January 14, 2026
JPM Healthcare Conference

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.

Poised to Deliver on the Promise of Oncolytic Immunotherapy

Sushil Patel, PhD
CEO, Replimune

RPx Oncolytic Immunotherapy Overcoming Historical Hurdles

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~150 Accounts Ready on Day 1

Near-term PDUFA date of April 10, 2026 for melanoma with commercial team "launch ready"

Go-to market model optimized to enable oncologist/interventional radiologist (IR) coordination

Other logistics addressed to enable operational efficiency

~1,200 Deep Injections Administered

Ability to inject RPx into deep lesions safely and repeatedly

Liver & lung injections successfully completed using image guidance

IRs excited to enable a new treatment paradigm

~1,000 Patients Treated Across the RPx Platform

Durable and systemic activity seen in difficult to treat settings

Randomized trials well underway for RP1 & RP2 (in uveal)

Expansion beyond skin cancer into HCC and BTC

RPx Platform Intended to Activate Systemic Immune Response

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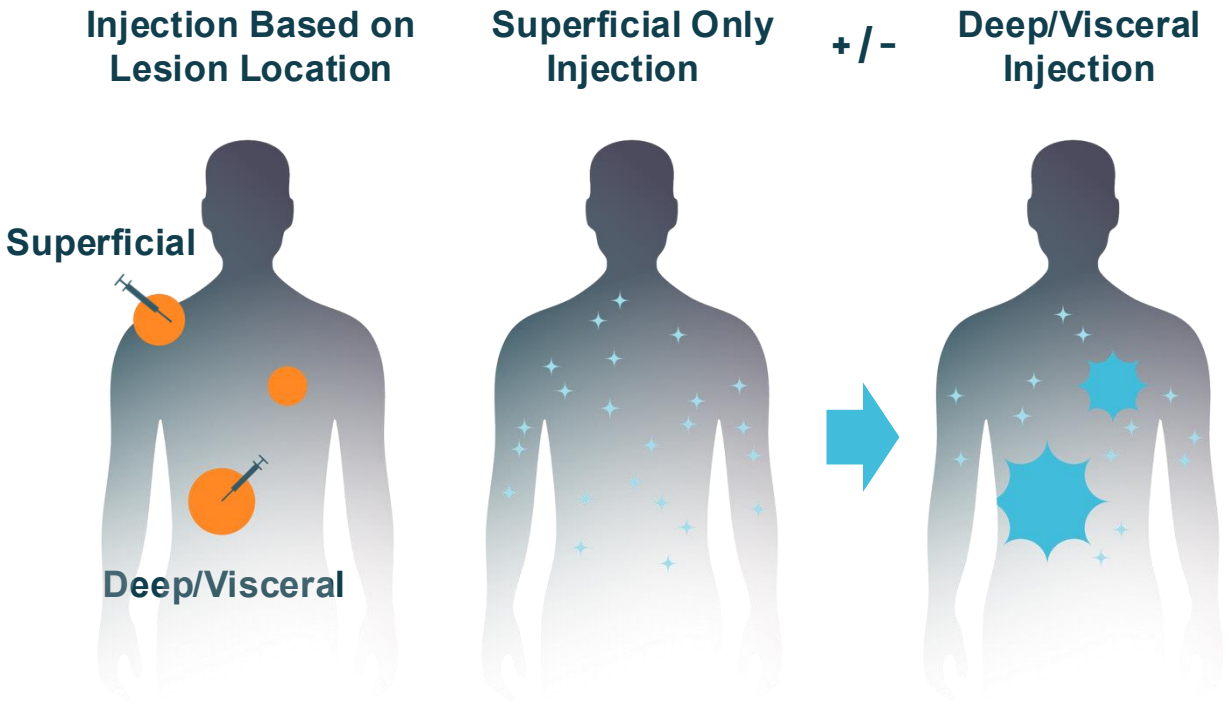
RPx Immune Activating Pay Loads

