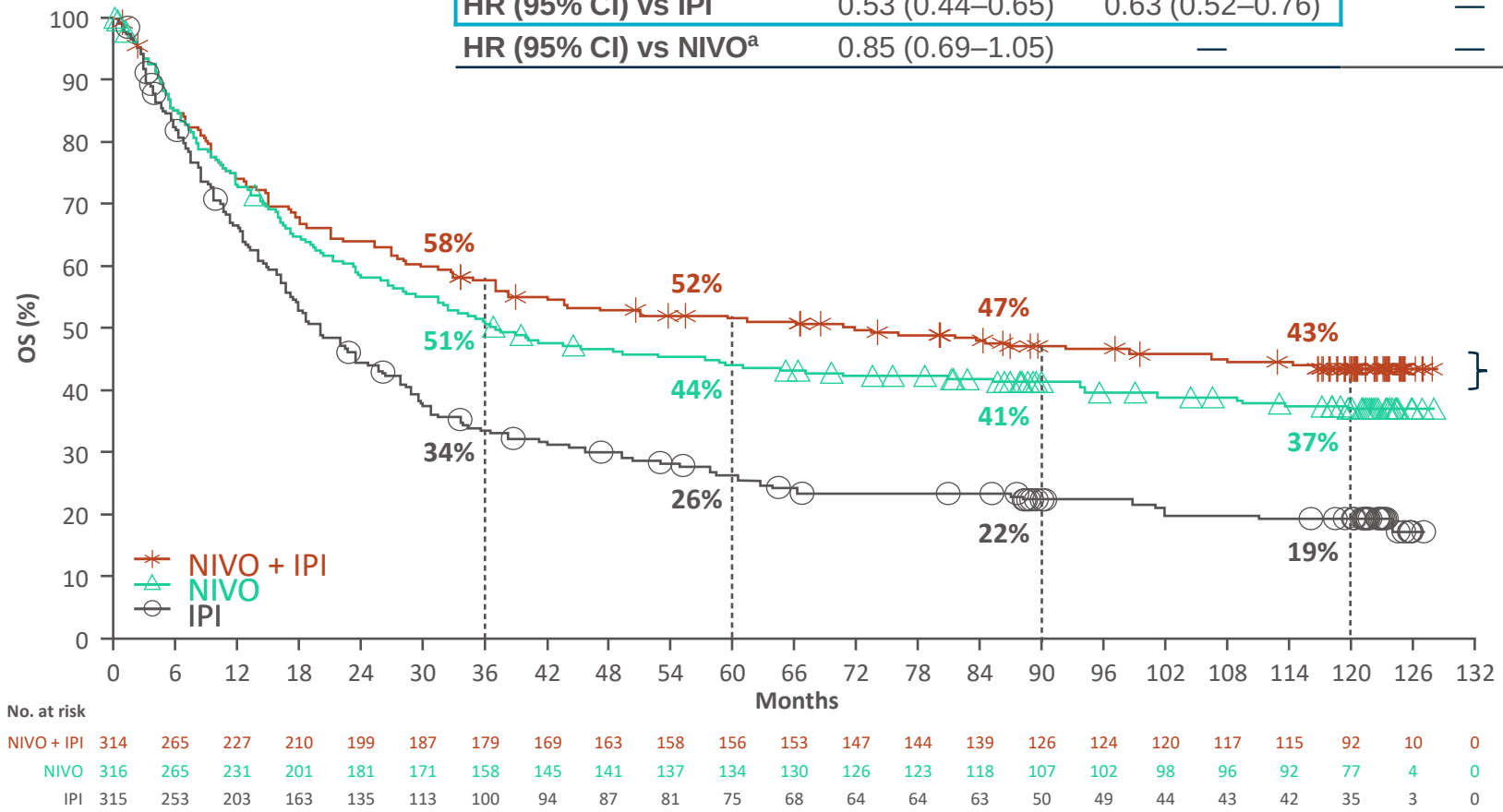
Advanced Melanoma: Landscape & RP1 Opportunities

Nikhil Khushalani, MD

Vice Chair, Department of Cutaneous Oncology, Moffit Cancer Center

Frontline Therapy in Metastatic Melanoma
Overall Survival: CheckMate 067

	NIVO + IPI (n = 314)	NIVO (n = 316)	IPI (n = 315)
Events	173	192	243
Median, mo (95% CI)	71.9 (38.2–114.4)	36.9 (28.2–58.7)	19.9 (16.8–24.6)
HR (95% CI) vs IPI	0.53 (0.44–0.65)	0.63 (0.52–0.76)	—
HR (95% CI) vs NIVO[a]	0.85 (0.69–1.05)	—	—



10-year OS analysis

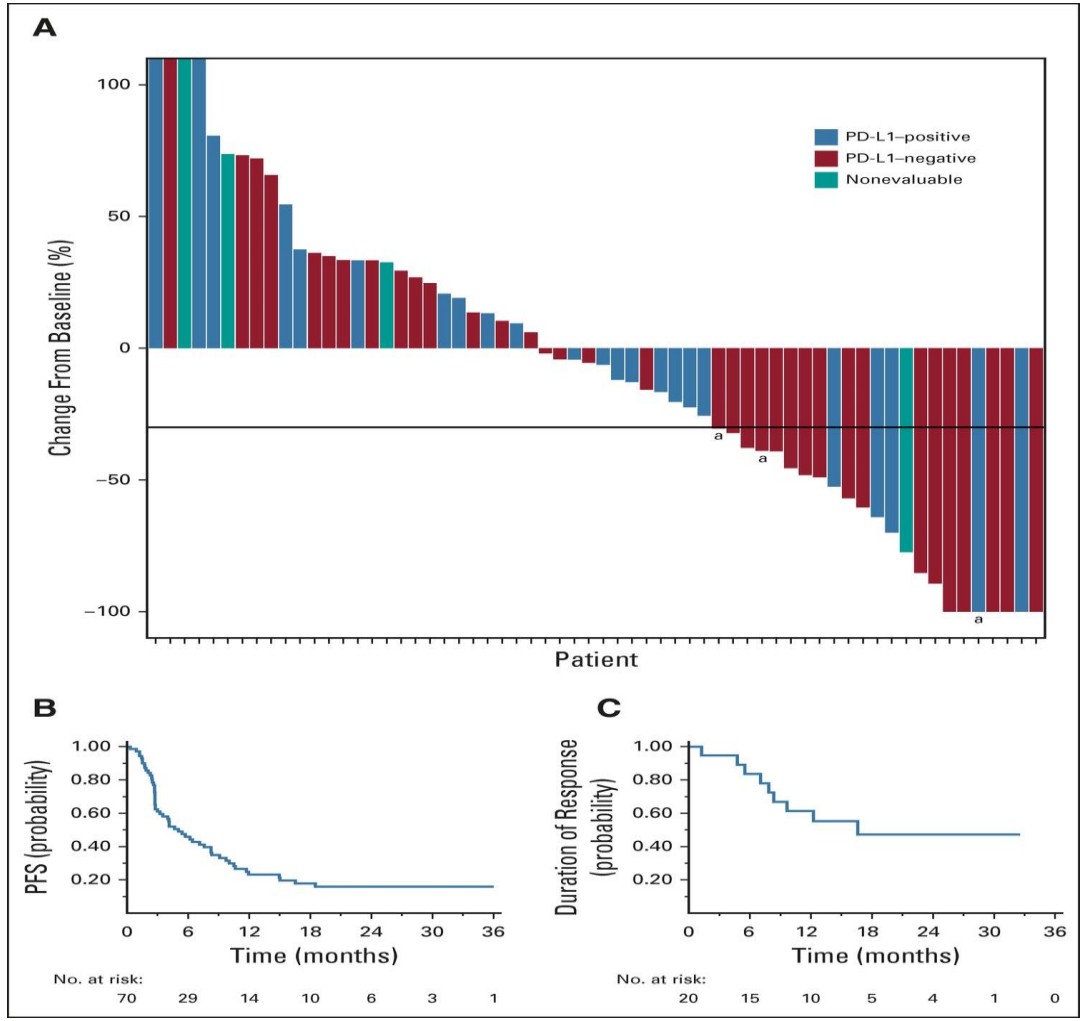
HR = 0.85[a]

(95% CI, 0.69–1.05)

[a]Descriptive comparison.

Wolchok et al. *N Engl J Med* 2025;392:11-22

Combination Anti-CTLA4 plus Anti-PD1 for Anti-PD1 Refractory Melanoma



N = 70

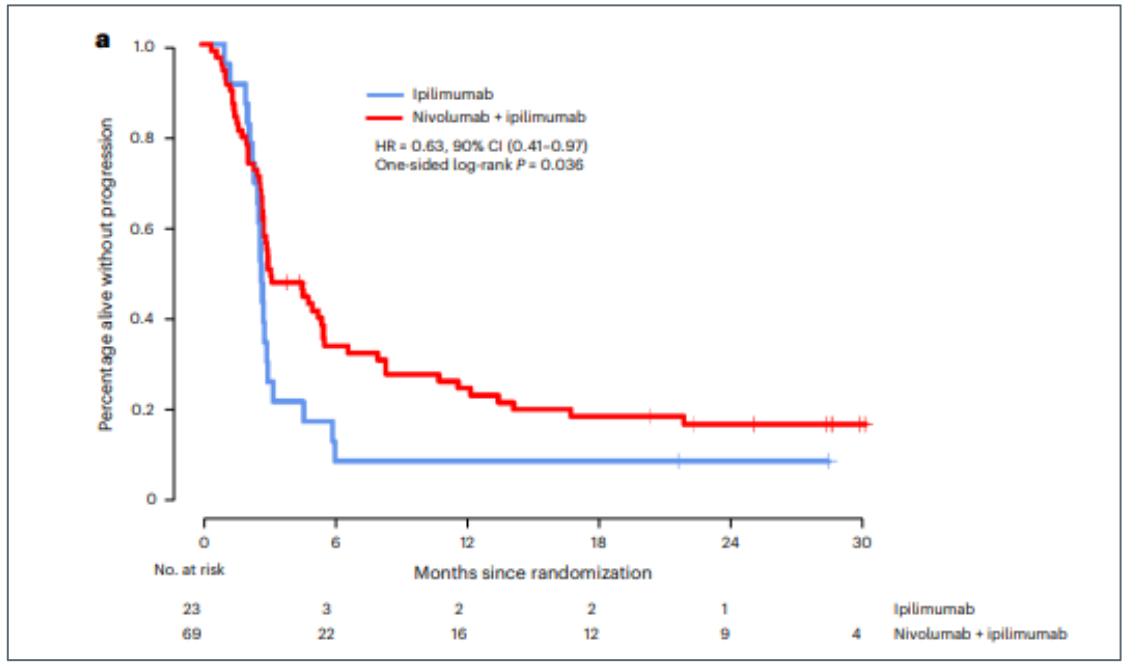
ORR: 29%

mPFS: 5 months

mOS: 24.7 months

Olson, …Khushalani*, Luke*. *J Clin Oncol* 2021;39:2647-55

Southwest Oncology Group Study S1616



	NIVO+IPI (N=69)	IPI (N=23)
Median PFS, mo (90% CI)	3.0 (2.8, 5.3)	2.7 (2.5, 2.9)
6-Month Estimate (90%CI)	34% (25%, 44%)	13% (4%,27 %)
HR (90% CI) vs. IPI	0.63 (0.41, 0.97)	--
ORR	29%	9%

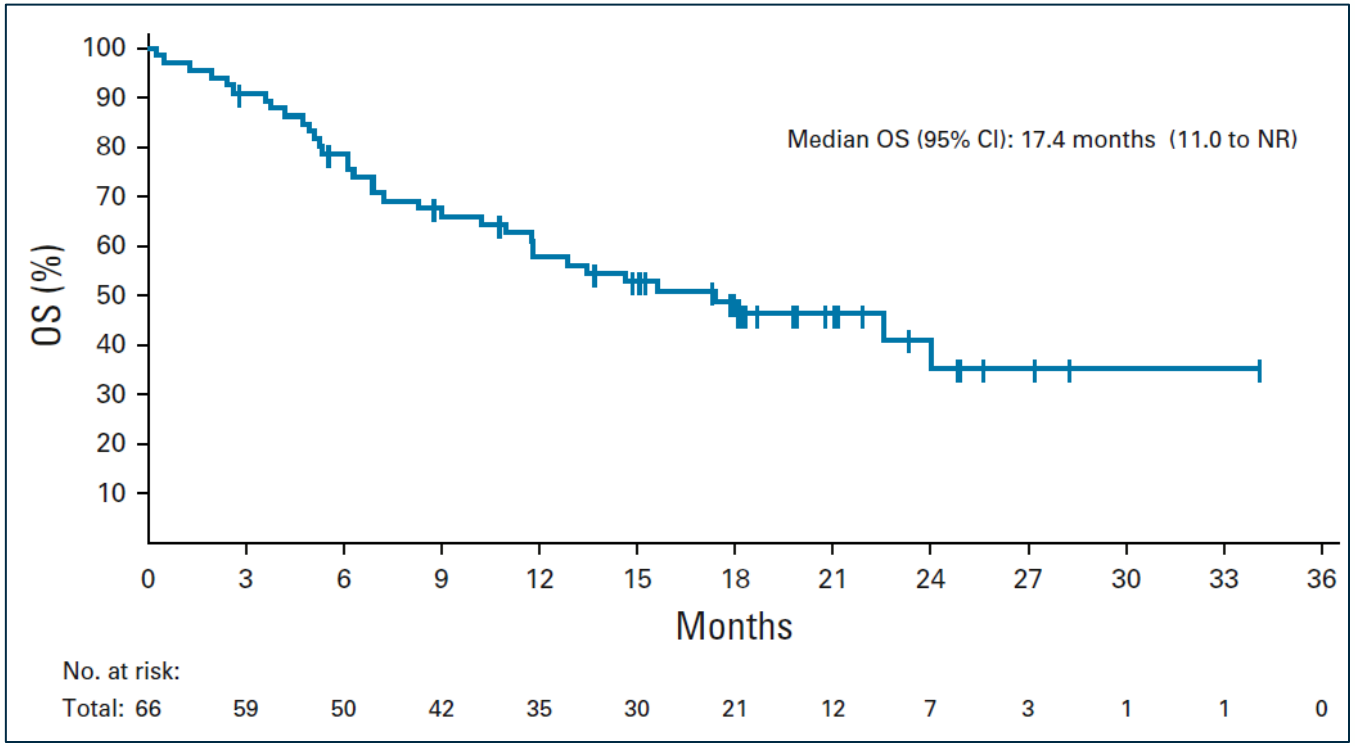
PFS was statistically significantly improved with Nivolumab + Ipilimumab compared to Ipilimumab (one-sided p-value = 0.036)

Vanderwalde, Bellasea, Kendra, Khushalani, et al. *Nature Medicine* 2023;29:2278

Tumor Infiltrating Lymphocyte Therapy (Lifileucel) in aPD-1-Refractory Metastatic Melanoma

RESPONSE	PATIENTS, N = 66 n (%)
Objective Response Rate	**24 (36.4)**
Complete Response	2 (3.0)
Partial Response	22 (33.3)
Stable Disease	29 (43.9)
Progressive Disease	9 (13.6)
Non-Evaluable*	4 (6.1)
Disease Control Rate	53 (80.3)
Median Duration of Response	**Not Reached**
Min, Max (months)	2.2, 26.9+

***NE due to not reaching first assessment.**

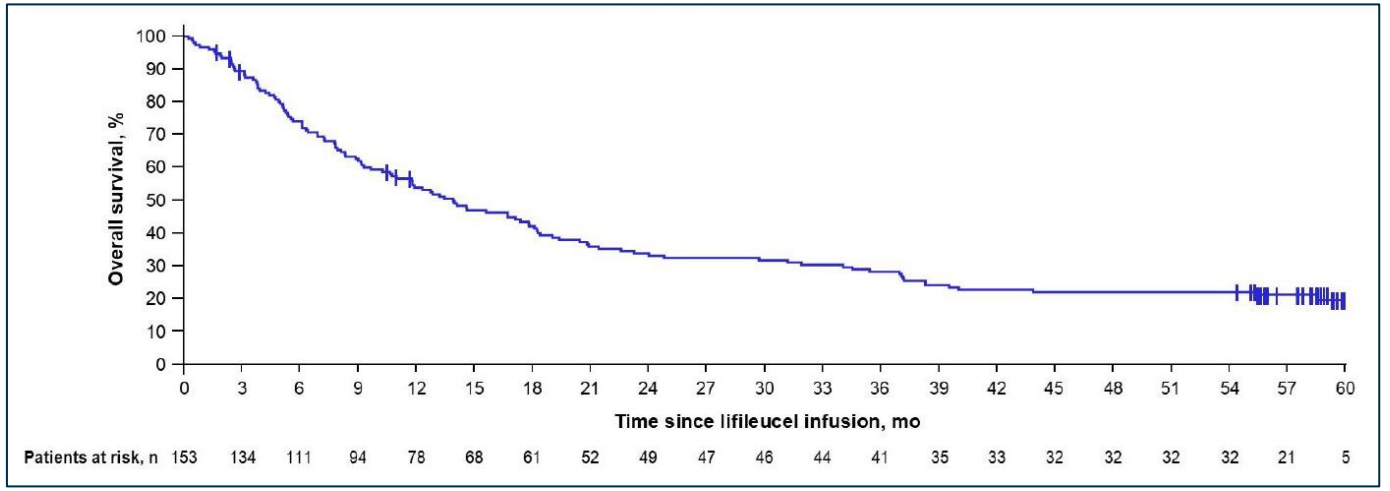


Sarnaik. Hamid, Khushalani et al. *J Clin Oncol.* 2021;39(24):2656-2666

Overall Survival with Lifileucel in aPD-1-Refractory Metastatic Melanoma

Five-year Outcomes (ASCO 2025)

- ORR 31.4% (CR, 5.9%)
- Median duration of response: 36.5m (95% CI, 8.3-NR)
- 31.3% responses ongoing at 5 years
- Median OS 13.9m
- Estimated 5-year OS: 19.7%



Sarnaik. Hamid, Khushalani et al. *J Clin Oncol.* 2021;39(24):2656-2666
Medina et al. *ASCO Annual Meeting* 2025, Abstract 9515
Medina et al. *J Clin Oncol.* 2025;epub June 02, 2025

Summary of Immune Therapy Options for Refractory Disease (BRAF non-mutant)

1L	2L Options	ORR	Gr 3/4 AEs
Anti-PD1	Anti-PD1 +Anti-CTLA4[1]	28%	56%
Anti-PD1+/- Anti-CTLA4	aPD1/aLAG[2] or Lifileucel[3]	12% 31%	13% >75%
Anti-PD1+Anti-LAG3	Anti-PD1+ Anti-CTLA4[4] or Lifileucel[3]	11% 31%	N/A* >75%

[1]Vanderwalde AM, Nature Medicine 2023 (SWOG S1616)
[2]Ascierto P, JCO 2023; (RELATIVITY-020)
[3]Amtagvi (lifileucel) prescription information
[4]Menzies et al. N Engl J Med. 2022;386:17
*Data no described in ref #4

Significant Unmet Need for Melanoma Patients that Progress on PD-1 Containing Regimens

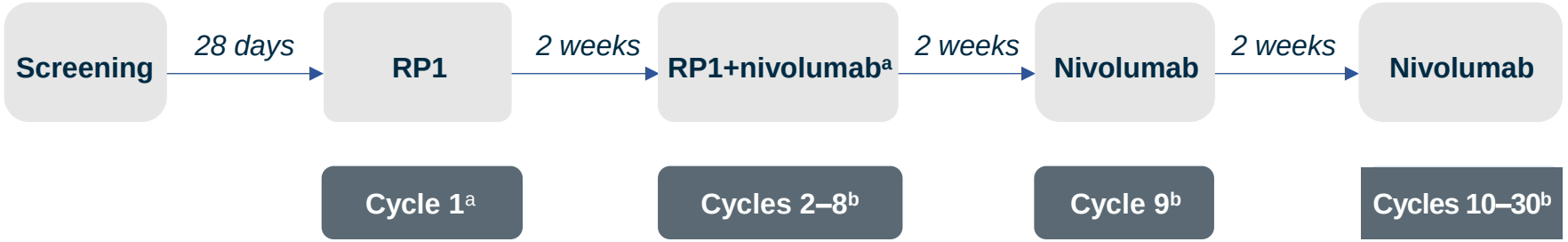
- There are limited treatment options for patients with anti–PD-1– progressed melanoma[1,2]
- Responses to targeted anti–BRAF + MEK for BRAF-mutant melanoma are usually not durable[3]
- Single-agent anti–PD-1 after confirmed progressive disease on anti–PD-1 yields a 6%–7% response rate[4,5]
- Nivolumab + ipilimumab is a potential option[2], but toxicity is high[2,6]
- Nivolumab + anti–LAG-3 offers sub-optimal efficacy[7]
- TIL therapy gives response rates of ~30%,[8] but most patients have grade 3-4 toxicity[9,10]

LAG-3, lymphocyte activation gene 3; PD-1, programmed cell death protein 1; TIL, tumor-infiltrating lymphocyte. 1. Mooradian MJ, et al. Oncology. 2019;33(4):141-8. 2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Melanoma: Cutaneous. Version 2. 2024. 3. Dixon-Douglas JR, et al. Curr Oncol Rep. 2022;24(8):1071-9. 4. Beaver JA, et al. Lancet Oncol. 2018;19(2):229-39. 5. Ribas A, et al. Lancet Oncol. 2018;19(5):e219. 6. Pires da Silva I, et al. Lancet Oncol. 2021;22(6):836-47. 7. Ascierto PA, et al. J Clin Oncol. 2023;41(15)2724-35. 8. Chesney J, et al. J Immunother Cancer. 2022;10(12):e005755. 9. US Food and Drug Administration. BLA clinical review and evaluation - AMTAGVI. BLA 125773. Updated February 6, 2024. Accessed May 31, 2024. https://www.fda.gov/media/176951/download. 10. Sarnaik AA, et al. J Clin Oncol. 2021;39(24):2656-66.