	GALV-GP R-	GM-CSF	Anti-CTLA-4
RP1	✓	✓	
RP2	✓	✓	✓

+ Anti-PD-1 Therapy



RPx engineering and the administration approach aims to drive <u>both</u> robust local and distant / systemic anti-tumor response to drive better patient outcomes

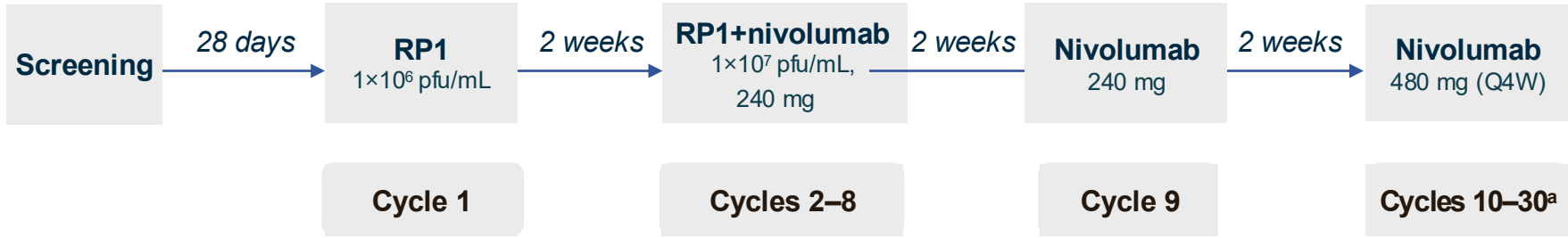
Anti-PD-1 Failed Melanoma (IGNYTE)

IGNYTE Study in Anti-PD-1 Failed Melanoma: Rigorous Criteria for Anti-PD-1 failure

IGNYTE

Anti-PD-1 failed melanoma cohort

(140 pts)



Primary objectives
- Safety and tolerability
- ORR

Secondary objectives
- DOR
- CR rate
- DCR
- PFS
- 1-year and 2-year OS

Criteria for prior anti–PD-1 failure

- Disease progression confirmed by 2 assessments at least 4 weeks apart
- Confirmed progression while on anti-PD1 treatment
- Anti-PD1 treatment continued for at least 8 consecutive weeks
- Anti-PD1-containing therapy must be the immediate prior line of treatment before enrollment

[a]RP1 can be reinitiated beyond 8 cycles if protocol-specified criteria are met.

Clinically Meaningful ORR in Resistant Subgroups

BOR n (%)	All patients (N = 140)	Prior anti-PD-1 with anti-CTLA-4 (n = 65)	Stage IVb–IVd (n = 68)	Primary resistance (n = 92)[a]	Secondary resistance (n = 48)[b,c]
CR	23 (16.4)	6 (9.2)	4 (5.9)	16 (17.4)	7 (14.6)
PR	24 (17.1)	11 (16.9)	13 (19.1)	16 (17.4)	8 (16.7)
SD	30 (21.4)	15 (23.1)	14 (20.6)	15 (16.3)	15 (31.3)
PD	54 (38.6)	26 (40.0)	29 (42.6)	39 (42.4)	15 (31.3)
ORR	**47 (33.6)**	**17 (26.2)**	**17 (25.0)**	**32 (34.8)**	**15 (31.3)**
DOR, median (95% CI), months	**24.8 (14.1, NR)**	**16.5 (7.9, 25.6)**	**14.8 (7.9, 22.6)**	**22.6 (9.5, NR)**	**25.6 (14.8, NR)**

Consistent response rates were also seen across clinical patient subgroups, including the following:

- **26.2% ORR** in patients who had **prior anti-PD-1 and anti-CTLA-4**
- **25.0% ORR** in patients who had **stage IVb-IVd visceral disease**

Wise-Draper, T. (2025, Nov. 7). *Biomarker and updated clinical data for RP1 plus nivolumab in anti–PD-1–failed melanoma from the IGNYTE trial demonstrate reversal of mechanisms of resistance to immune checkpoint blockade*. Society for Immunotherapy of Cancer Annual Meeting, National Harbor, MD, USA.
IGNYTE study: RP1+Nivo in anti-PD1 failed melanoma. Centrally reviewed RECIST 1.1 responses; all patients have ≥12 months follow-up.
Data cutoff: October 15, 2024 (7 months post the primary analysis). [a]Primary resistance: progressed within 6 months of starting the immediate prior course of anti–PD-1 therapy. [b]Secondary resistance: progressed after 6 months of treatment on the immediate prior course of anti–PD-1 therapy. [c]Includes 1 patient with unknown resistance status.

Responses with RP1 plus Nivolumab in the IGNYTE Study vs. Immediate Prior Anti-PD-1 Regimen

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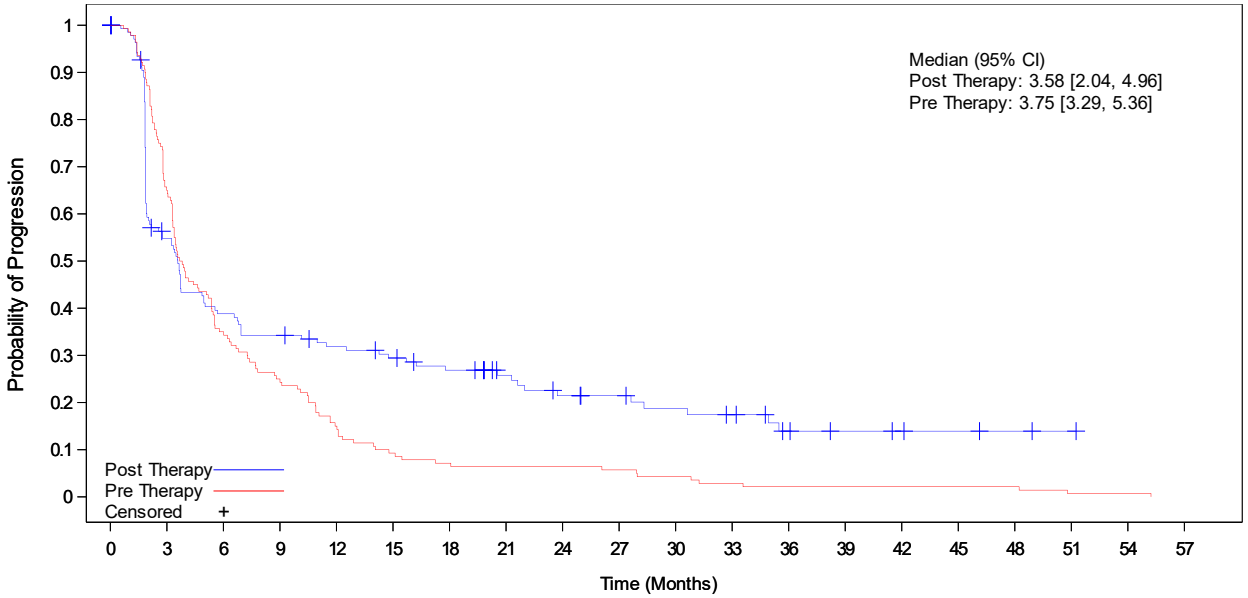
Summary of Response on Immediate Prior Anti-PD-1 and in the IGNYTE Study (N=104)

IGNYTE Non-Adjuvant Patient Population	Time on Prior Treatment months	ORR on prior PD-1 based therapy (95% CI)	ORR during IGNYTE (95% CI)
All Patients (N=104)	5.6	**11.5%**	**29.8%**
Responders Only (N=31)	5.6	**12.9%**	**100%**
Primary Resistance (N=64)	4.0	**0%**	**28.1%**
Secondary Resistance (N=40)	14.0	**30.0%**	**32.5%**