IGNYTE Study Anti-PD1 Failed Melanoma Cohort

Anti–PD1 failed melanoma cohort

(140 pts; 16 pts treated in prior cohorts: Total=156)



Primary objectives

- Safety and tolerability
- Efficacy by ORR using modified RECIST 1.1 criteria

Secondary objective

DOR, CR rate, DCR, PFS, by central & investigator review, ORR by investigator review, and 1-year and 2-year OS

Key eligibility criteria

***Confirmed progression* while *on* prior anti-PD1 therapy[c]**

At least 8 weeks of prior anti–PD1, confirmed progression while on anti–PD1; anti–PD1 must be the last therapy before clinical trial. Patients on prior adjuvant therapy must have progressed while on prior adjuvant treatment.

N = 27 sites

N = 26 sites

Primary analysis conducted when all patients have ≥ 12 months follow up

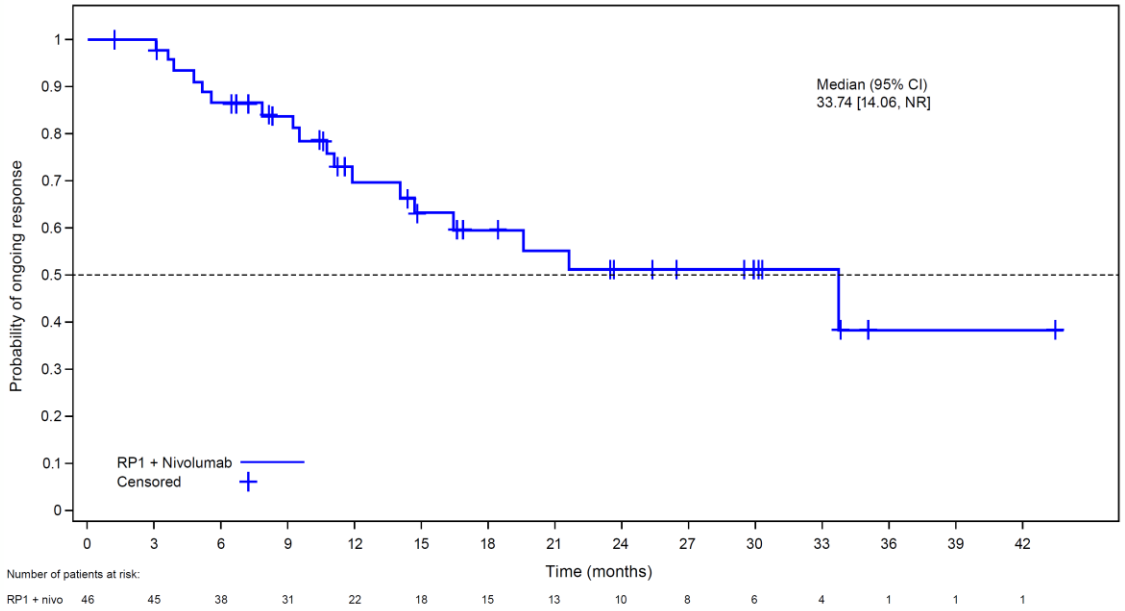
RP1 plus Nivolumab Delivers Consistent Responses Across Anti-PD1 Failed Melanoma Subgroups Independent of PD-L1 Expression

BOR n (%)	All patients (N = 140)	Prior Single-agent anti–PD-1 (n = 75)	Prior Anti–PD-1/ CTLA-4 (n = 65)	Stage IIIb–IVa (n = 72)	Stage IVb–IVd (n = 68)	Primary resistance (n = 92)	Secondary resistance (n = 48[a])	Prior Anti–PD-1 adjuvant (n = 36)	Prior Anti–PD-1 not adjuvant (n = 104)	PD-L1 ≥1% (n = 44)	PD-L1 <1% or N/A or Missing (n = 96)
CR	21 (15.0)	16 (21.3)	5 (7.7)	17 (23.6)	4 (5.9)	16 (17.4)	5 (10.4)	11 (30.6)	10 (9.6)	-	-
PR	25 (17.9)	13 (17.3)	12 (18.5)	12 (16.7)	13 (19.1)	16 (17.4)	9 (18.8)	5 (13.9)	20 (19.2)	-	-
SD	31 (21.1)	16 (21.3)	15 (23.1)	17 (23.6)	14 (20.6)	15 (16.3)	16 (33.3)	8 (22.2)	23 (22.1)	-	-
PD	54 (38.6)	28 (37.3)	26 (40)	25 (34.7)	29 (42.6)	39 (33.7)	15 (31.3)	11 (30.6)	43 (41.3)	-	-
ORR	**46 (32.9)**	**29 (38.7)**	**17 (26.2)**	**29 (40.3)**	**17 (25)**	**32 (34.8)**	**14 (29.2)**	**16 (44.4)**	**30 (28.8)**	**23 (52.7)**	**24 (25)**

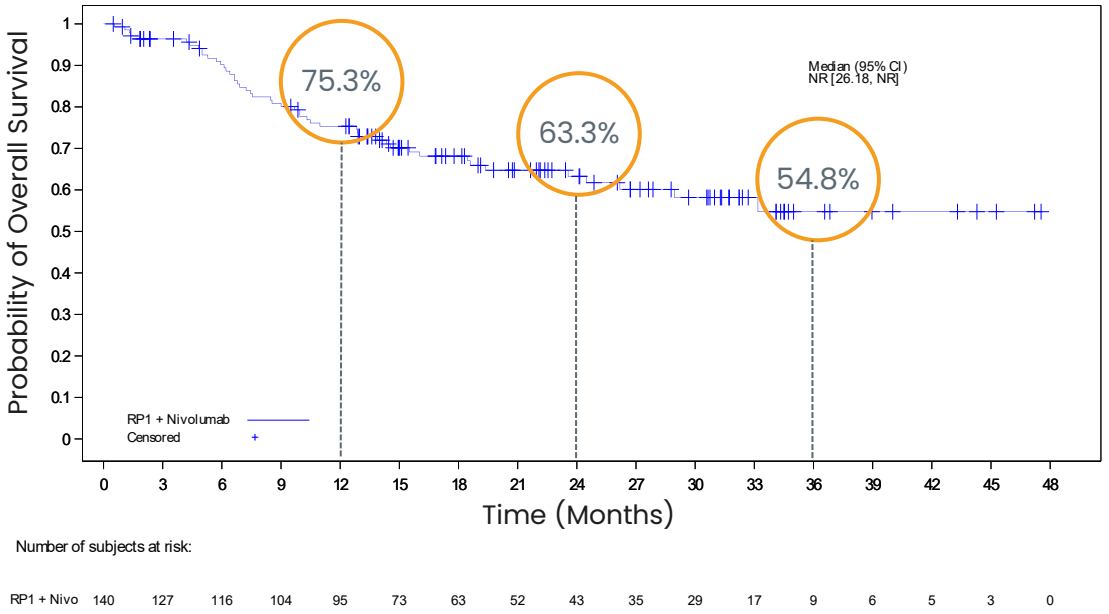
RECIST v1.1. IGNYTE Primary Analysis. BOR, best overall response; CR, complete response; CTLA-4, cytotoxic T-lymphocyte antigen 4; ORR, objective response rate; PD, progressive disease; PD-1, programmed cell death protein 1; PR, partial response; SD, stable disease. Median follow-up = 15.5 mos (0.5 – 47.5 mos)

Durable Responses Translate to Promising Overall Survival

Median Duration of Response - 33.7 months



Overall Survival - Not Reached



RECIST v1.1. IGNYTE Primary Analysis.

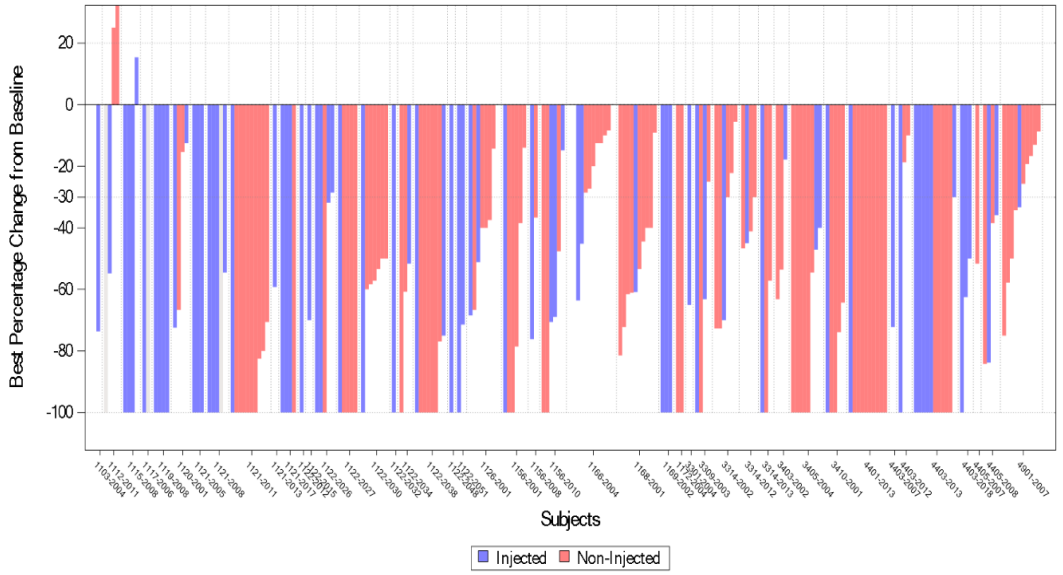
Systemic Benefit with Deep Responses in Visceral Lesions

Anti-tumor effect on non-injected visceral lesions*

Location of visceral lesions	n** (Lesions)	Any Reduction	>0% to <30%	≥30% to <100%	100%
Lung	**29**	**28 (96.6)**	**7 (24.1)**	**9 (31.0)**	**12 (41.4)**
Liver	**14**	**14 (100)**	**3 (21.4)**	**5 (35.7)**	**6 (42.9)**
Spleen	6	5 (83.3)	5 (83.3)	0	0
Pleura	2	2 (100)	0	1 (50.0)	1 (50.0)
Brain	1	1 (100)	1 (100)	0	0
Total	**52**	**50 (96.2)**	**16 (30.8)**	**15 (28.8)**	**19 (36.5)**

- 96.2% reduction in lesions from baseline

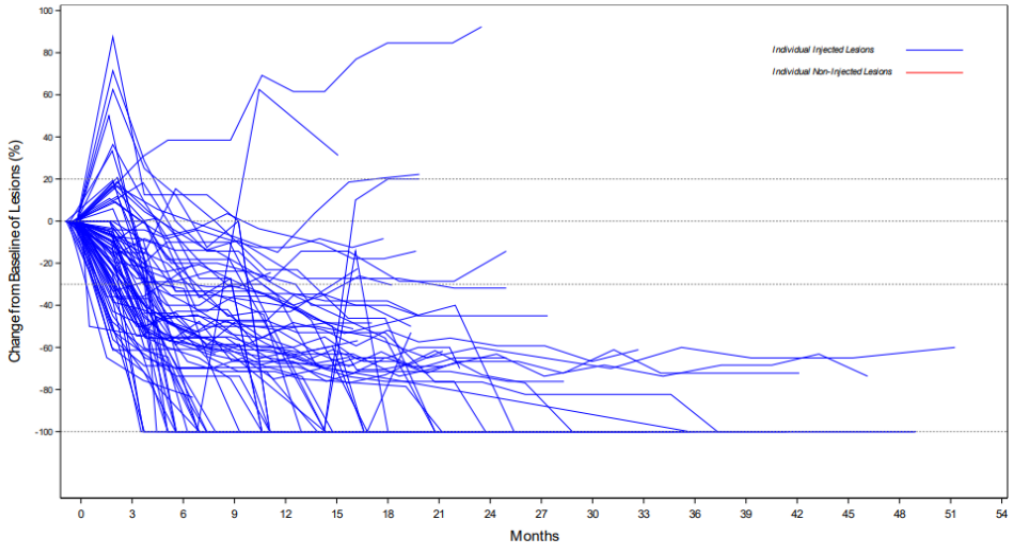
Responses in injected and non-injected lesions*



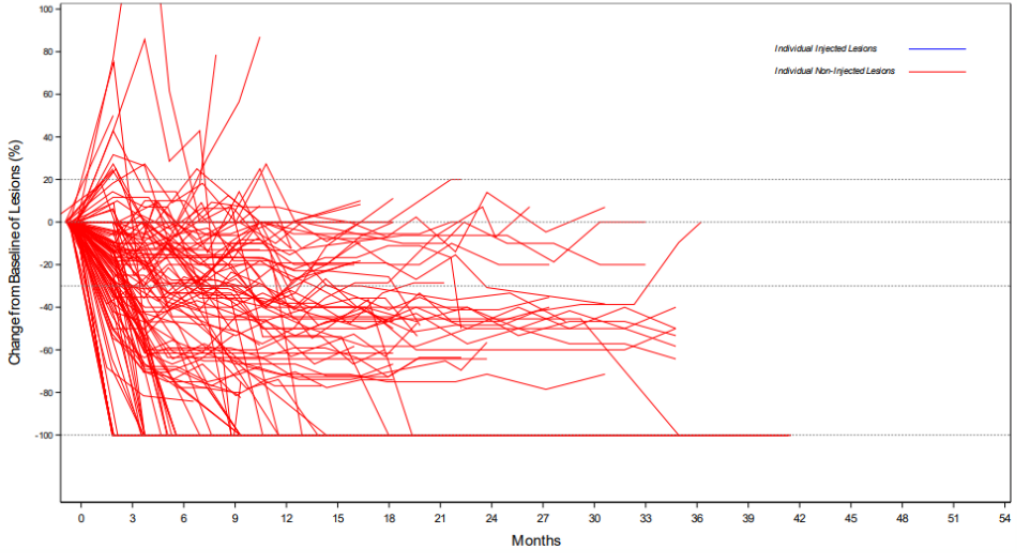
RECIST v1.1, IGNYTE Primary Analysis. *Responding patients (n=47), **Includes 6 new lesions that appeared while on study

Kinetics and Degree of Response is Similar in Both Injected and Non-Injected Lesions in Responders

Injected lesions



Non-injected lesions



- Responses are driven not only by the reduction of injected lesion but also by the reduction of the non-injected lesions

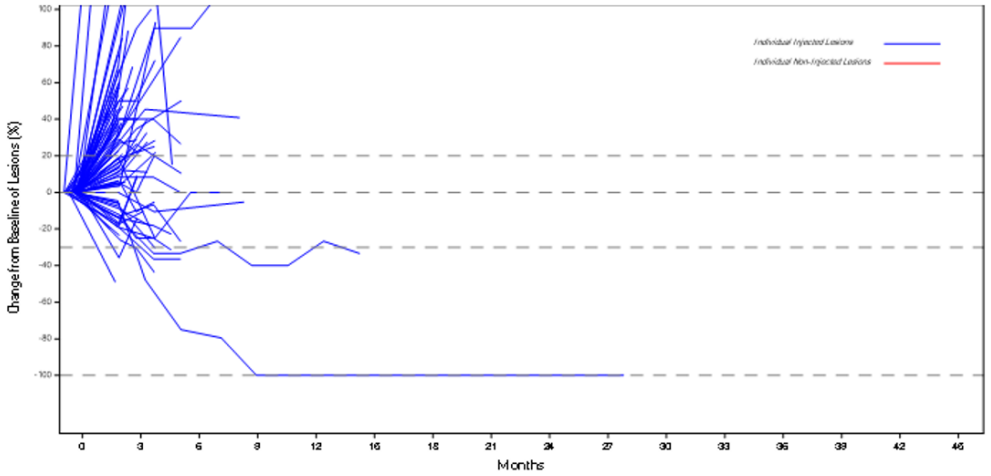
Data on file

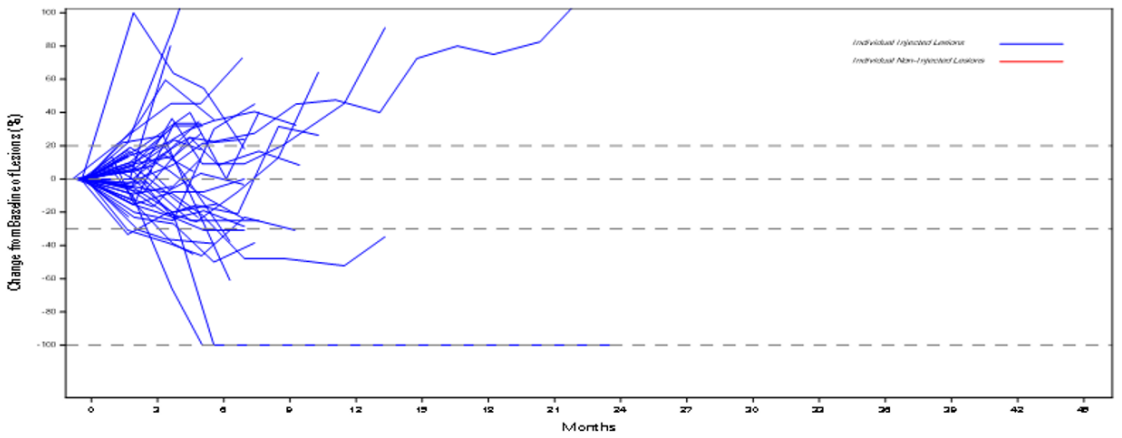
Non-Responders (PD/SD) also Demonstrated Some Lesion Reduction in Both Injected and Non-Injected Lesions

Progressive Disease (PD)

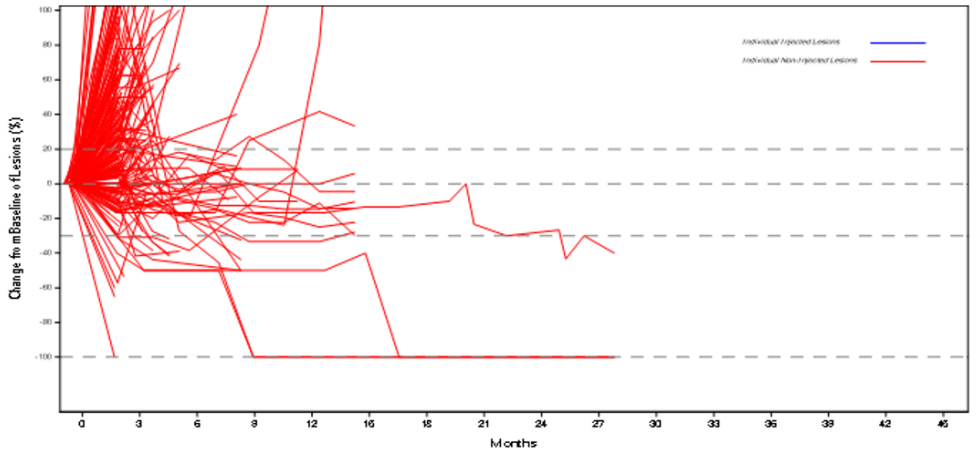
Stable Disease

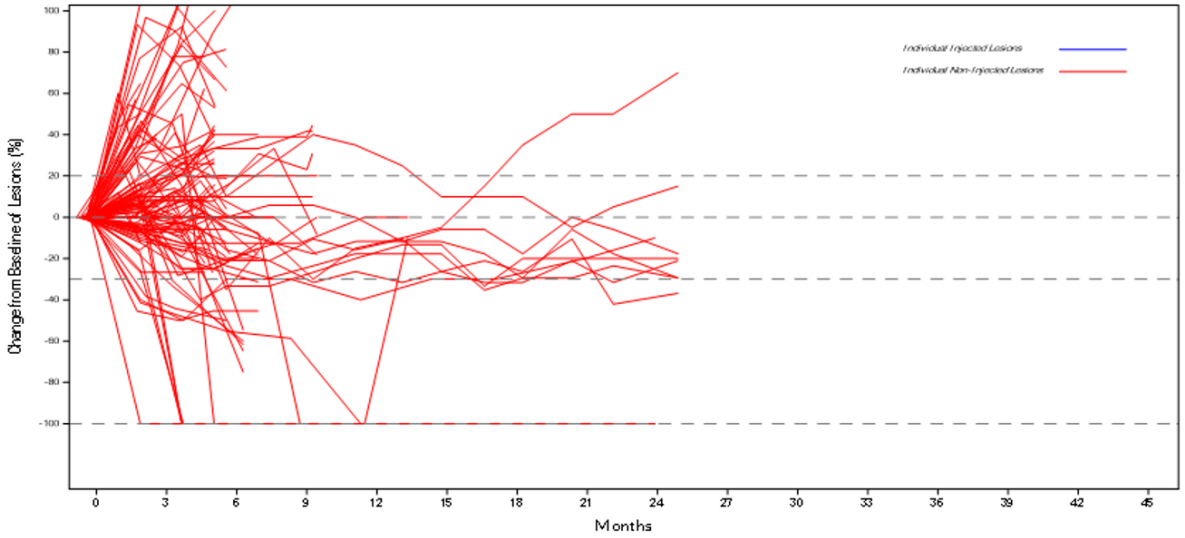
Injected lesions





Non-injected lesions





Data on file

Numerically Higher Response Rate with Deep/Visceral (± superficial) Injections vs. Superficial Injections alone

Efficacy by injection type by BICR using RECIST 1.1 (patient-level data)

Confirmed BOR, n (%)	Total (N = 140)	Superficial only (n = 104)	Deep/visceral ± superficial (n = 36)	
			Deep/ visceral plus superficial (n = 14)	Deep/ visceral only (n = 22)
CR	21 (15.0)	18 (17.3)	0	3 (13.6)
PR	25 (17.9)	13 (12.5)	6 (42.9)	6 (27.3)
SD	31 (22.1)	19 (18.3)	4 (28.6)	8 (36.4)
PD	54 (38.6)	46 (44.2)	3 (21.4)	5 (22.7)
ORR	**46 (32.9)**	**31 (29.8)**	**6 (42.9)**	**9 (40.9)**

Eight (7.7%) patients in the superficial only group and 1 (7.1%) patient in the deep/visceral plus superficial group were not evaluable (discontinued prior to the first efficacy assessment).

In GK et al. ASCO 2025. Abstract 9547. Poster 20.