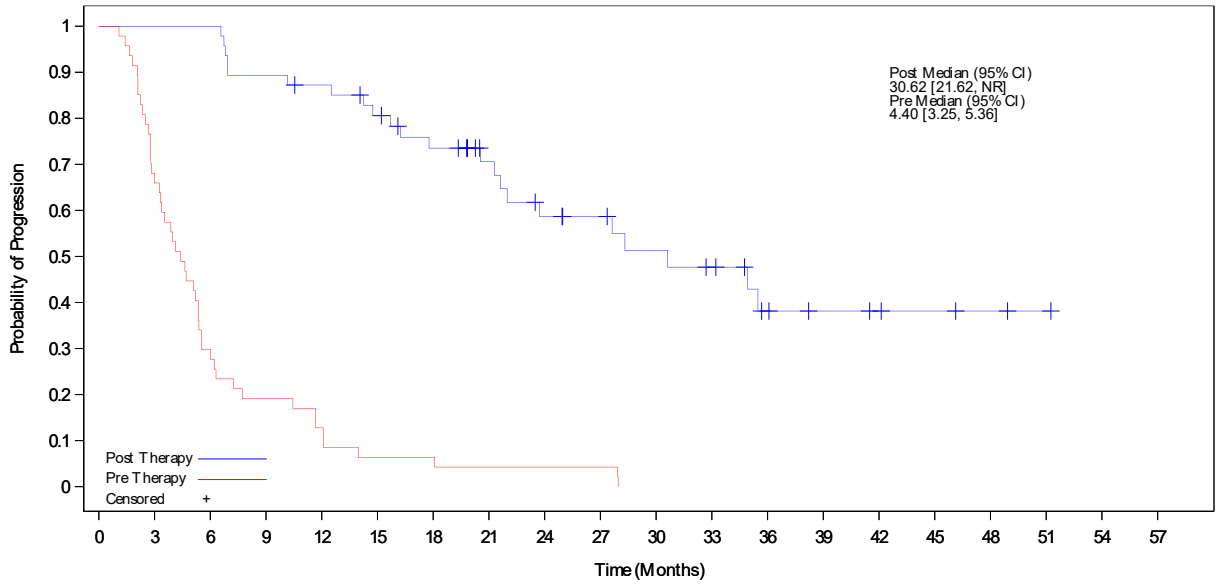
Replimune data on file.

Time to Progression with RP1 plus Nivolumab vs. Immediate Prior Anti-PD-1 Regimen

Pre versus post Therapy Time to Progression (all IGNYTE patients)



Pre versus post Therapy Time to Progression (responders only)



Replimune data on file. Key: Post Therapy (blue line)=PFS of VO in combination with nivolumab in the IGNYTE study, Pre Therapy (red line)=time to progression on immediate prior anti-PD-1 containing regimen

Confirmatory IGNYTE-3 Study: Enrollment on Track

IGNYTE-3

Advanced cutaneous melanoma

Progressed on anti-PD-1 AND anti-CTLA-4 OR not candidates for anti-CTLA-4

N=~400

Randomized 1:1

Interim Analysis – OS

RP1 + Nivolumab
(n=200)

Treatment of Physician's Choice (TPC*)
(n=200)

>60 patients enrolled

- Global trial with ~110 sites -> ex-US expansion initiated
- EMA engagement completed
- **Interim OS analysis planned for 2H 2027**