BICR, blinded independent central review; BOR, best overall response; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

Favorable Safety Profile of RP1 + Nivolumab (All Patients)

Preferred term, n (%)	TRAEs occurring in ≥5% of patients (N = 141)	
	All Grades	Grade 3-4
≥1 TRAE	**126 (89.4)**	**18 (12.8)**
Fatigue	46 (32.6)	1 (0.7)
Chills	45 (31.9)	0 (0.0)
Pyrexia	43 (30.5)	0 (0.0)
Nausea	31 (22.0)	0 (0.0)
Influenza-like illness	25 (17.7)	0 (0.0)
Injection-site pain	21 (14.9)	0 (0.0)
Diarrhoea	20 (14.2)	1 (0.7)
Vomiting	19 (13.5)	0 (0.0)
Headache	18 (12.8)	0 (0.0)
Pruritus	18 (12.8)	0 (0.0)
Asthenia	14 (9.9)	1 (0.7)
Arthralgia	10 (7.1)	1 (0.7)
Decreased appetite	9 (6.4)	1 (0.7)
Myalgia	9 (6.4)	0 (0.0)
Cough	8 (5.7)	0 (0.0)
Rash	8 (5.7)	0 (0.0)
Injection-site reaction	7 (5.0)	0 (0.0)
Vitiligo	7 (5.0)	0 (0.0)

- Predominantly grade 1 and 2 constitutional-type side effects
- Low incidence of grade 3 events (none occurring in >5% of patients); five grade 4 events in total
- No grade 5 events
- Safety was also acceptable for repeated deep/visceral injections (mostly similar toxicities to the overall population)

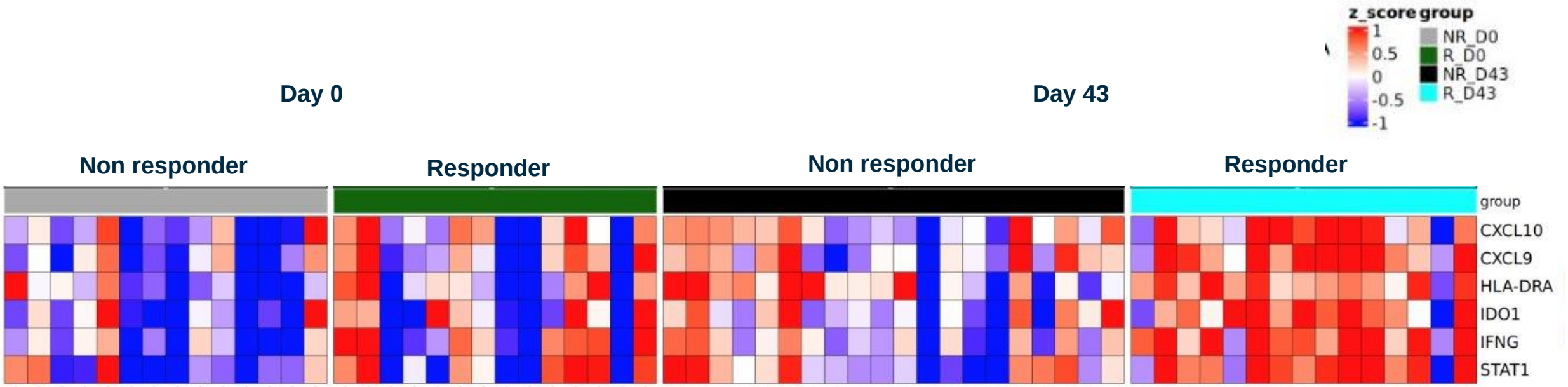
Additional grade 3/4 TRAEs (grade 4 italicized)**:**

Two events each (1.4%): Hypophysitis, rash maculo-popular

One event each (0.7%): Abdominal pain, acute left ventricular failure, amylase increased, cancer pain, *cytokine release syndrome*, eczema, enterocolitis, extranodal marginal zone B-cell lymphoma (MALT type), *hepatic cytolysis*, hyponatraemia, immune-mediated enterocolitis, infusion-related reaction, left ventricular dysfunction, *lipase increased*, memory impairment, meningitis aseptic, muscular weakness, *myocarditis*, palmar-plantar erythrodysaesthesia syndrome, paraesthesia, peripheral sensory neuropathy, radiculitis brachial, sinus arrhythmia, *splenic rupture*, tricuspid valve incompetence, tumor pain, type 1 diabetes mellitus

Data presented at ESMO 2024, SITC 2024

RP1 plus Nivolumab Increases Interferon Gamma Signature from Day 1 to Day 43

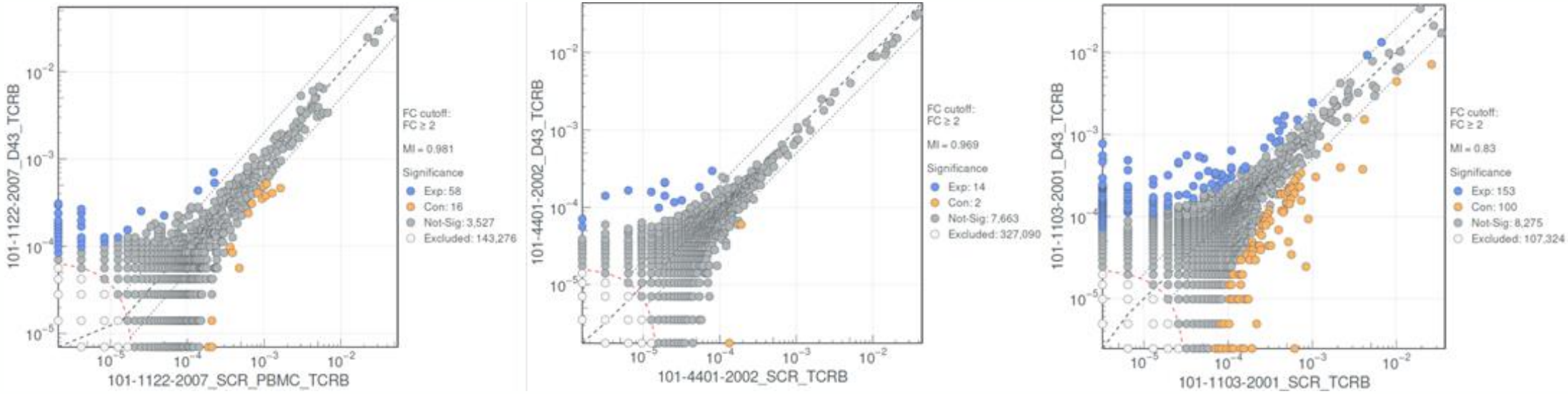


- Increase in expression of genes related to interferon gamma signature in responders suggests the ability of RP1+nivolumab to convert an immunologically silent to an immune inflamed tumor microenvironment and potentially drive responses to further nivolumab treatment

Gene signature scores were computed as the unweighted average of the log10 normalized expression with +1 pseudocounts. The log10 transformation was chosen to follow Ayers, et al, 2017.

Data on file

Expansion and Generation of T-Cell Clones Post RP1 + Nivolumab Demonstrates Systemic Activity



- Many of the expanded clones (range 20-80%) are newly detected at Day 43, suggesting that treatment not only expanded existing T cell clones but generated new T cell clones.
- A particularly striking expansion of T cell clones (n=170) was observed for melanoma pt (101-1103-2001) with an ongoing complete response.

Key Takeaways

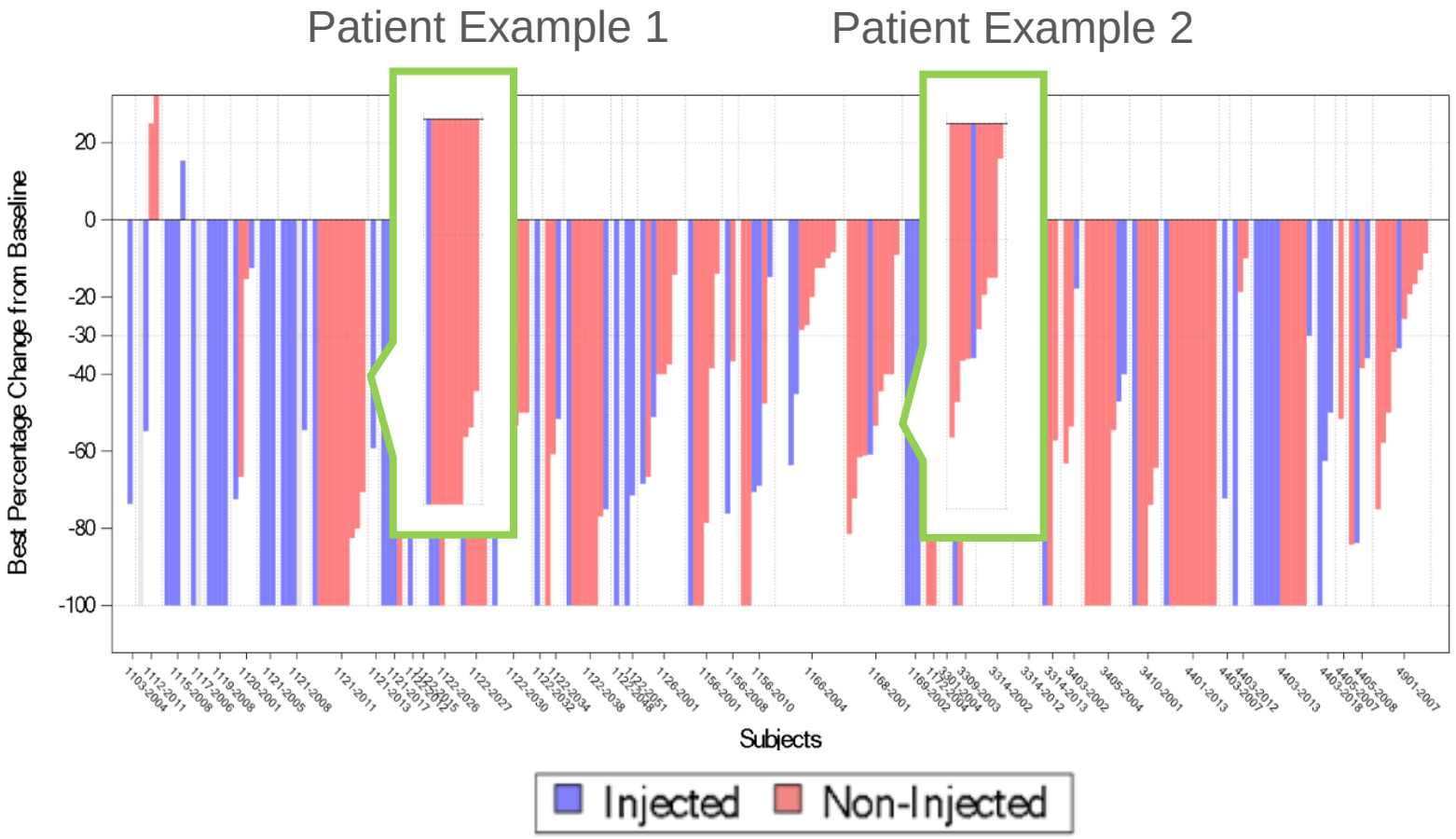
- ORR=32.9, mDoR =33.7 (RECIST 1.1)
    - Consistent responses across major subgroups, (e.g. ipi/nivo failed patients, patients with primary resistance, PD-L1 negative patients)
- In responders, responses in non-injected lesions (including in the viscera) occurred with a similar frequency and depth as injected lesions indicating systemic benefit
- Patients with deep/visceral (+/- superficial) injections had numerically higher response rates vs. those who received superficial injections only
- Favorable safety profile with a low incidence of Grade 3/4 events
    - Superficial and deep lesions can be safely and repeatably injected
- RP1 + nivolumab is able to expand existing T-cell clones and generate new ones and changes the TME
    - Differential gene expression signatures from Day 0 to Day 43 in responders vs. non responders suggests the ability for the treatment to create a more inflamed TME
    - Expansion & generation of T-Cell clones post RP1 + nivolumab provides further evidence of systemic anti-tumor activity

Interventional Radiology in Oncology Treatment

Rahul Sheth, MD

Associate Professor, Department of Interventional Radiology at MD Anderson Cancer Center

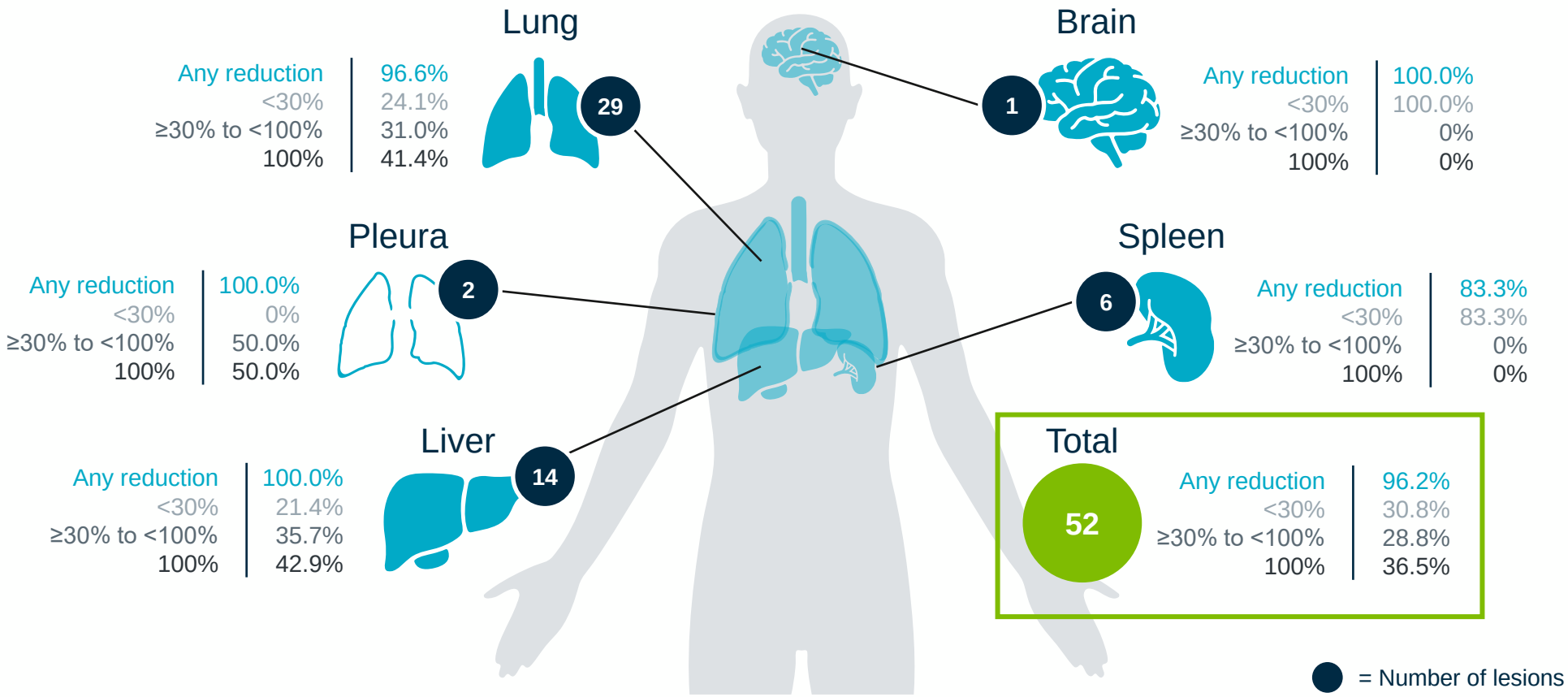
Responses in Injected and Non-Injected Lesions



- Responses not driven by injected lesions alone
  - Injected and non-injected lesions responded with similar frequency, depth and duration
  - Tumor reduction seen in 50 out of 52 non-injected visceral organ lesions

All measurable lesions (10 max if >10 were present) measured by central review for each patient with a best response of confirmed CR or PR. Central reviewers were blinded to lesion injection status. RECIST v1.1, IGNYTE Primary Analysis. * Responding patients (n=47), **Includes 6 new lesions that appeared while on study

Responses in Non-Injected Visceral Lesions



Deep responses to RP1 plus nivolumab treatment were observed in non-injected visceral lesions

In GK et al. ASCO 2025. Abstract 9547. Poster 20.

Safety in Superficial and/or Deep/Visceral Injections

- Patients with deep/visceral (with or without superficial) injections experienced a numerically higher incidence of chills, influenza-like illness, and injection-site pain treatment-related adverse events compared with patients who received superficial injections only
- Other adverse events were comparable between the 2 groups

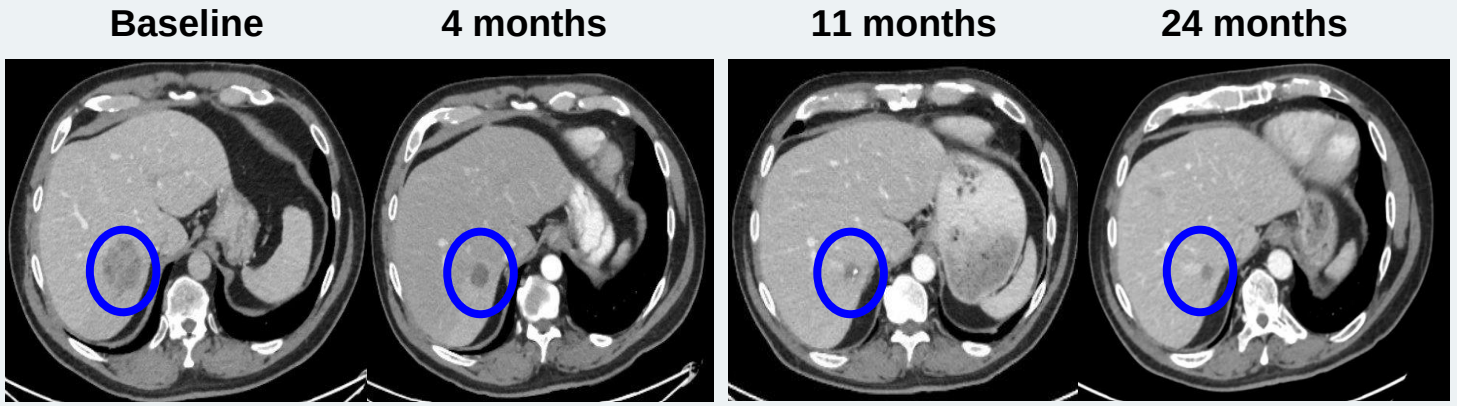
Safety by injection type (most common TRAEs related to RP1 or nivolumab)

TRAEs, n (%)	Superficial only (n = 104)		Deep/visceral ± superficial (n = 36)			
			Deep/visceral plus superficial (n = 14)		Deep/visceral only (n = 22)	
	All grades	Grades 3/4	All grades	Grades 3/4	All grades	Grades 3/4
Total	93 (89.4)	15 (14.4)	12 (85.7)	2 (14.3)	21 (95.5)	1 (4.5)
Fatigue	33 (31.7)	1 (1.0)	6 (42.9)	0	7 (31.8)	0
Pyrexia	31 (29.8)	0	3 (21.4)	0	9 (40.9)	0
Chills	30 (28.8)	0	5 (35.7)	0	10 (45.5)	0
Nausea	22 (21.2)	0	3 (21.4)	0	6 (27.3)	0
Diarrhea	14 (13.5)	1 (1.0)	2 (14.3)	0	4 (18.2)	0
Vomiting	14 (13.5)	0	1 (7.1)	0	4 (18.2)	0
Headache	13 (12.5)	0	1 (7.1)	0	4 (18.2)	0
Influenza-like illness	13 (12.5)	0	2 (14.3)	0	10 (45.5)	0
Injection-site pain	13 (12.5)	0	3 (21.4)	0	5 (22.7)	0

In GK et al. ASCO 2025. Abstract 9547. Poster 20.

RP1 Injections into Liver have a Tolerable Safety Profile

Patient Case: RP1 Liver Injection in Patient with Prior PD-1



25% ORR, 50% CBR in patients who received liver injections

48 liver injections in 8 patients (patients received 6-7 cycles)

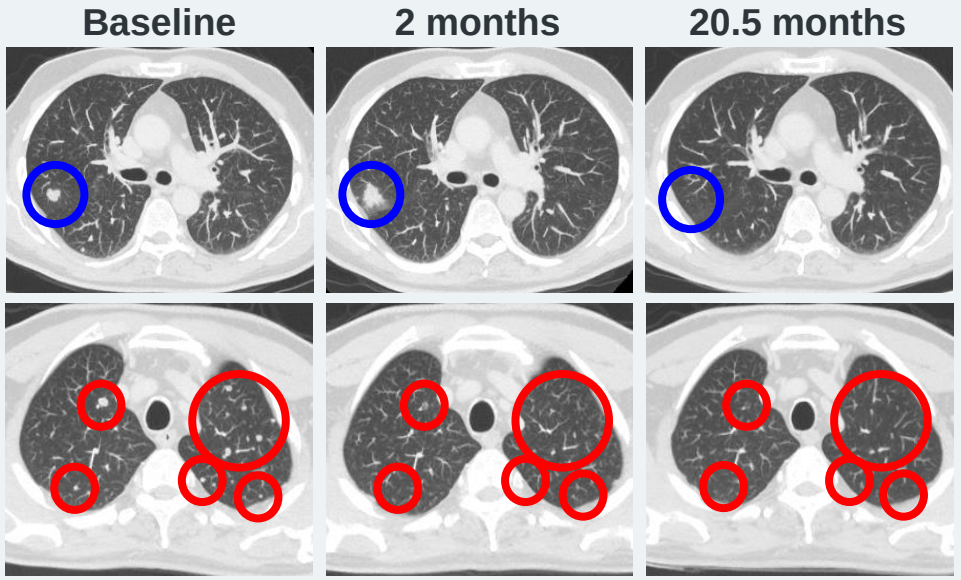
No liver/abdominal cavity bleeding events or elevated liver function tests

Injected Non-Injected

In GK et al. ASCO 2025. Abstract 9547. Poster 20.

Lung Injections were Associated with Low Rates of Pneumothorax Events

Patient Case: RP1 Lung Injection in patient with Prior ipilimumab + nivolumab



57% ORR, 71% CBR in patients who received lung injections

52 lung injections in 7 patients (patients received 7-8 cycles)

Pneumothorax* events: 3/52 (5.8%)

- Grade 1: 1/52 (1.9%)
- Grade 2: 2/52 (3.8%)
- Grade ≥3: 0

Injected Non-Injected

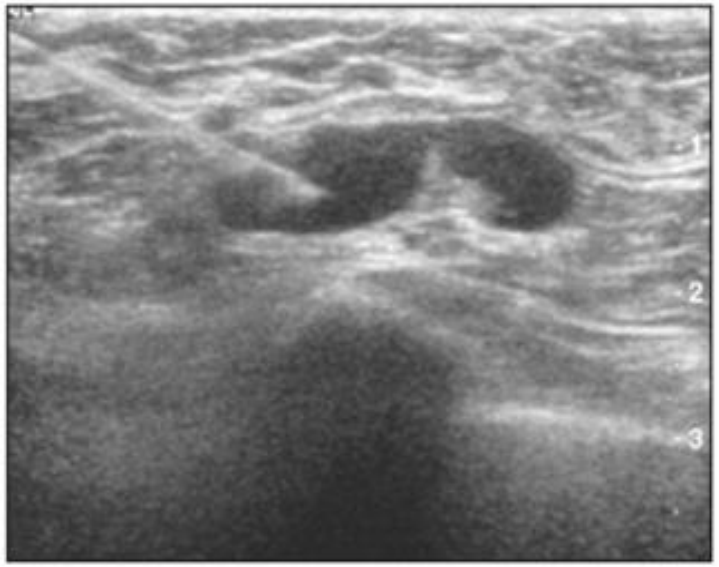
* Patients continued treatment following events

In GK et al. ASCO 2025. Abstract 9547. Poster 20.

RP1 Injections Procedure – Ultrasound

For injections with ultrasound guidance

- Multiple insertion points may be needed for larger tumors
- Cover ultrasound probe with a disposable protectant barrier
- Capture the measurements of the tumor to be injected
- After inserting the needle, attach empty syringe and pull back to ensure the needle has not been placed in a blood vessel; withdraw and redirect if so
- Change syringe and attach syringe with RP1

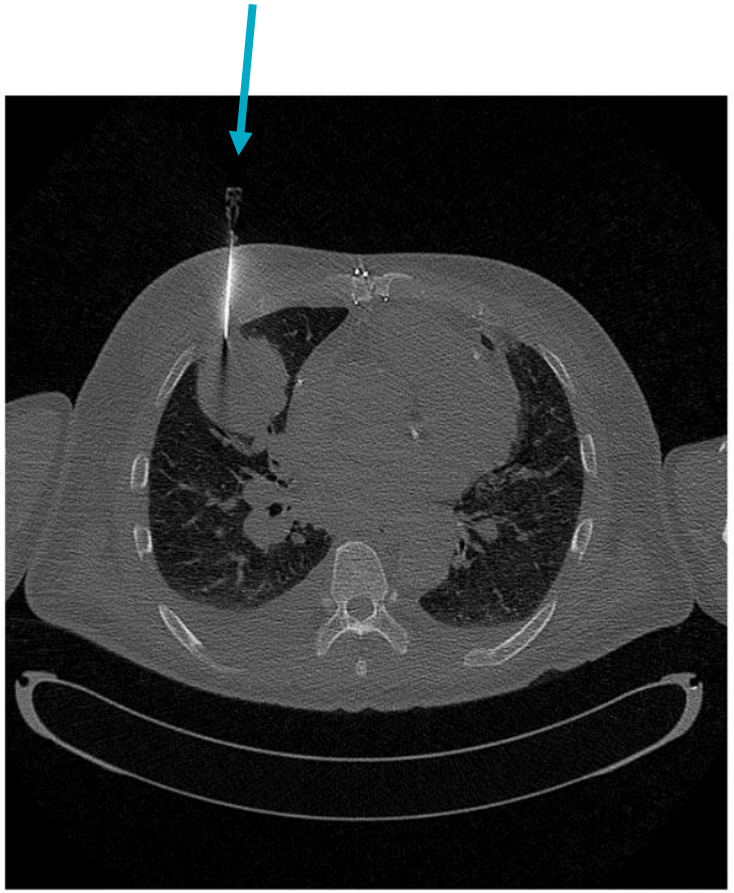


Ultrasound image with needle placed in tumor

RP1 Injections Procedure – CT Imaging

For injections with CT imaging guidance

- Multiple insertion points may be needed for larger tumors
- Image the tumor and determine where the needle will be placed and capture the measurements of the tumor to be injected
- After inserting the needle, attach empty syringe and pull back to ensure the needle has not been placed in a blood vessel; withdraw and redirect if so
- Change syringe and attach syringe with RP1
- Observe to see if tumor appears to be “filled” and do not attempt to inject maximum volume



CT Image with needle placed in lung tumor

Deep ‘Tumor Directed’ RPx Injections

Ultrasound or CT guidance

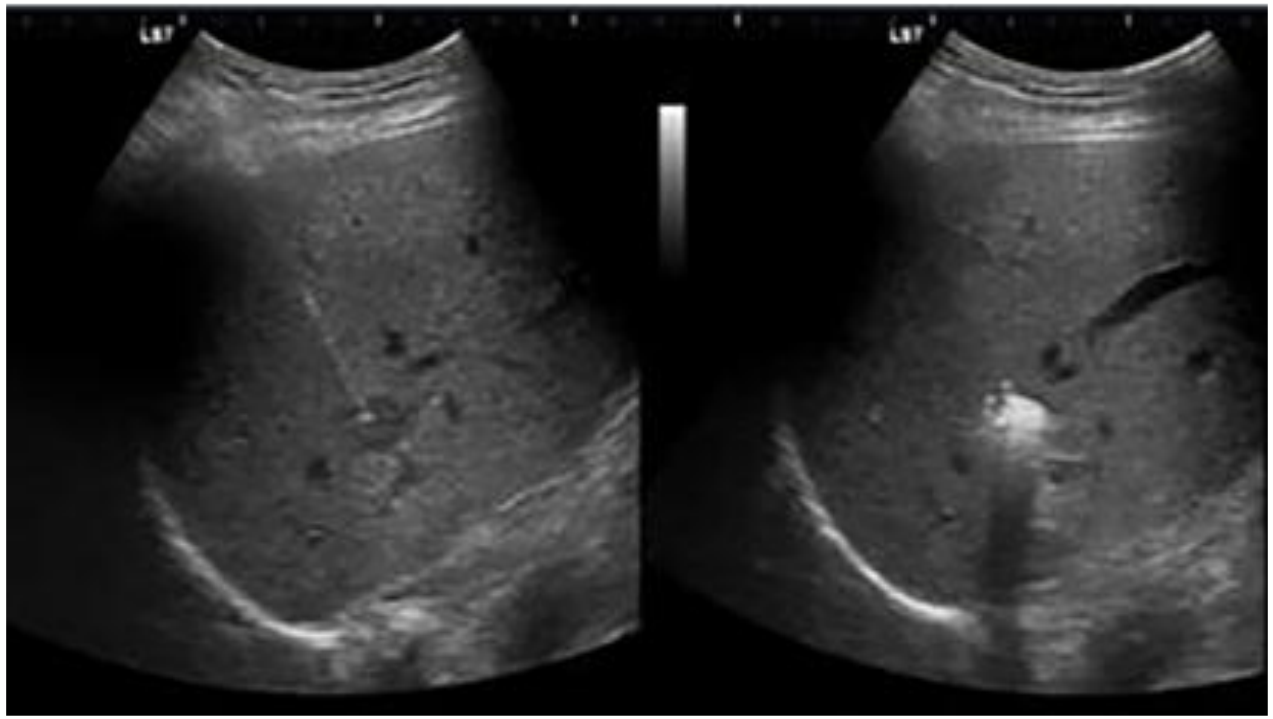
- Approx. 80% of liver tumors can be injected with ultrasound guidance
- Lung injection often use CT guidance
- Needle placed in target lesion (typically 17-27 gauge)
- Up to 10 mL RPx can be injected per cycle
- Agent distributed across the tumor(s)

Can be done by the majority of radiologists

- Outpatient procedures usually with conscious sedation
- Logistics similar to FNA or biopsy (infrastructure and processes in place)
- 15-30 min procedure; monitoring for 2-4hr

Ultrasound image with needle placed in tumor

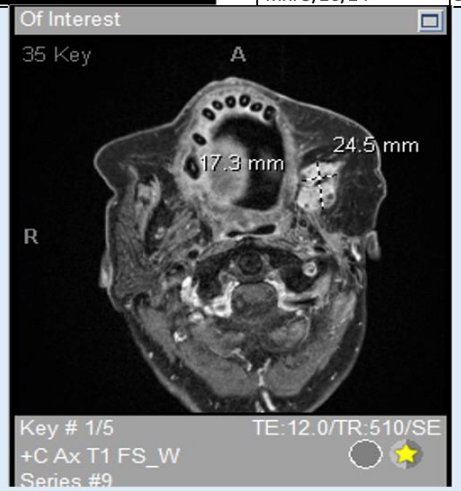
Immediate post injection image



Tselikas L. Clin Canc Res 2021;27:2698–705.
Sheth RA. JAMA Network Open. 2020;3(7):e207911.

Injection Planning and Workflow Management

A	B	C	D	E	F
MRN	DOB	LAST, FIRST NAME	TYPE AND DATE OF CROSS-SECTIONAL FOR TARGET LESION(S) REFERENCE	SITE A/lesion 1: CT IMAGE OF TARGET INJECTABLE LESION	SITE B/lesion 2: CT IMAGE OF TARGET LESION FOR CONTROL BIOPSY -
[redacted]			MRI 3/26/24	Inject the following Lesion: MRI 3/26/24, Se #9, Im #35	



Next Encounter: 11/6/2024; 3/12/25

Updated : 5/31/2024; 6/14/2024; 7/12/2024; 7/19/2024; 9/4/2024; 10/11/2024

	Date:	Time:	Cx Dx		
Inj	5/24/24	1545-1545	C1D1		
Inj	5/30/24	1515-1553	C1D8		
Inj	6/5/24	1200-1200	C1D15		
BX Only	6/12/24		C2D1		
Inj	7/3/24	1304-1305	C3D1		
Inj	7/9/24	1222-1223	C3D8		
Inj	7/17/24	1314-1317	C3D15		
	7/22/24	visit performed	C4D1		
Inj	8/13/24	1155-1156	C5D1		
Inj	8/22/24	1452-1452	C5D8		
Inj	8/28/24	1429-1430	C5D15		
	9/3/24	no dosing in even cycle	C6D1		
Inj	9/24/24	1632-1632	C7D1		
Inj	10/1/24	1226-1227	C7D8		
Inj	10/8/24	1317-1318	C7D15		
Inj	11/6/24	1133-1133	C9D1		
Inj	1/14/25	1521-1525	C11D1		
Inj	1/29/25	1129-1130	C11D15		
Inj	3/12/25	1136-1136	C13D1		

Poised for Commercial Success

Chris Sarchi
Chief Commercial Officer

Well Positioned Pending Approval to be the 1st Choice after PD-1 Progression

Replimune

Compelling data and favorable safety profile

Comprehensive understanding of the patient population and prescriber/IT adoption

Launch model prioritized for IT adoption across key account settings

Commercial organization hired and trained

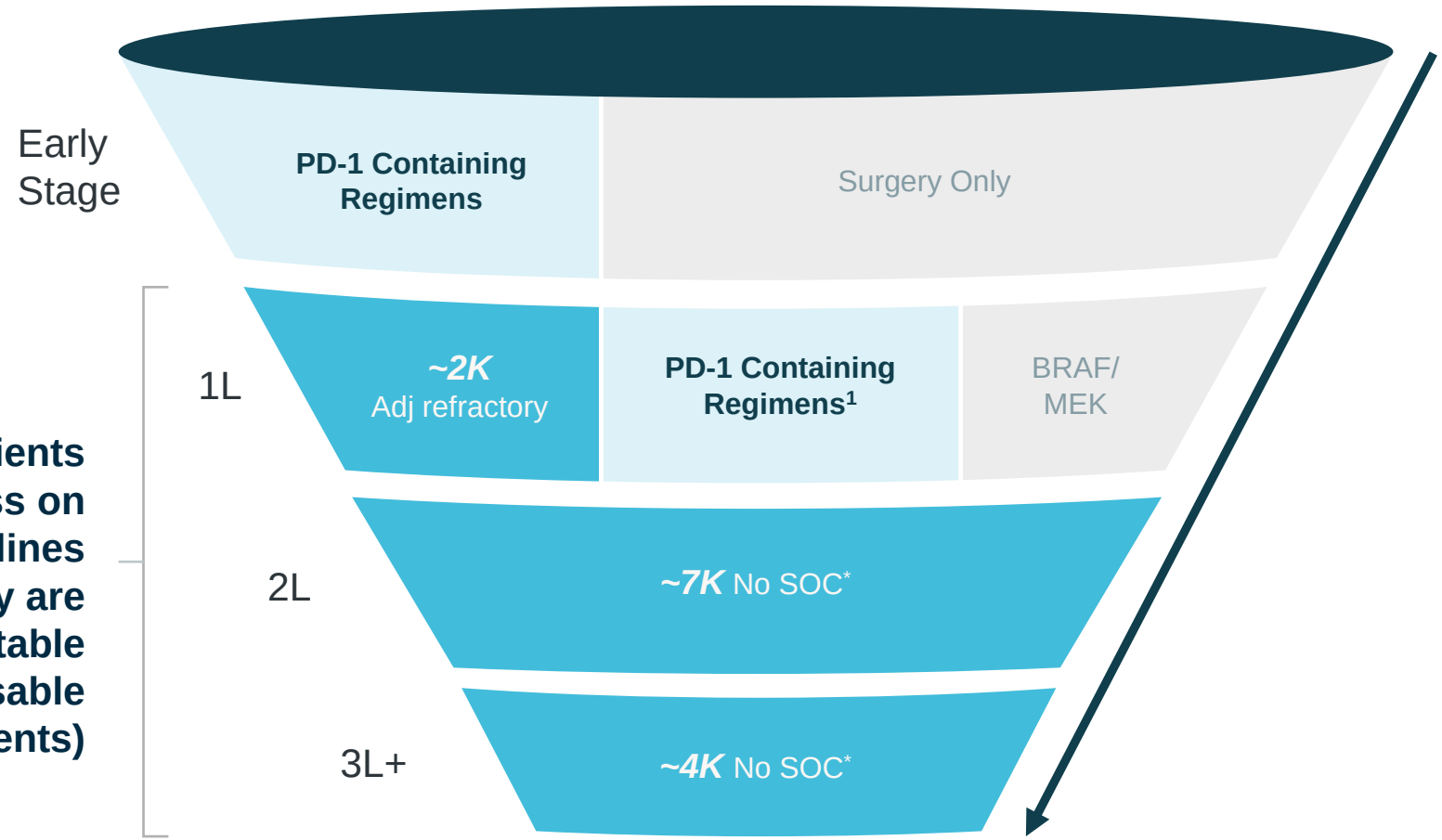
~60 customer-facing team members

Allows a significant patient opportunity

Drives demand and supports pull through

~10K Addressable Patients Across Lines of Therapy

US Melanoma Patient Treatment Funnel



80% of patients who progress on PD-1 across lines of therapy are injectable (~10K addressable patients)

RP1 potential patients

1De-novo metastatic or recurrent from surgery. *Therapy is dependent on prior exposure (e.g. PD-1 regimen, BRAF+MEK, TIL, or chemo), 80% of patients are injectable
Source: Quotes from primary market research with HCPs; Epi data for year 2030 from CancerMPact® Patient Metrics, Cerner Enviza (available from www.cancermpact.com Accessed 15 Oct 2025), with adjustments to future 2L+ treatment rates based on primary market research.

Image Guidance Will Enable Broader Usage of RP1 Through Interventional Radiology

Replimune

Injection **In-Office**	Injection via **Image Guidance** for Deep Lesions*	
		
~20% of pts require **only superficial injections**	**~20% of pts** have **superficial and deep lesions**	**~60% of pts only have deep lesions** (e.g., lymph, liver, lung etc.)
Medical Oncology *(Med Onc, APP)*		
	Interventional Radiology	

Image guided injections conducted by Interventional Radiology using ultra-sound, CT, or MRI. Source: Melanoma US treated patient population for 2030 based on CancerMPact Patient Metrics, Oct 2023 ; Injectability based on primary market research with IRs, Medical Oncologists and Surgical Oncologists *Brain and Bone not considered injectable

Patients Treated Across Hospital/Non-Hospital Settings

Hospital (50%)

Integrated Oncologists and IRs

Community (50%)

Referrals established with IR services*

Source: Patient volume based on systemically treated melanoma patients (Symphony Claims) and Onekey affiliations

Extensive Customer Insights Drive Launch Preparation

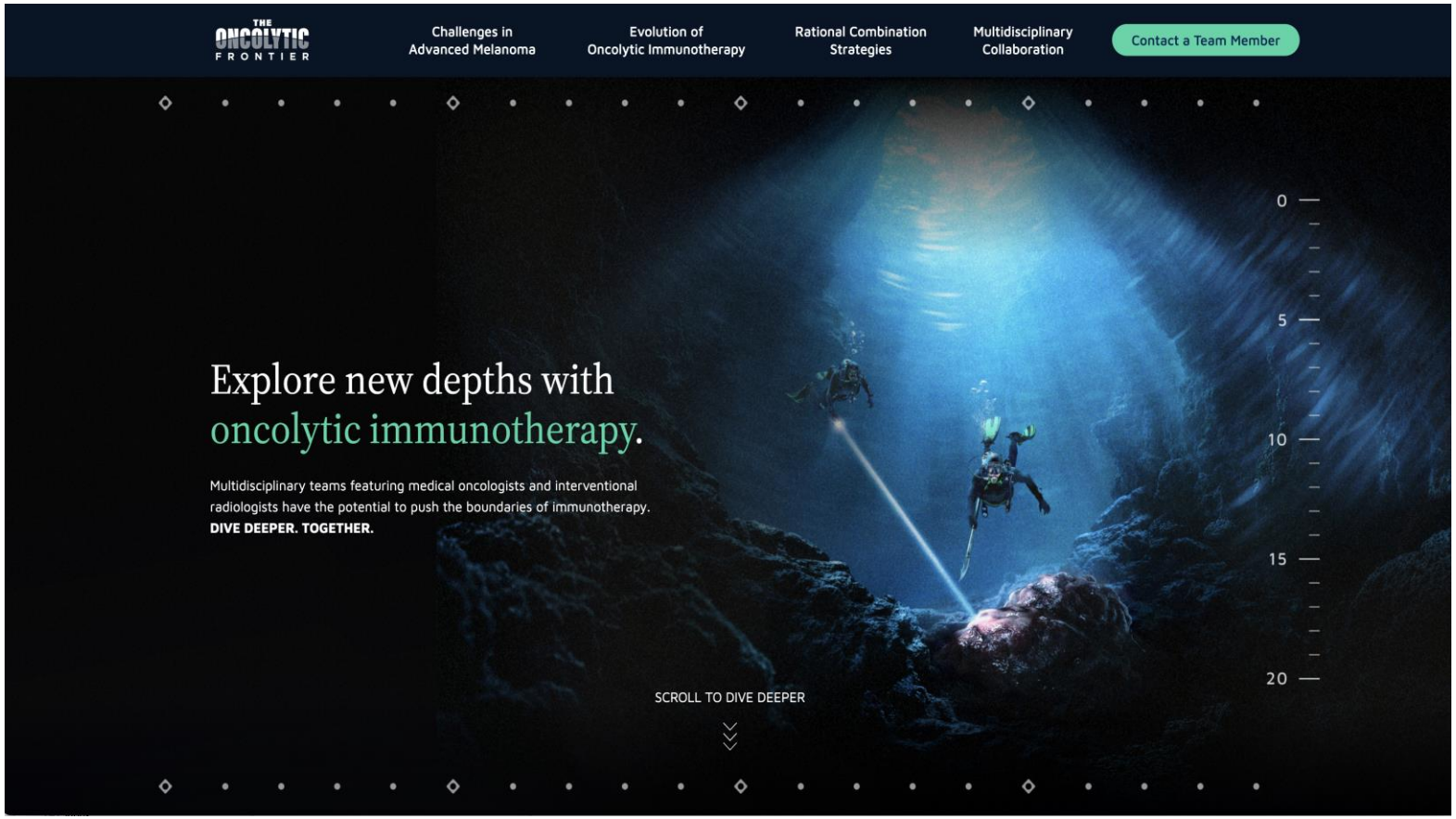
30+ Advisory Boards and 3rd Party Programs Completed

Key Insights

- Unmet needs identified in HCP workflow led to the creation of innovative commercial roles
- High level of excitement across target providers, with IRs demonstrating a strong willingness to play an active role in the treatment process
- Medical oncologists have IRs they refer to, however, opportunity identified to enhance collaboration to support patient treatments

Source: Qualitative market research with medical oncologists and IRs; Quantitative primary market research with IRs (N=110), Medical Oncologists (N=100); Claims analysis of interventional radiology procedures; Those rating as a 5+ on a 1-7 scale where considering willing; Backtable Podcast" Intratumoral Oncolytic Treatments for Metastatic Melanoma (Episode 547)

Unbranded Education Activities with HCPs in Place to Drive Cross-Functional Collaboration



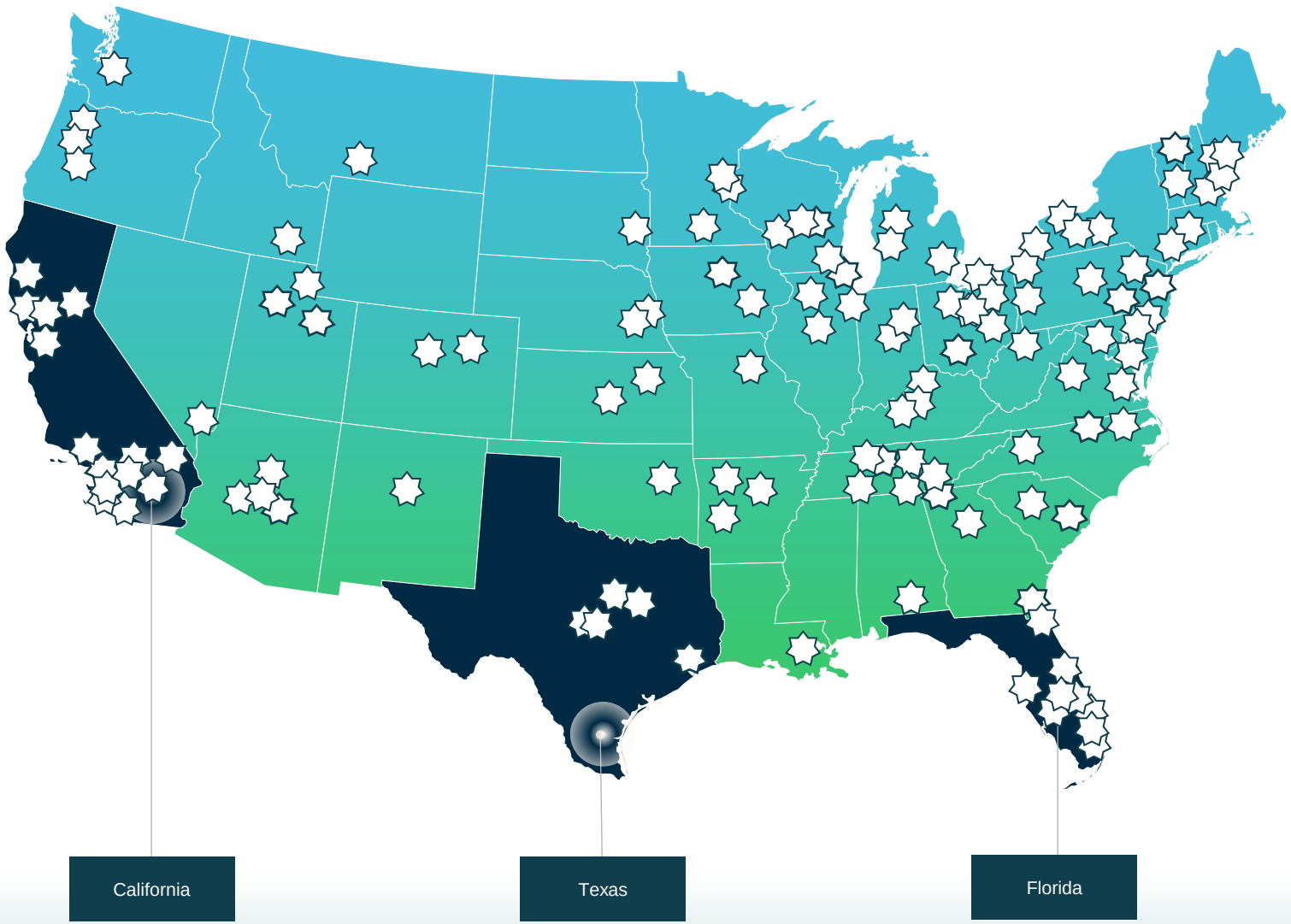
"Advanced cancer management used to primarily be under Hem-Onc. Now, it is truly multidisciplinary. It is a really an exciting time to be in oncology as we get to offer these really novel therapies to these patients with very advanced diseases."

Dr. Sunandana Chandra (Medical Oncologist, Northwestern)

"As an interventional oncologist, it really provides us an opportunity to collaborate in a new manner. The novelty to this treatment is not the procedure. It is the process and the collaboration. Ultimately, it benefits patients."

- Dr. Riad Salem (Interventional Radiologist, Northwestern)

Sites with Intratumoral Experience Support Targeted Early Adoption



~150 Sites have Intratumoral Injection Experience to date

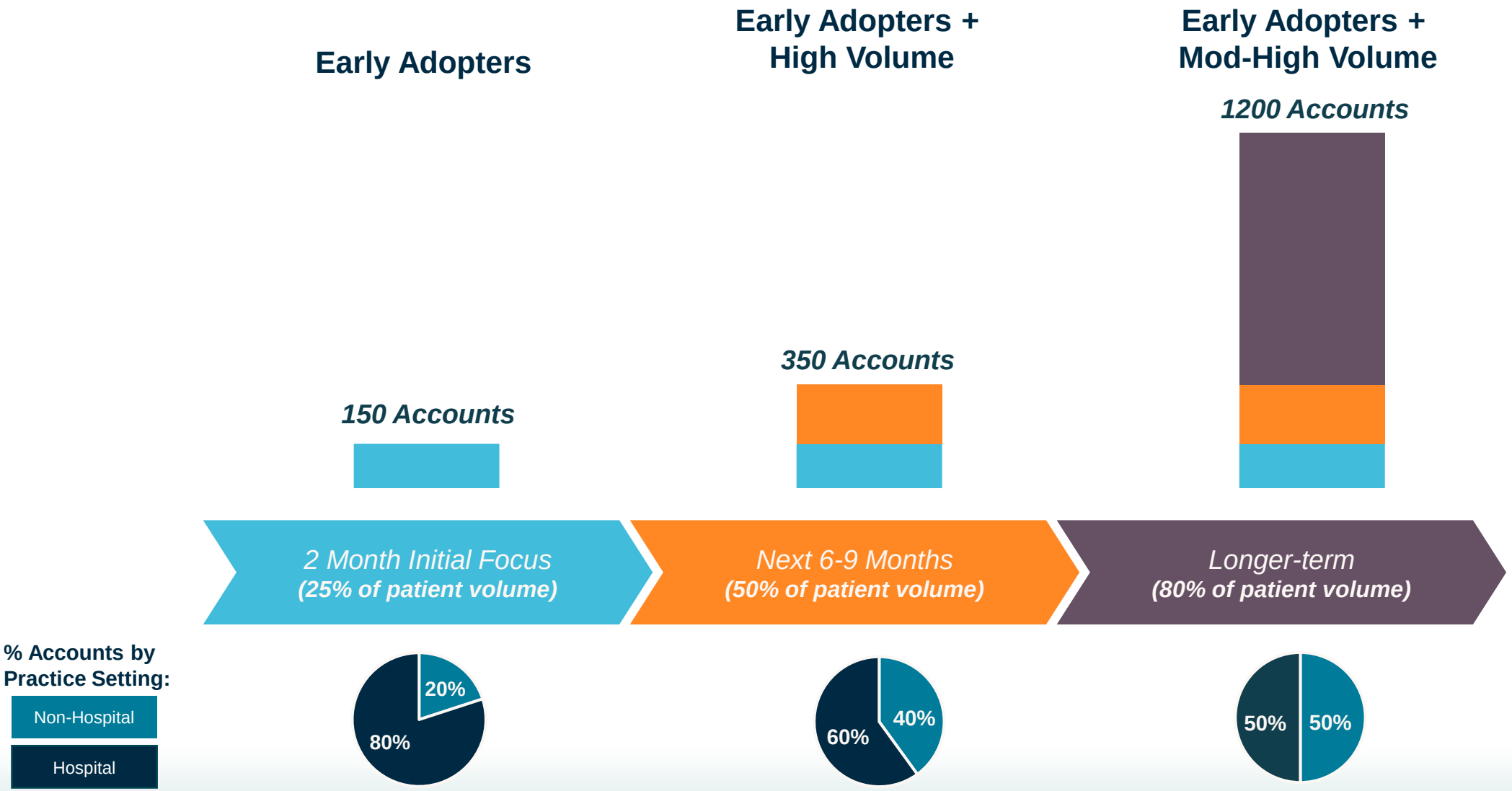
- RPx Injection Training and/or Clinical Experience *(N~115)*
- Prior intratumoral injection experience (e.g. TVEC) *(N~40)*

High geographic treatment concentration

- 3 states represent ~25% of patients
- 10 states represent ~50%

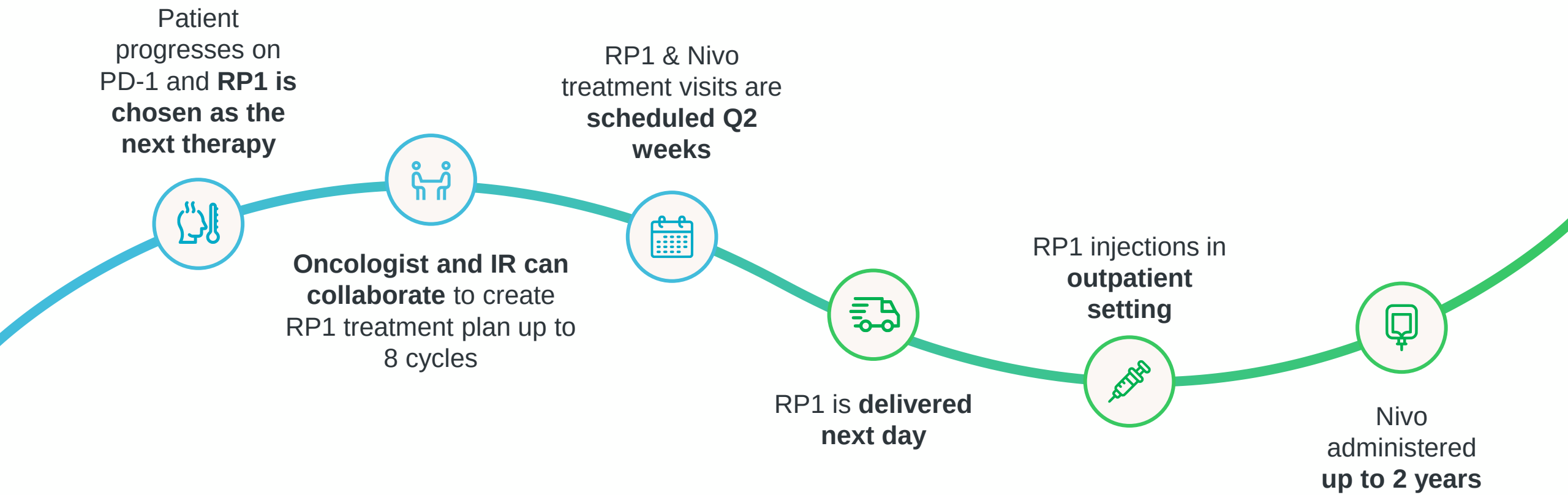
Targeted Launch for Long-term Success

Early Adopters have integrated interventional radiology and high patient volume



Coordinated RP1 Patient Treatment Journey

Replimune



Customer-facing Team Built to Address Anticipated HCP Needs

Replimune

Superficial Lesions

Med Oncs / Surg Oncs / APPs

HIPAA-Certified Oncology Nurse Educator

- Educate on superficial injection techniques
- Provide on-site oversight of first RP1 administration (on-demand as requested)
- Empower staff to have patient/caregiver treatment discussions

Deep Lesions

Interventional Radiologist

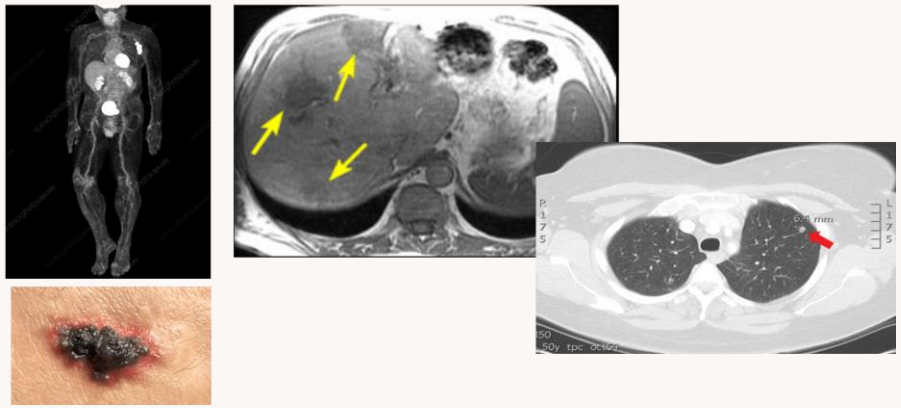
Interventional Radiology Oncology Coordinator

- Educate on superficial injection techniques and deep/visceral injection guidance
- Provide on-site oversight of first RP1 administration (on-demand as requested)
- Support reimbursement and logistics
- Ensure awareness and collaboration between medical oncologists and IRs prepared to inject

Optimizing Coordination of Care

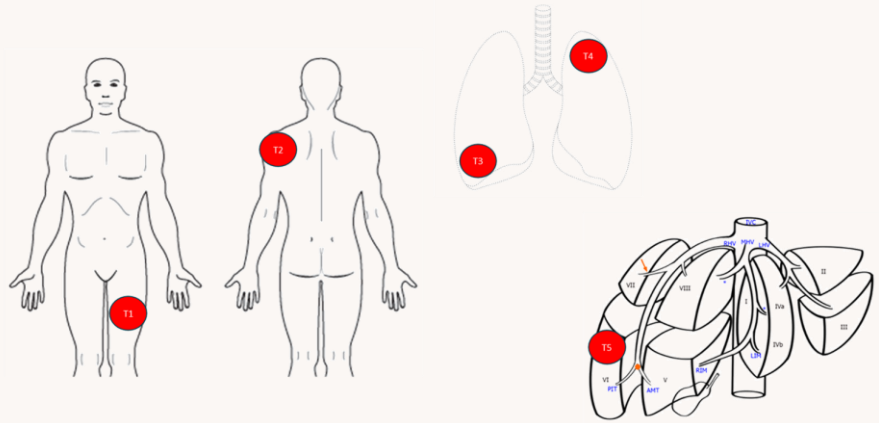
1

Review Patient Scans



2

Identify and Select Injectable Tumors



3

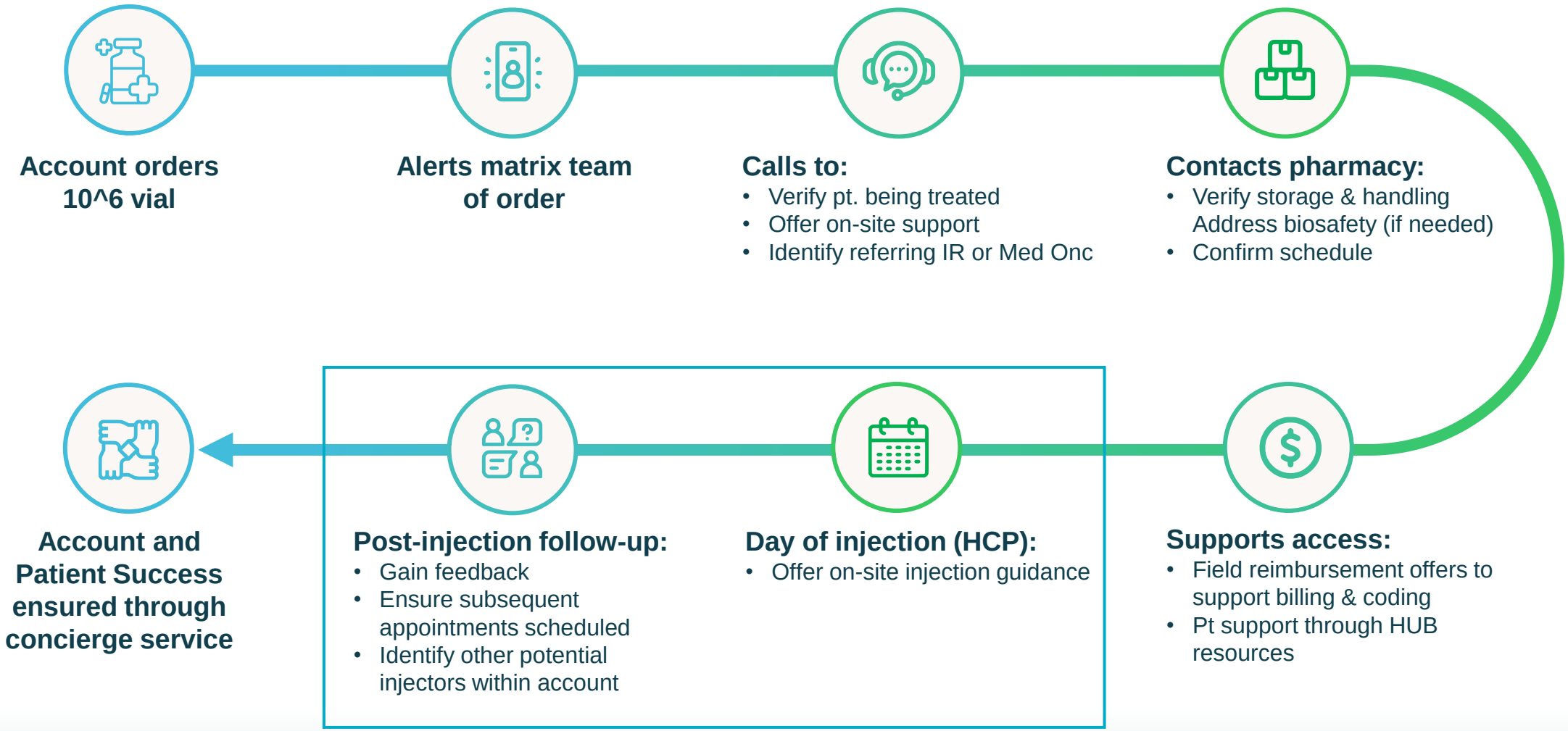
Plan out RP1 treatment for all 8 cycles

Please list all lesions targeted for injection, and any new lesions targeted for injection that appear after the first injection visit
Each course of vusolimogene oderparepvec is comprised of 8 injection visits
Maximum volume of vusolimogene oderparepvec that can be given at each injection visit is 10 mL
Lesions selected for injection may vary between injection visits, such that not every target lesion may be injected at each visit

Patient ID: **VO Course #:**

Lesion ID (from map)	Lesion Location (from map)	Injected (Y/N)	Injection Modality	Size (cm)	Visit 1 Date: 7/22/25 Volume (mL)	Visit 2 Date: 8/5/25 Volume (mL)	Visit 3 Date: 8/12/25 Volume (mL)	Visit 4 Date: 8/19/25 Volume (mL)	Visit 5 Date: 8/26/25 Volume (mL)	Visit 6 Date: 9/2/25 Volume (mL)	Visit 7 Date: 9/9/25 Volume (mL)	Visit 8 Date: 9/16/25 Volume (mL)	Notes
T1	L thigh	YES	S.C.	3.2	3	3	3	2	1	1	1	1	IR will inject both superficial lesions on each injection visit
T2	L deltoid	YES	S.C.	1.2	1	1	1	1	1	1	X	X	No injectable tumor on 9/9 visit
T3	R lower lung	YES	C.T. guided	2.6	1.5		1.5		1.5		1.5		Alternate lung injections
T4	L upper lung	YES	C.T. guided	1.5		1		1		1		X	No injectable tumor on 9/16 visit
T5	Liver section VI	YES	C.T. guided	2.2	2		2		2		2		To be injected only on same day at T3
					7.5 ml	**5 ml**	**7.5 ml**	**4 ml**	**5.5 ml**	**3 ml**	**4.5 ml**	**2 ml**	

Concierge Services Offered Through Every 1st Order



Reimbursement Landscape Supports Adoption of RP1

Community Accounts

- ASP+6% for RP1 and nivolumab
- Potential of 2 years of continued nivolumab use to maintain patient treatment continuity
- Established procedure code exist for superficial injections

Hospital Setting

- ASP+6% (+) and 340B pricing for RP1 and nivolumab
- Established procedure codes exist for both superficial and deep/visceral intratumoral injections

Existing Codes To Support RP1 Deep Injections

Code	Description	Physician Payment in Office	Physician Payment in Facility	Hospital Outpatient	ASC
32999	Unlisted procedure lung	contracted	contracted	$618.26	No fee
47399	Unlisted procedure liver	contracted	contracted	$703.59	No fee
38999	Unlisted procedure lymph node	contracted	contracted	$437.18	No fee
48999	Unlisted procedure pancreas	Contracted	Contracted	$703.59	No fee
49999	Unlisted procedure peritoneum	Contracted	contracted	$703.59	No fee
76942	US guidance for needle placement	$57.25	$29.11	No fee	No fee
77012	CT guidance for needle placement	$122.27	$66.63	No fee	No fee
99152	Moderate sedation by same provider*	$48.52	$11.64	No fee	No fee

*** If anesthesia is administered by Anesthesiologist, rates are higher - $75 then $17 per 15 minutes additional**

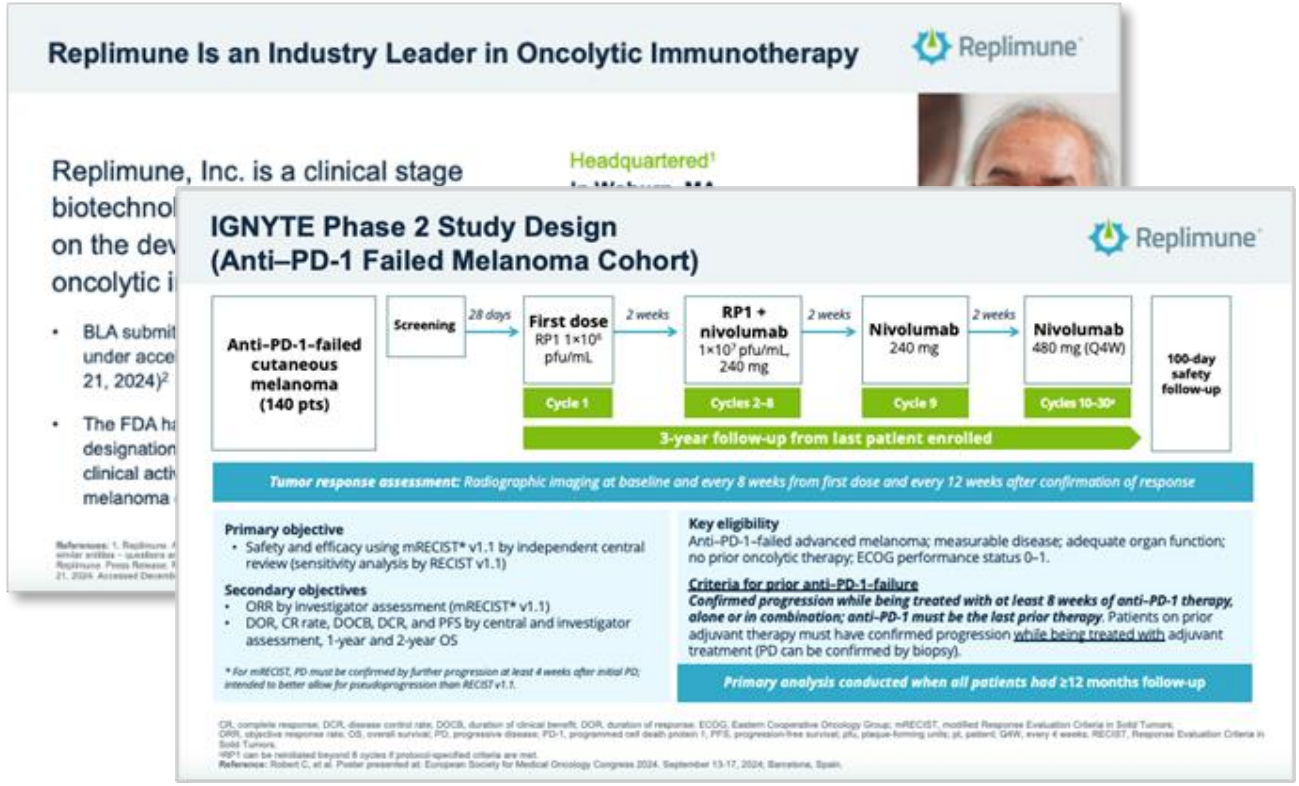
Real-world utilization will be determined by physicians

Extensive Payer Engagement Ongoing to Enable Patient Access

Pre-Approval Information Exchange

- **70% of commercial and Medicare advantage targets engaged representing nearly 160 million lives**
- **55% of Medicaid Fee for Service targets engaged**
- Ongoing engagement at key meetings including MOASC, PCMA, NAMCP, ACCC, AMCP, Asembia

Introduce Replimune as an industry leader in oncolytic immunotherapy, provide an overview of current melanoma treatments & share IGNTYE study design and findings



ReplimuneConnect Plus Patient Support Program Ready for Launch

Core Services

Patient Enrollment
Welcome and inform the patient

Insurance Navigation
Benefits investigation and OOP costs

Access Barriers
Educate on Prior Authorizations, denials, appeals

Patient Affordability
Co-pay and PAP programs

Personal Connection
Compassionate voice and resource for patients

Concierge Services

Clinical Support and Education
Nurse Educators

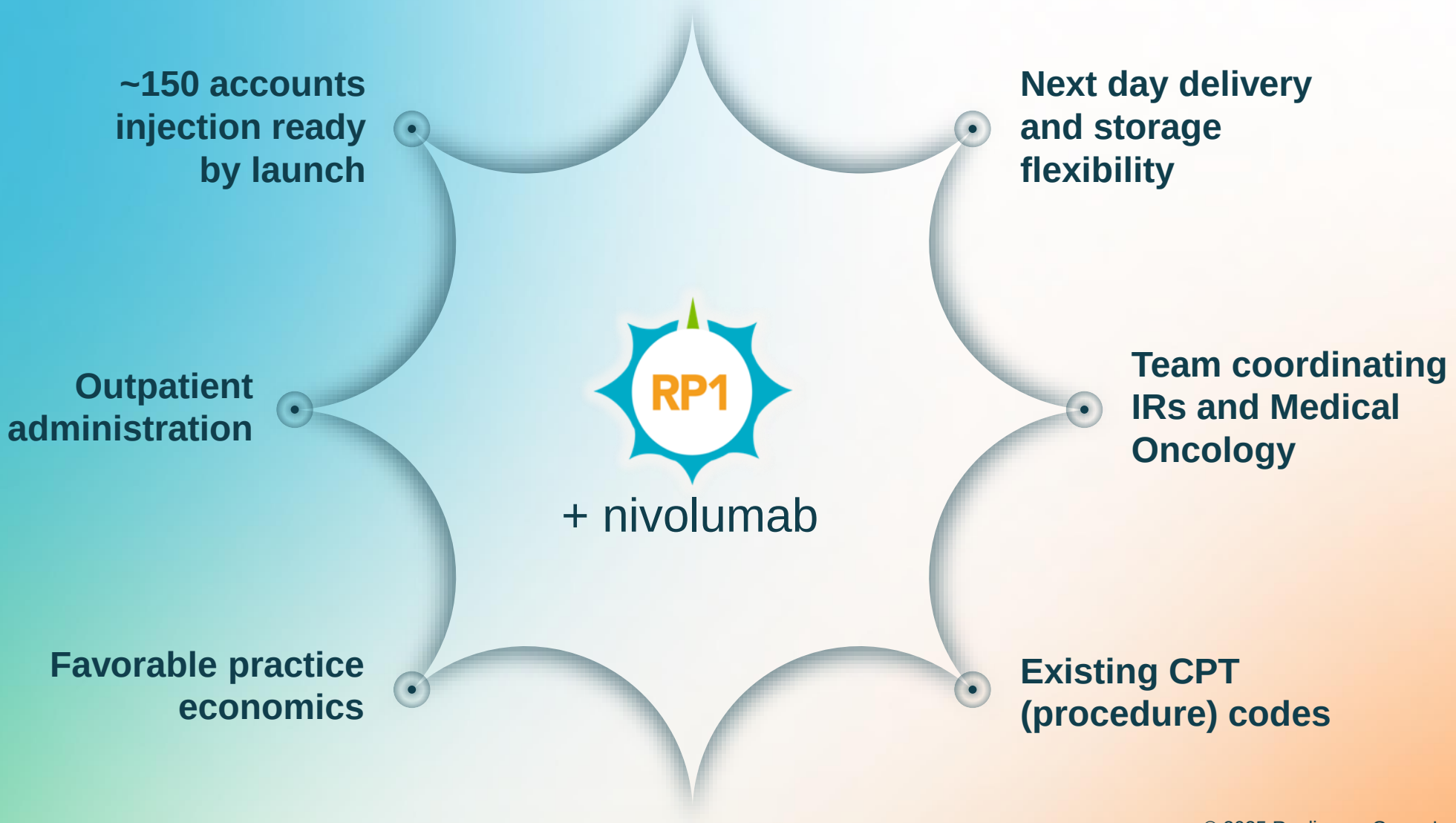
PAP Assurance Program
Claim denial assistance

Care Coordination
Scheduling and reminders

Caregiver Support
Information and resources

Note: Patients can be enrolled in the program by the physician's office or by contacting the patient hub directly themselves

RP1 Profile and Logistics are Attractive for Targeted Early Adoption



Introducing…

“Too-drih-kev”

Advanced Melanoma Fireside Chat

Moderated by:
Emily Hill
Chief Financial Officer

Our KOL Panel

Sherrif Ibrahim, MD, PhD
Dermatologist

Dermatologist, Mohs Surgeon and Owner, Rochester Dermatologic Surgery & Associate Professor, University of Rochester

Nikhil Khushalani, MD
Medical Oncologist

Vice Chair, Department of Cutaneous Oncology at Moffitt Cancer Center

Kim Margolin, MD
Medical Oncologist

Medical Director, Borstein Family Foundation Melanoma Program at Saint John's Cancer Institute

Bhavesh Shah, RPh
Pharmacist

Chief Pharmacy Officer, Hematology Oncology at Boston Medical Center

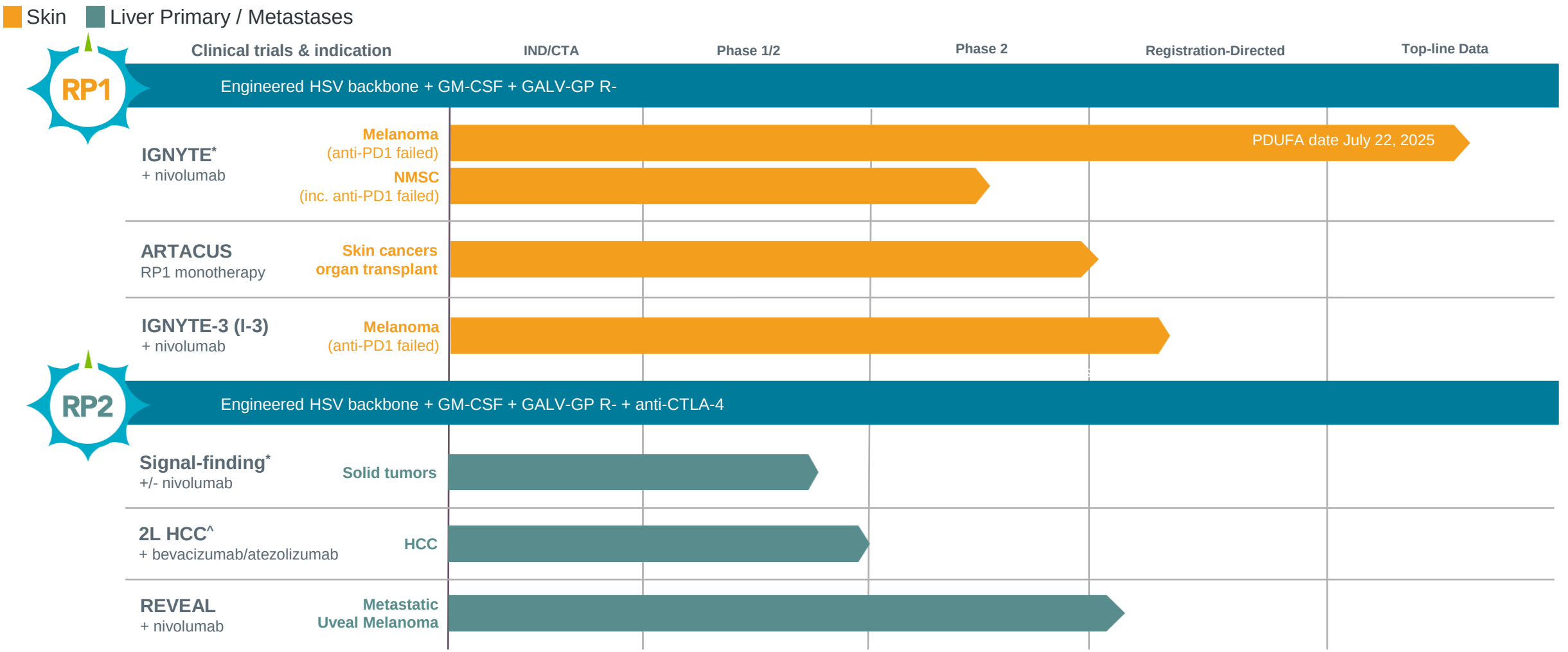
Rahul Sheth, MD
Interventional Radiologist

Associate Professor, Department of Interventional Radiology at MD Anderson Cancer Center

RPx in Skin Cancers

Kostas Xynos, MD, PhD
Chief Medical Officer

RPx Pipeline in Skin and Beyond



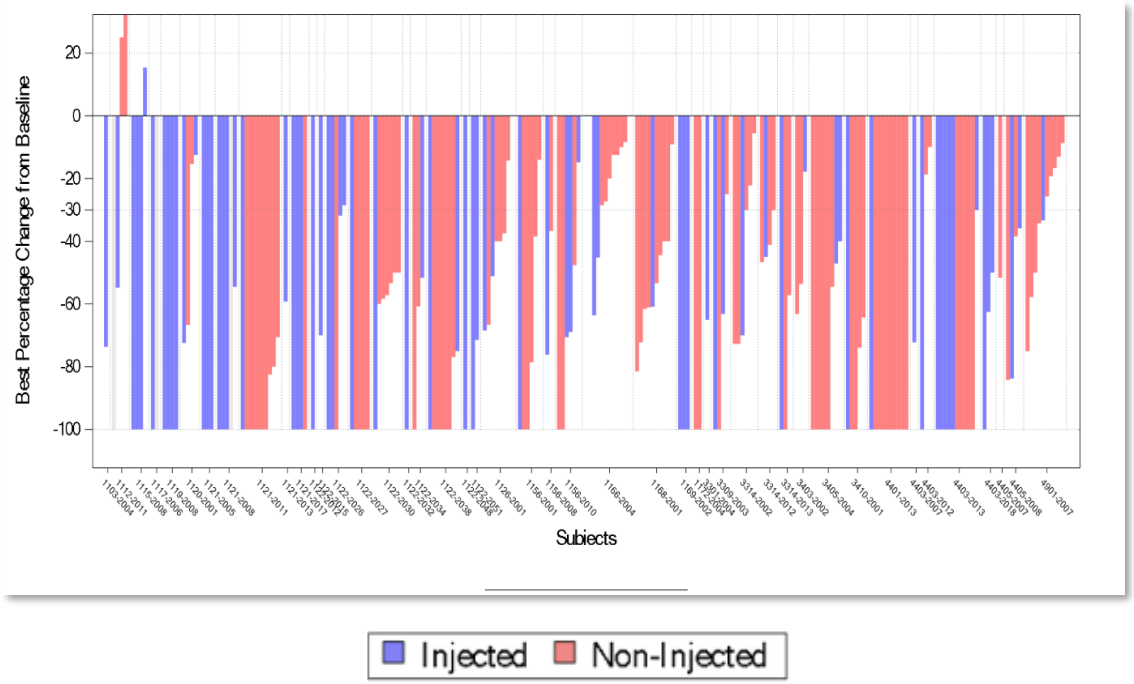
RPx expansion into additional skin cancers, liver and thoracic primary / metastatic cancers planned

* Under a clinical trial collaboration & supply agreement with BMS for the supply of nivolumab – full commercial rights retained by Replimune
^ Under clinical trial collaboration & supply agreement with Roche for atezolizumab & bevacizumab supply – full commercial rights retained by Replimune

Key Learnings Drive Expansion Further into Skin Cancers

- RP1 can lead to **systemic and durable responses** in injected and non-injected lesions, including visceral
- **Clinical benefit** achieved across patient sub-groups
- **Meaningful signals** seen in early disease (neo-adjuvant/ locally advanced settings)
- Numerically **higher response rate** with deep/visceral (± superficial) injections vs. superficial injections alone
- Favorable & tolerable safety profile
- Expansion of existing & generation of new T-cell clones and **increase in PDL1 expression**

IGNYTE Responses in Injected and Non-injected Lesions



Confirmatory IGNYTE-3 (I-3) Study Underway in Melanoma

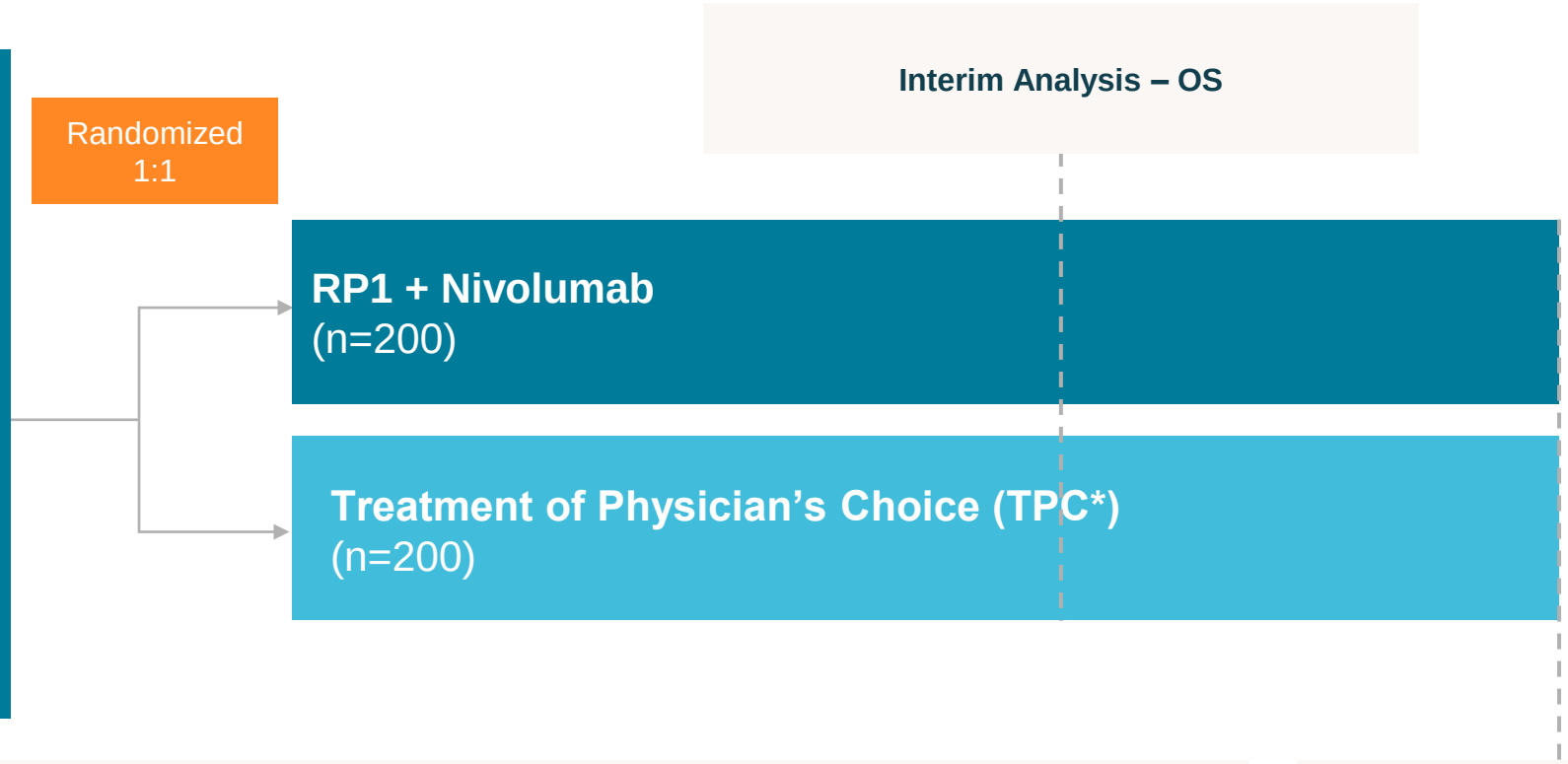
IGNYTE-3

Advanced cutaneous melanoma

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

N=~400

Randomized 1:1



- Global trial with ~110 sites
- EMA engagements planned for 2H 2025
- Expanded Access Program in US and Global Compassionate Use Program

*Nivolumab-Relatlimab (Opdualag), Chemotherapy (DTIC, TMZ, paclitaxel/nab-paclitaxel), Rechallenge with anti-PD1 monotherapy (nivo or pembro); NCT6264180

High Unmet Need in Non-Melanoma Skin Cancers and Angiosarcoma

- ~4,600 post-PD1 non-melanoma skin cancer cases in the US each year (CSCC, MCC, BCC)
- Majority of patients have injectable disease
- No FDA approved treatments in anti-PD1 failed non-melanoma skin cancers
- Angiosarcoma comprises up to 2% of all soft tissue sarcomas (STS) and 4-5% of all cutaneous STS[1]

*"Really what's most important [in MCC] is an efficacious treatment because **right now we don't have any SOC and chemo doesn't provide durable results,** even in patients who respond."*

*"Everyone in BCC will eventually progress and **only have chemo** if I can't get them in a trial…These patients have already gone though multiple lines of therapy."*

*"**New active drugs would be a big unmet need** for angiosarcoma. The biology of the tumor type is very interesting and not immunologically responsive. Combinations and predictive biomarkers would be even better."*

Source: CancerMPact® Patient Metrics, Oracle (formerly known as Kantar Health; available from www.cancermpact.com) and Replimune analysis. Note: all epi numbers are for the year 2030 Addressable defined as treated patients. 1. Angiosarcoma - StatPearls - NCBI Bookshelf

Durable Signals in MCC, BCC, CSCC and Angiosarcoma

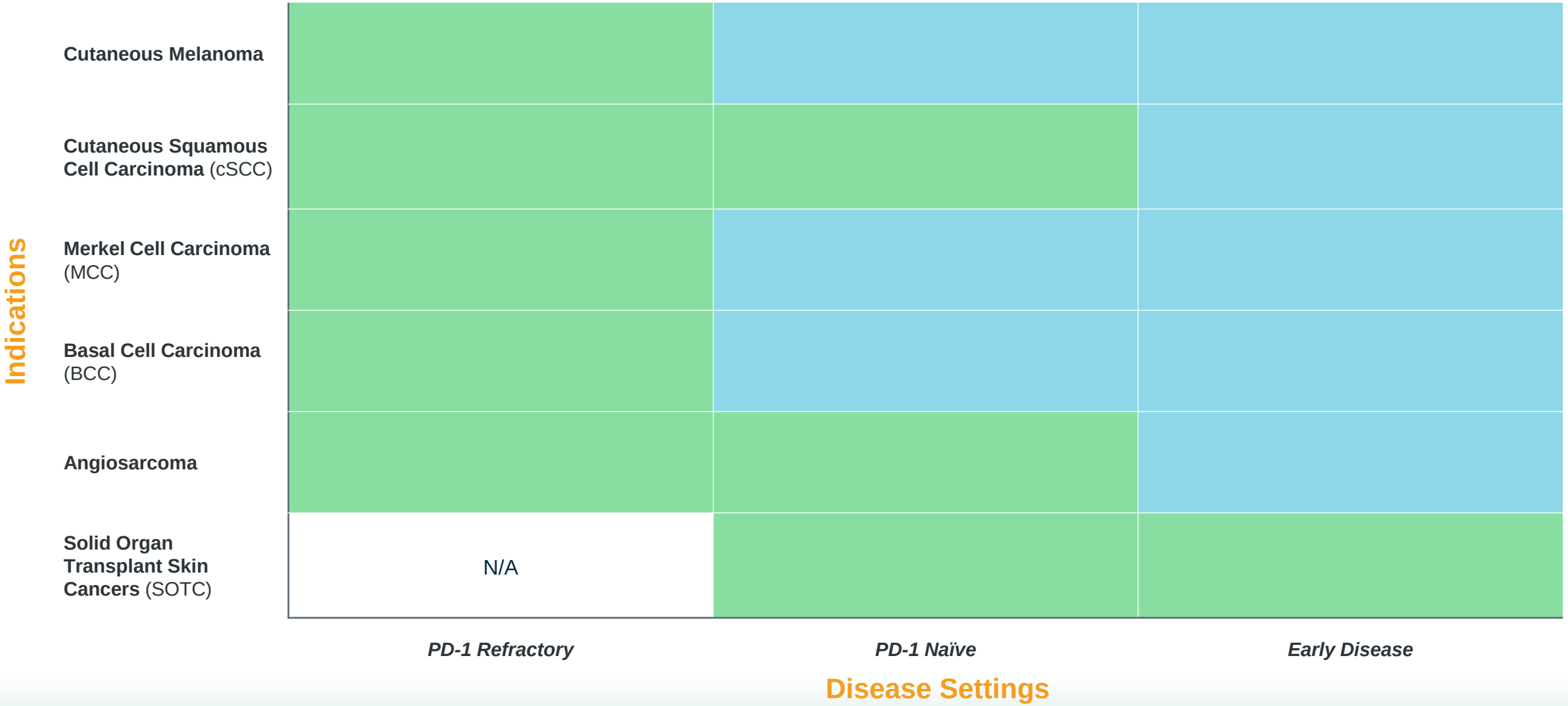
	MCC (N = 23)		BCC (N = 13)		Angiosarcoma (N = 14)		PD-1 Failed CSCC (N=28)	
	PD-1 Naïve (N = 4)	PD-1 Failed (N = 19)	PD-1 Naïve (N = 3)	PD-1 Failed (N = 10)	PD-1 Naïve (N = 6)	PD-1 Failed (N = 8)	Locally Advanced (N = 6)	Metastatic (N = 22)
CR	4 (100)	3 (15.8)	1 (33.3)	0	2 (33.3)	2 (25.0)	1 (16.7)	1 (4.5)
PR	0	2 (10.5)	0	3 (30.0)	2 (33.3)	1 (12.5)	1 (16.7)	2 (9.1)
NE	0	1 (5.3)	0	0	0	0	0	0
SD	0	3 (15.8)	1 (33.3)	5 (50)	2 (33.3)	3 (37.5)	3 (50)	7 (31.8)
PD	0	10 (52.6)	1 (33.3)	2 (20)	0	2 (25)	1 (16.7)	12 (54.5)
Confirmed Best Overall Response (BOR), n (%)	**4 (100)**	**5 (26.3)**	**1 (33.3)**	**3 (30.0)**	**4 (66.7)**	**3 (37.5)**	**2 (33.3)**	**3 (13.6)**
DOR (months), median	41	12.5	17.3	17.3	16.3	5	12.4	18.6

All patients had ≥ 6 months of follow up

CERPASS Trial: RP1 + cemiplimab vs cemiplimab in anti-PD1 naïve CSCC missed its primary endpoints of ORR/CR across all patients but in LA CSCC showed ORR of 63% and doubling of the CRs for the combination (48.1% vs 22.6%)

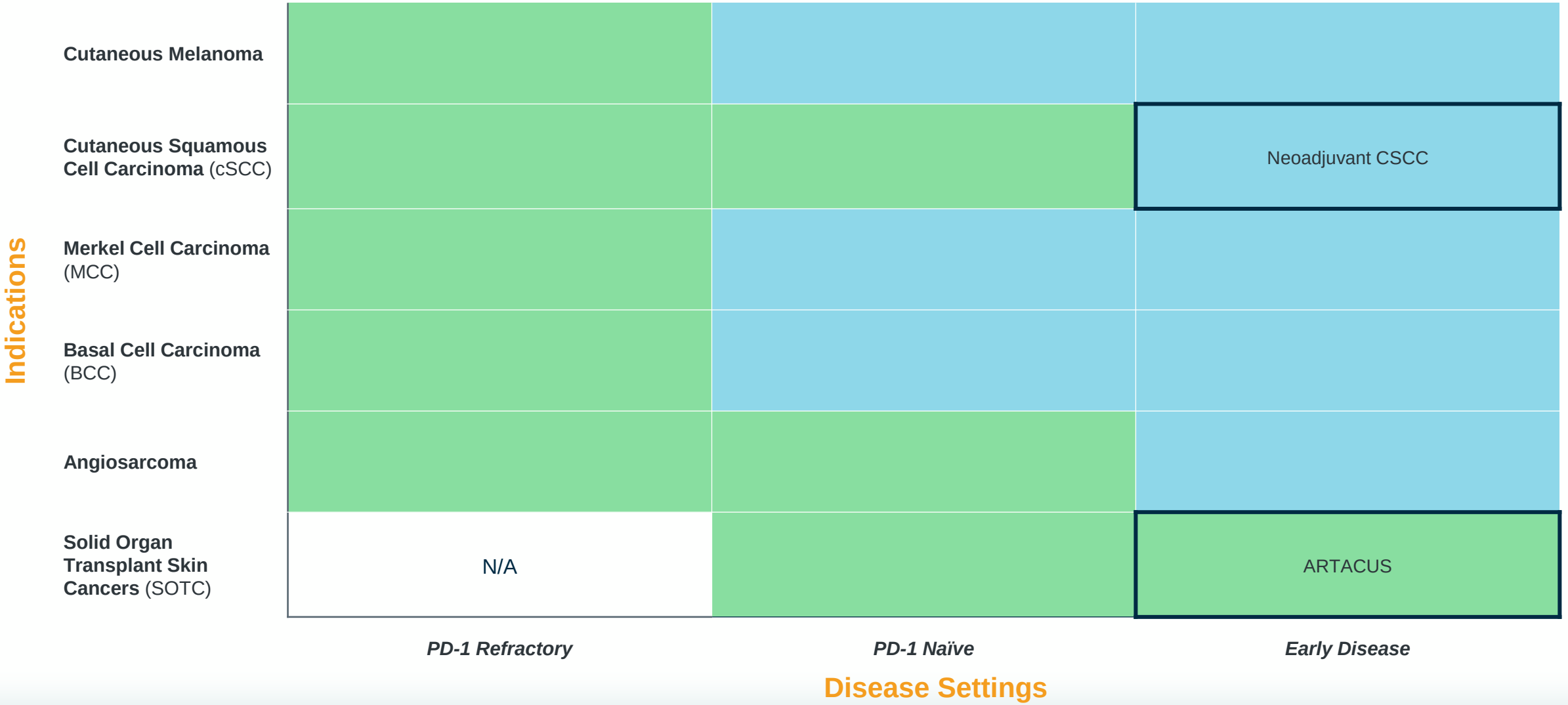
Data as of Oct 15, 2024 – D90; Enrollment as of Apr 14 2025

Opportunity to Address Areas of High Unmet Need in Skin Cancer



REPL ongoing trials Opportunities

Opportunity to Address Areas of High Unmet Need in Skin Cancer



REPL ongoing trials Opportunities

Treatment of Cutaneous Squamous Cell Carcinoma

Sherrif Ibrahim, MD
Rochester Dermatologic Surgery
Victor, NY

Treatment of Resectable cSCC with RP1: A Nonsurgical Approach to Management

Results from the Replimune Investigator Sponsored Trial

Background/Unmet Need:

Non-melanoma skin cancer incidence is higher than for all other malignancies combined and continues to increase

Current treatment options include surgical or destructive approaches.

Non-surgical options are ineffective

Currently no FDA approved drugs for neoadjuvant cSCC

Rationale

cSCC has one of the highest mutational burdens of any human malignancy

RP1 injection has been shown to mount a highly active immune reaction

Serial injections of RP1 may provide effective, definitive treatment for small cSCC’s

Study Objectives

A Phase 1b, single-center, open-label study, evaluating efficacy and safety of RP1 for the treatment of resectable cutaneous Squamous Cell Carcinoma

Primary Objectives and Endpoints

- **Pathologic complete response (pCR)** per Immune-Related Pathologic Response Criteria' (irPRC) criteria
    - 0% residual viable tumor (RVT) remaining in post-therapy specimen (no signs of cancer) in tissue samples removed during surgery

Secondary Objectives and Endpoints

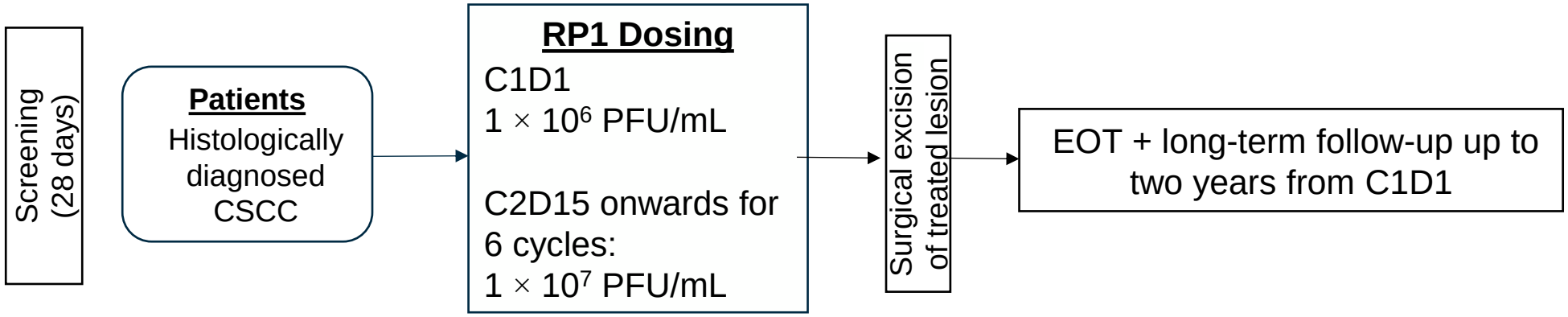
- **Duration of response (DOR), complete response (CR) rate, disease control rate (DCR), and progression-free survival (PFS)**, by investigator review.
- To evaluate efficacy **by one-year disease free survival (DFS)** rates, according to investigator review.

Study Design

Key Eligibility: Histologically confirmed diagnosis of invasive cSCC (BWH T1/T2a), prior OV therapy will be excluded

Treatment: RP1 Monotherapy up to12 weeks (for 6 cycles) every other week

Sample Size: 12 patients



Demographics

- 12 subjects, 15 tumors
- 7 male, 5 female
- Mean age 76.4
- 100% Caucasian non-Hispanic
- Head/Neck: 6
- Extremities: 7
- Torso: 2

Safety Results

All subjects completed all 6 cycles

Early termination: 0

Adverse Events: Grade 1 Erythema/edema in 1 subject

Serious Adverse Events: 0

Injections tolerated well

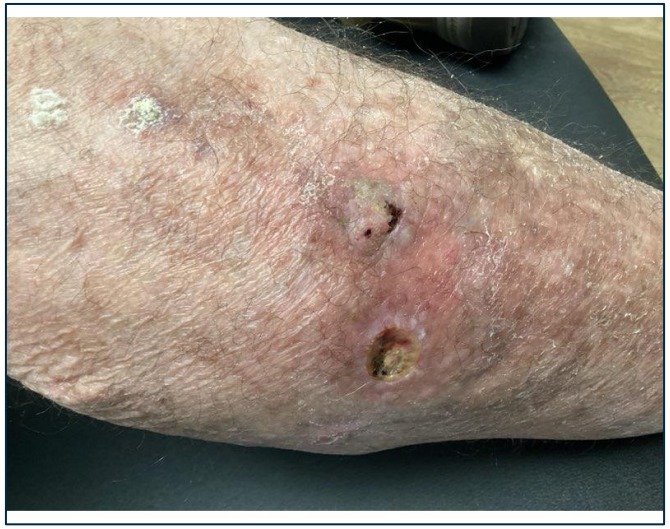
HSV-related AE’s: 0

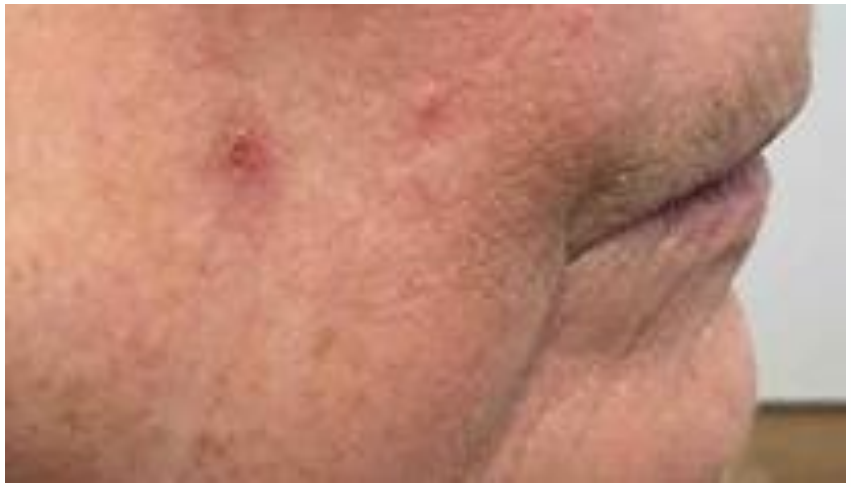
Efficacy Results

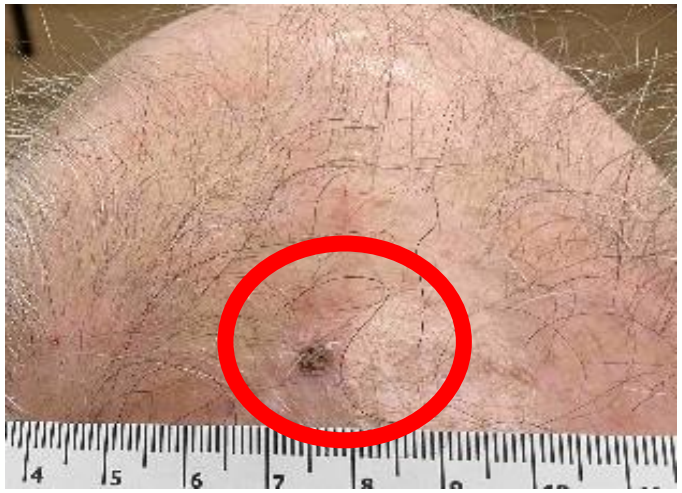
N=12	Clinical	Pathological
CR	8/12 (67%; no Sx needed)	10/12 (83%)
PR	4/12 (33%)	2/12 (17%)
ORR	12/12 (100%)	12/12 (100%)

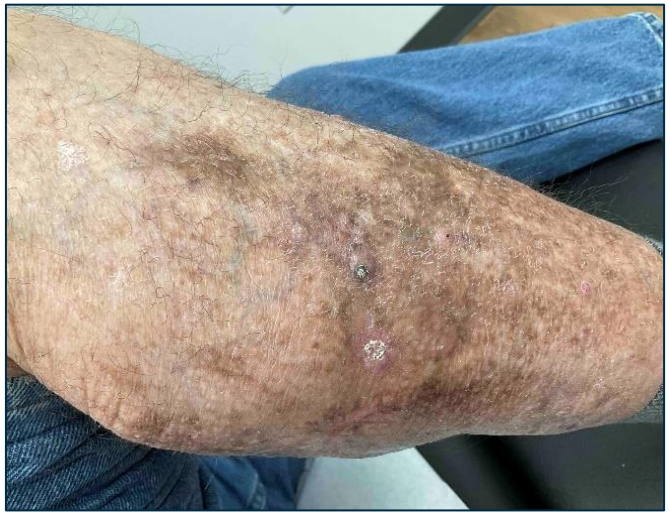
- pCRs were confirmed by biopsy in 8 patients that did not undergo Surgery
- **8/12 patients in this study were able to forgo surgery**
- All patients remain in response; follow up ongoing to assess durability of responses

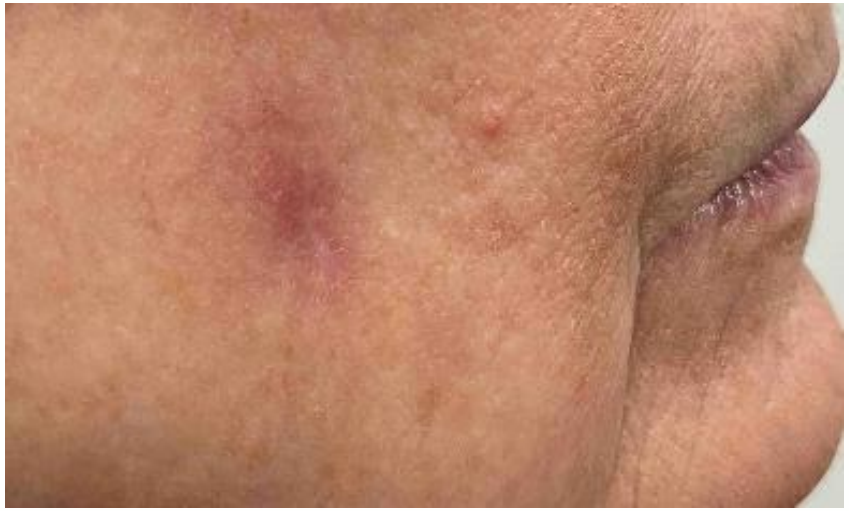
A Non-surgical Treatment Option for Patients

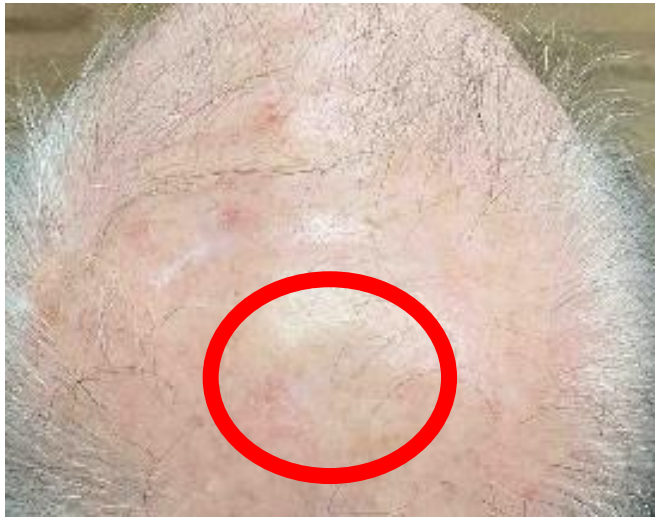












Conclusions

Summary:

- 100% overall response rate (83% path complete response)
- Treatments well tolerated and safety exceptional
- No progressive disease
- Successfully executed investigator sponsored trial / pilot study

Opportunities:

- Consider larger investigator sponsored, multi-site trial in Neoadjuvant CSCC
- Expand potential use of RP1 across skin cancers (e.g. BCC)

Solid Organ Transplant Skin Cancers

Results from ARTACUS

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

- NMSC is the most common cancer in SOT recipients, occurring at a 7–53× higher rate than in the general population.
- >90% of cases are cutaneous squamous cell carcinoma (CSCC) or basal cell carcinoma (BCC)
- Checkpoint inhibitors are contraindicated in this setting due to a significant risk of allograft rejection.
- Currently, no prospective immunotherapy data in non-kidney transplant patients.
- No SOC for locally advanced or metastatic CSCC in SOT patients
- ~1,500 addressable NMSC cases in the US per year with 50% growth in transplants over the last 8 years

Friman T, et al. *Int J Cancer*. 2022;150(11):1779-91. Garrett G, et al. *JAMA Dermatol*. 2017;153(3):296-303. Mittal A and Colegio O. *Am J Transplant*. 2017;17(10):2509-30.
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Squamous Cell Skin Cancer. Version 1. 2023. CancerMPact® Patient Metrics, Oracle (formerly known as Kantar Health; available from www.cancermpact.com) and Replimune analysis. Note: all epi numbers are for the year 2030 Addressable defined as treated U.S. patients.

RP1 in Solid Organ Transplant Skin Cancers (SOTC): ARTACUS Study Design

Key Eligibility:

- Kidney, liver, heart, lung and other solid organ transplant patients, hematopoietic cell transplant patients:
  - With cSCC
  - With BCC & MCC

RP1 Monotherapy -> Q2W up to 52 doses

($1x10^6$ PFU/mL for one dose followed by $1x10^7$ PFU/mL for subsequent doses)

EOT and long-term follow-up for up to 3 years from C1D1

Deep and Durable RP1 Monotherapy Responses in Locally Advanced CSCC in Solid Organ Transplant Patients

Confirmed Best overall response, n (%)	Intend To Treat Population (n=26)
CR	6 (23.1%)
PR	3 (11.5%)
SD	8 (30.8%)
PD	4 (15.4%)
Not Evaluable	5 (19.2%)
ORR (CR + PR)	**9 (34.6%)**
DCR (CR + PR + SD)	17 (65.4%)

Duration of Response Rate, % (95% CI)	Intend To Treat Population (n=26)
6 mos	76.2% (33.2, 93.5)
12 mos	61% (20.2, 85.8)
24 mos	**61% (20.2, 85.8)**

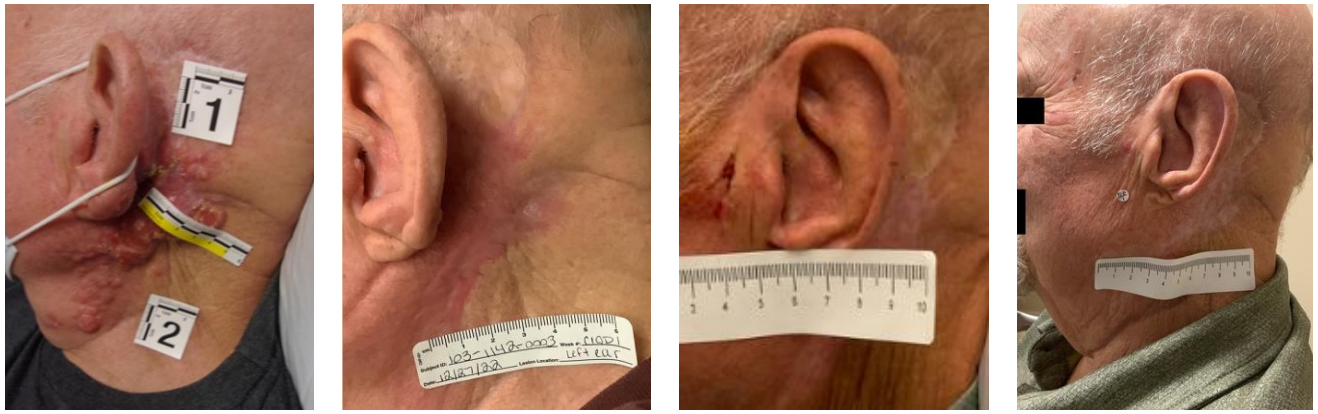
- No cases of RP1 related allograft rejection; responses see in broad set of allograft types:
  - Renal (n = 18, 69.2%)
  - Hepatic (n = 5, 19.2%)
  - Heart (n = 2, 7.7%)
  - Lung (n = 1, 3.8%)
- Well-tolerated in immunocompetent patients; no changes to immunosuppression steroid use required
- Study enrollment ongoing

Data as of Dec 31 2024

RP1 Monotherapy Responses in Locally Advanced CSCC in Solid Organ Transplant Patients

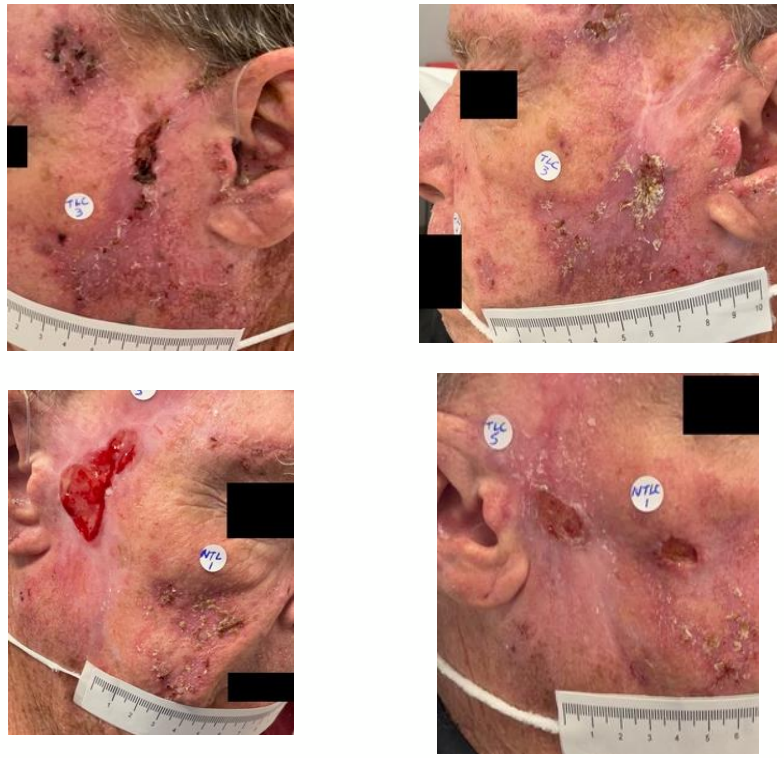
Liver Transplant Patient

Baseline (C1) | Week 18 (C10) | Week 48 (C25) | Week 101 (F/U)



Heart Transplant Patient

Baseline (C1) | Week 30 (C16)



RP1 Monotherapy Responses in Locally Advanced CSCC in Solid Organ Transplant Patients

Cycle 1	Cycle 5	Cycle 13	Cycle 14

RPx Platform: Following the Data

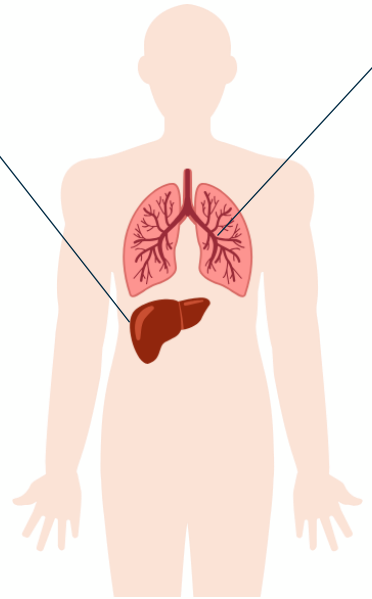
Kostas Xynos
Chief Medical Officer

Liver and Lung Are the Most Common Sites of Metastasis for Cancer

Replimune

Cancers Metastasizing to Liver

- Uveal melanoma (70%+)
- Colorectal cancer (30-50%)
- Neuroendocrine tumor (20-46%)
- Pancreatic cancer (30-40%)
- Gastric cancer (5-40%)
- Breast cancer (6-38%)
- Small cell lung cancer (17%)
- Non-small cell lung cancer (4%)



Cancers Metastasizing to Lung

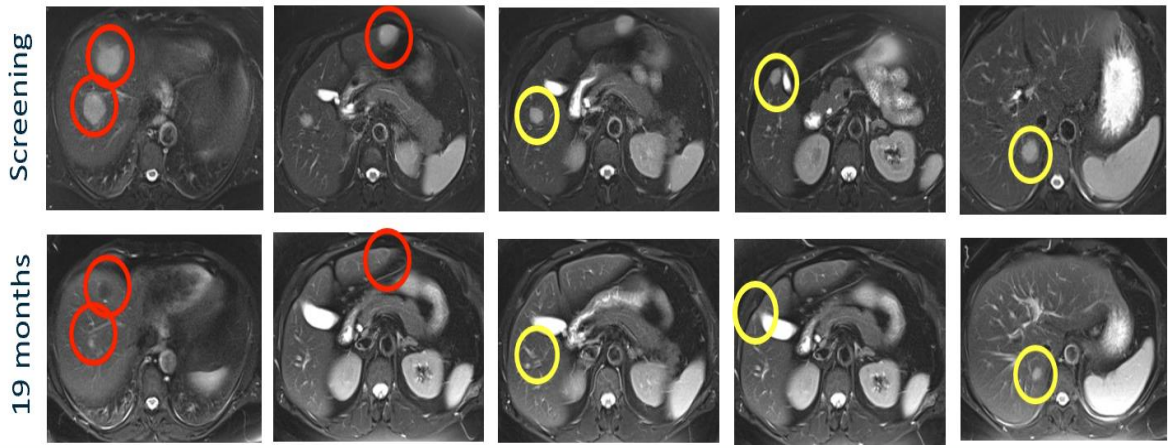
- Osteosarcoma (75-85%)
- Prostate cancer (46%)
- Renal cell carcinoma (45.2%)
- Hepatocellular carcinoma (39.5%)
- Breast cancer (21-32%)
- Colorectal cancer (31.7%)

Patients with liver & lung metastases have poorer clinical outcome, higher mortality and respond less to immunotherapy

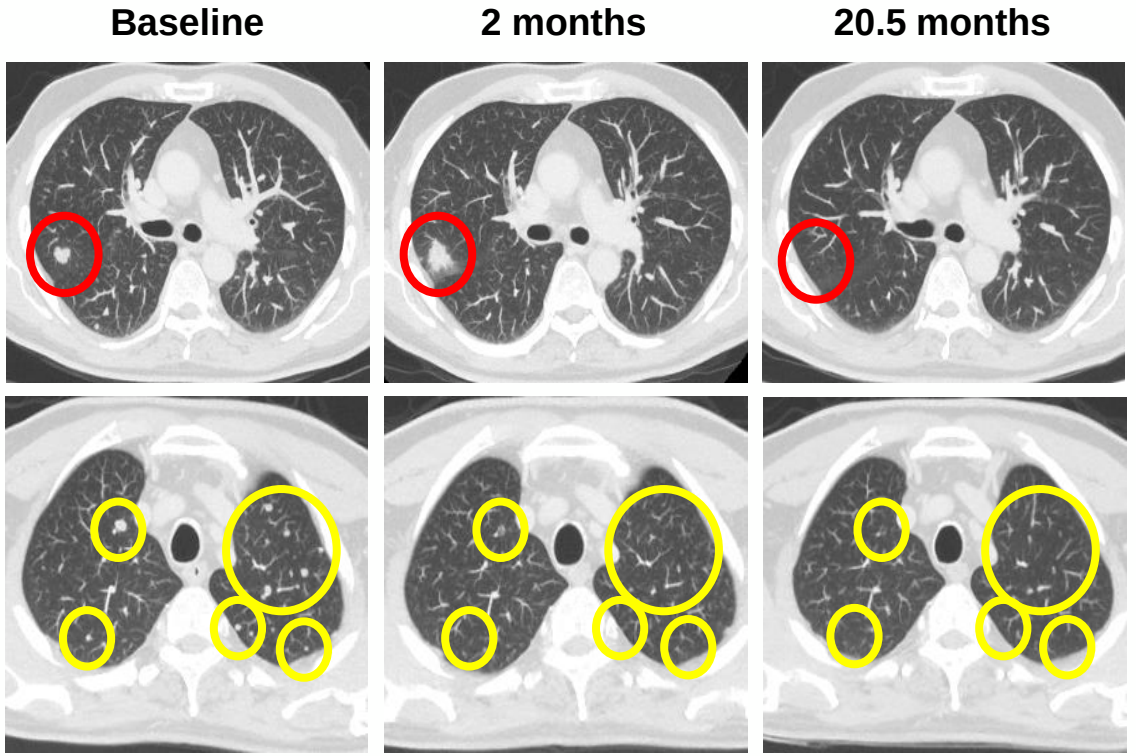
Tsilimigras DI Nat Rev Dis Primers. 2021 Apr 15;7(1):27 . Yu et al Nat Med Jan 2021; Lung-specific metastasis: the coevolution of tumor cells and lung microenvironment | Molecular Cancer | Full Text

RP1 Activity Seen in Patients Liver and Lung Metastases

Durable activity in injected and non-injected liver
Ipi/nivo failed metastatic uveal melanoma



Durable activity in injected and non-injected lung
Ipi/nivo failed metastatic melanoma



Injected Non-injected

Data Supports Expansion into Cancers with Liver and Lung Metastases

- Biomarker data (i.e. increase in IFN-γ) demonstrate ability to convert immunologically silent TMEs to immunologically inflamed
- RPx leads to systemic and durable responses in injected and non-injected lesions including liver and lung
- Enhanced ORR observed with deep/visceral (±superficial) injections:
  - ORR was 40% (6/15) in patients receiving lung and liver injections
  - Median number of RP1 injections in the lung and liver was 8 and 6.5 respectively
- Deep/visceral lesions Including liver and lung can be safely injected

Data from IGNYTE

Confirmed BOR, n (%)	Deep/visceral +/- superficial (n = 36)	
	Deep/visceral plus superficial (n = 14)	Deep/visceral only (n = 22)
CR	0	3 (13.6)
PR	6 (42.9)	6 (27.3)
SD	4 (28.6)	8 (36.4)
PD	3 (21.4)	5 (22.7)
ORR	**6 (42.9)**	**9 (40.9)**

Source: In G, "Response analysis for injected and non-injected lesions and the safety and efficacy of superficial and deep RP1 injection in the registrational cohort of anti-PD-1-failed melanoma patients of the IGNYTE trial." Poster presented at: American Society of Clinical Oncology, June 1, 2025; Chicago, IL.

Unmet Need in Uveal Melanoma with High Rates of Liver Metastases

- ~1,000 cases in the US per year[1]
- 70-90% of cases metastasize to liver only ~10% of patients survive > 1 year[3,4]
- Recent approval of Kimmtrak® in 1L HLA-A2 positive Uveal Melanoma based on OS
  - 40%-50% HLA-A2 positive
- No standard of care in 1L HLA neg or 2L[2]

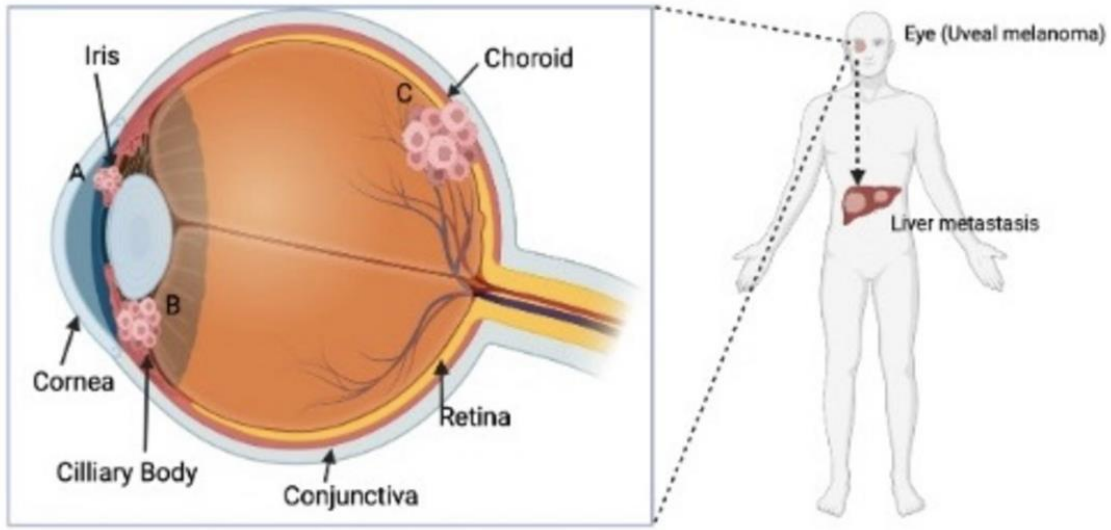


Figure 4. Locations of uveal melanoma. Created using BioRender.

1. Carvajal RD et al. Br J Ophthalmol 2017; 2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Melanoma: Uveal. Version 1.2023.; 3. Jager MJ, et al. Nat Rev Dis Primers. 2020;6(1):24; 4. Khoja L, et al. Ann Oncol. 2019;30(8):1370-80. Image sourced: Sah, V. (2022, November 25). *Novel immunotherapies for metastatic uveal melanoma - From bench to clinical biomarkers*. https://gupea.ub.gu.se/handle/2077/73552

RP2 + Nivolumab Demonstrated Promising Signal in Metastatic Uveal Melanoma

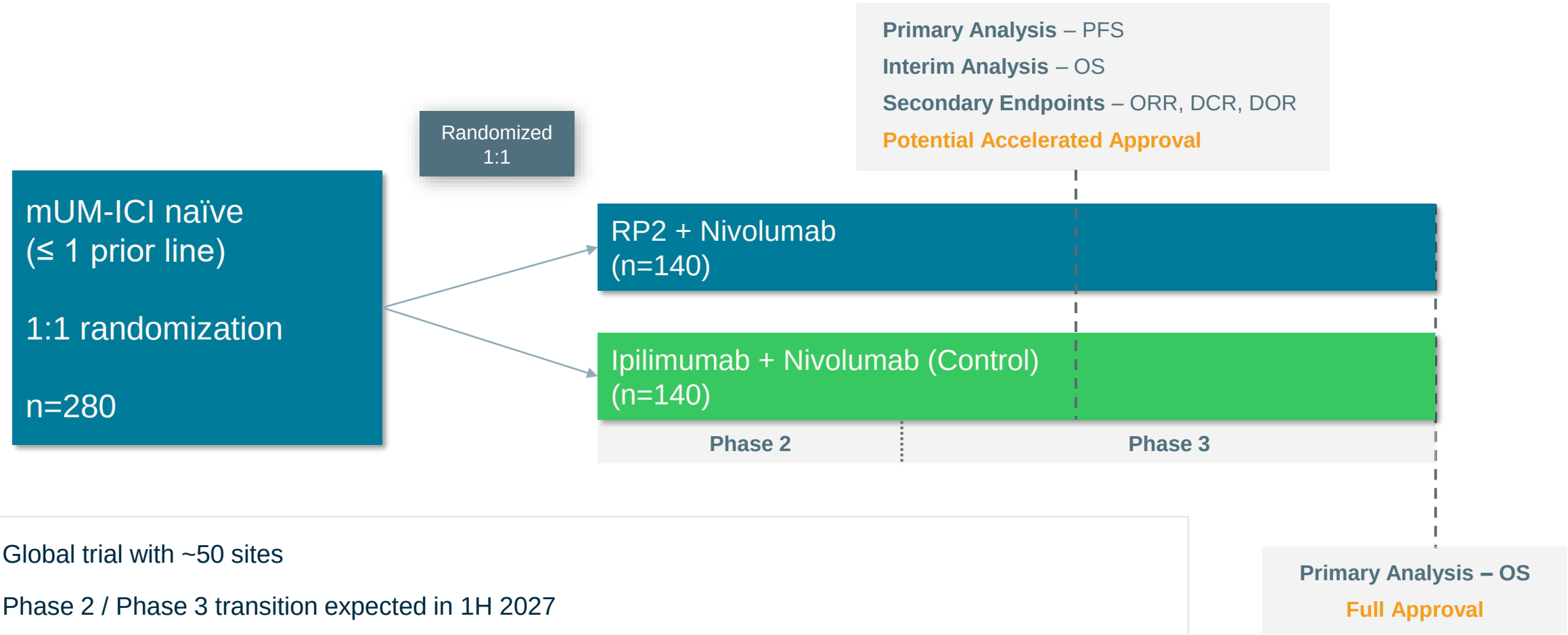
Phase 1	RP2 monotherapy (n = 3)	RP2 + nivolumab (n = 14)	Total (N = 17)
Confirmed BOR, n (%)			
CR	0 (0)	0 (0)	0 (0)
PR	1 (33.3)	4 (28.6)	5 (29.4)
NE	1 (33.3)	1 (33.3)	2 (11.8)
SD	0	5 (35.7)	5 (29.4)
PD	1 (33.3)	4 (28.6)	5 (29.4)
ORR (CR + PR)	**1 (33.3)**	**4 (28.6)**	**5 (29.4)**
DCR (CR + PR + SD)	**1 (33.3)**	**9 (64.3)**	**10 (58.8)**

HLA-A*02:01 status	Positive (n = 6)	Negative (n = 11)	Total (N = 17)
Confirmed BOR, n (%)			
PR	1 (16.7)	4 (36.4)	5 (29.4)
SD	2 (33.3)	3 (27.3)	5 (29.4)
PD/NE	3 (50.0)	4 (36.4)	7 (41.2)

- Total **of 47 liver lesion injections** across **12/17 patients***
- **3 Previous Lines** of treatment
- **ORR was 29.4% (all PRs) and DCR was 58.8%**
- Median DOR was **11.5 months**
- **Responses observed regardless of HLA status**
- Most common grade 1 or 2 TRAEs (≥20%) were pyrexia, chills, fatigue, hypotension, and pruritus
- No grade 4 or 5 TRAEs

*70.6% [12/17] patients received prior anti–PD-1 and anti–CTLA-4 therapy; data presented at ASCO 2024

RP2 in Metastatic Uveal Melanoma: Registrational REVEAL Study Ongoing

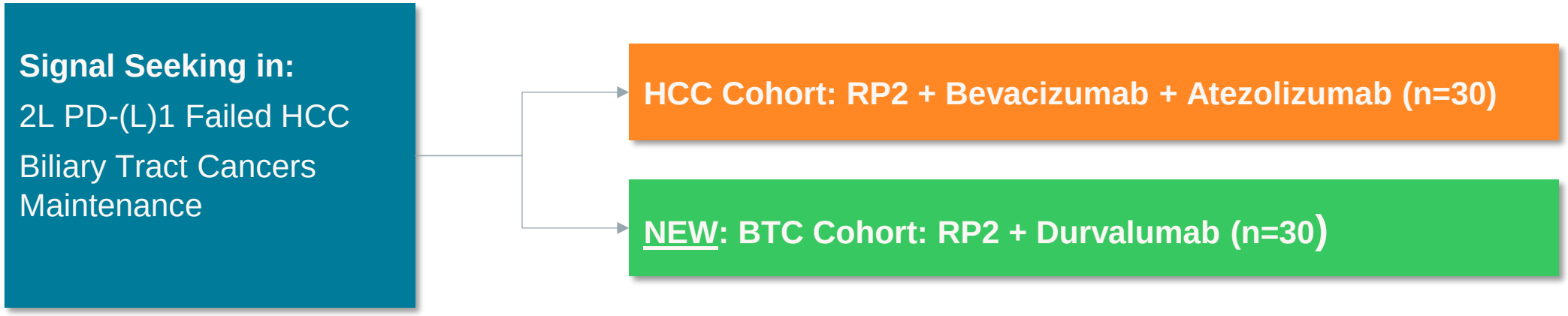


- Global trial with ~50 sites
- Phase 2 / Phase 3 transition expected in 1H 2027
- PFS analysis in 2028 as basis for potential accelerated approval

https://clinicaltrials.gov/study/NCT06581406

RP2 Liver Primary / Metastases Study Cohorts Enrolling

- **2L PD-1 Failed Hepatocellular Carcinoma (HCC): ~3,500 cases in the US; SOC limited to TKI**
- **Biliary Tract Cancers (BTC): ~5,000 cases in the US; no current trials in BTC 1L maintenance**



- HCC cohort expansion into South Korea; currently 11/13 US sites activated
- Preliminary HCC data expected 1H 2026
- FPI BTC cohort expected 2H 2025

Source: CancerMPact® Patient Metrics, Oracle (formerly known as Kantar Health; available from www.cancermpact.com) and Replimune analysis.
Note: all epi numbers are for the year 2030 Addressable defined as treated U.S. patients.

RPx Platform: What's Next?

Nina Aragam
SVP, Portfolio Strategy & Program Management

RPx has the Potential to Reach Up to ~125K Patients in the U.S.

Melanoma & Skin Cancers

Build Around Foundational Approval In Melanoma

- PD1-Failed Melanoma
- Merkel Cell Carcinoma
- Basal Cell Carcinoma
- Angiosarcoma
- Solid Organ Transplant Skin Cancer
- PD1-Failed cSCC
- Neoadjuvant Skin Cancers

~70K+ patients

Liver Primary / Metastases

Expand into Specific Cancers with High Liver Metastases

- Uveal melanoma
- HCC
- Biliary Tract Cancer

~10K+ patients

Lung Primary / Metastases

Expand into Specific Cancers with High Lung Metastases

- NSCLC
- Mesothelioma
- HNSCC
- Renal Cell

~45K+ patients

Source: CancerMPact® Patient Metrics, Oracle (formerly known as Kantar Health; available from www.cancermpact.com) and Replimune analysis. Note: all epi numbers are for the year 2030 Addressable defined as treated U.S. patients.

RPx Platform Can Broaden and Provide a Novel Approach to Cancer Care

Monotherapy in Patients Unable to Receive IO

- Immunocompromised patients
- Patients ineligible or discontinue due to AEs (~8-13%)[1,2,3]

Rare Cancers with High Unmet Need

- Uveal, NMSC and melanoma subtypes (i.e. Mucosal, Acral)
- Adrenocortical carcinoma
- Sarcomas

Surgery Sparing

- Patients not amenable to surgery due to tumor size, location/deforming, impact to QoL, loss of organ
- High-risk patients for cancer prevention

Optimize/Broaden Drug Delivery

- Endobronchial ultrasound (EBUS) for thoracic cancers
- Advanced imaging technology/robotics

1. Brahmer JR, Long GV, Hamid O, et al. Safety profile of pembrolizumab monotherapy based on an aggregate safety evaluation of 8937 patients. *Eur J Cancer*. 2024;199:113530. doi:10.1016/j.ejca.2024.113530. 2. Libtayo PI 3. *Clin Cancer Res* (2025) 31 (12): 2413–2425.

Anticipated Future Milestones

2025	2026	2027+
1st TUDRIQEV® Potential Approval (anti-PD-1 failed melanoma)	Preliminary RP2 HCC data	mUM PFS readout for potential AA
RP2 BTC cohort FPI	IGNYTE NMSC & ARTACUS Data / Publications	TUDRIQEV® I-3 Data for Global Access

Potential RPx Future Compendia or Approval Opportunities

Q&A

Investor Day
June 24, 2025

Thank You

Replimune®