Primary Analysis – OS

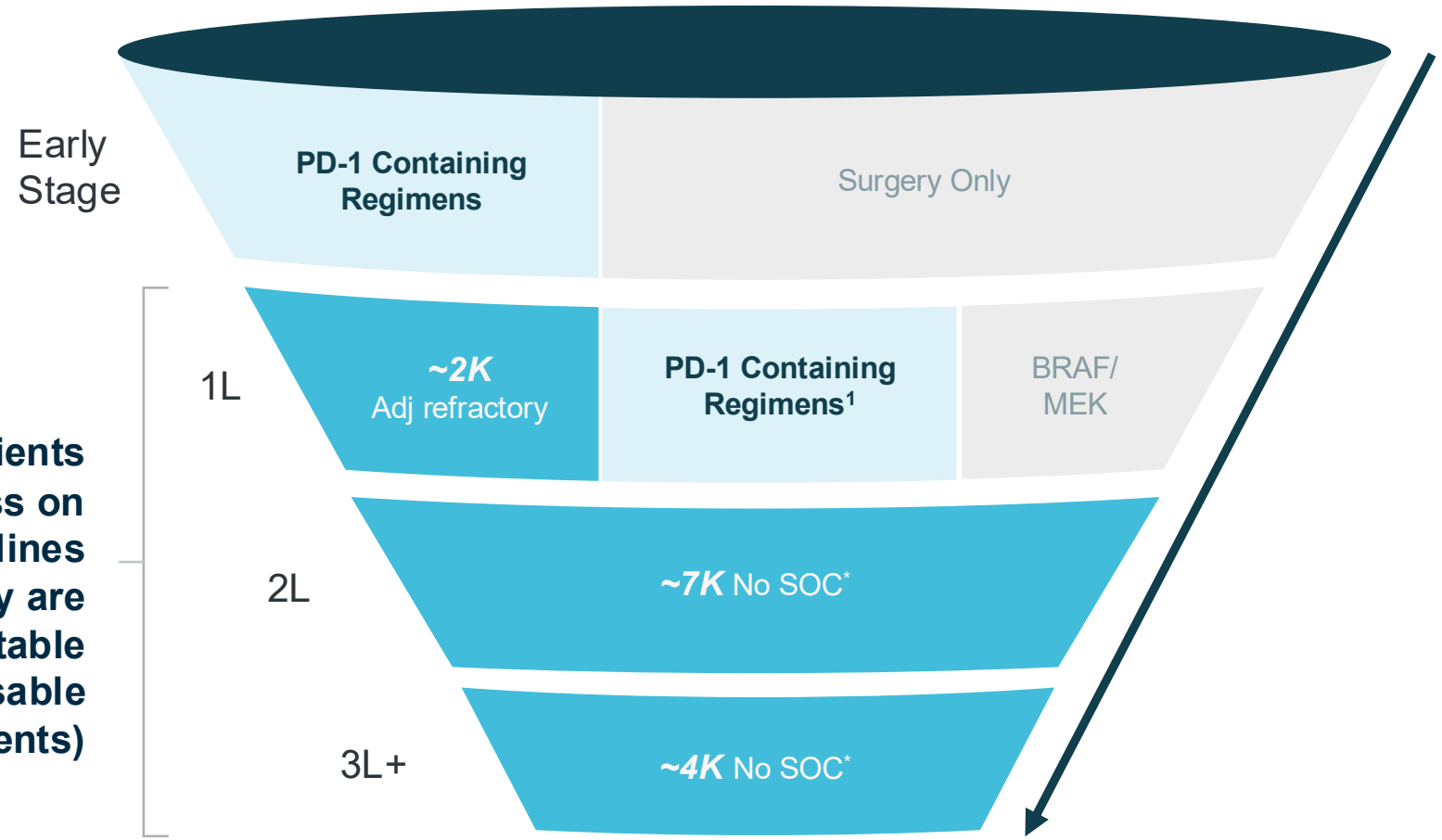
Secondary Endpoints – PFS/ORR

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

Prepared for Commercial Launch Success in Melanoma

~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

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Injection **In-Office**

~20% of pts require **only superficial injections**

Injection via **Image Guidance** for Deep Lesions*

~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

"If we can biopsy the tumor, we can inject it"

- Interventional Radiologist

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

Interventional Radiologists Excited to Play a New Role in Immunotherapy Treatment

>520K

US interventional oncology procedures performed in 2024[1]; expected to increase

"There is a rising interest in intra-tumoral therapies with IRs"

- Interventional Radiologist

"Seeing this level of RP1 activity in visceral un-injected lesions is very motivating for IRs. This is not something we have seen with other intra-tumoral agents to date"

- Rahul Sheth, M.D., F.S.I.R.

Source: Symphony Health Claims data, full year 2024. Biopsy and IO Procedures performed by Interventional Radiologists, Vascular & Interventional Radiologists, Radiologists, or Diagnostic Radiologists. IO Procedures include Ablation, Embolization, and Radiotherapy.

Initial U.S. Melanoma Launch Focus: 150 Accounts
Expansion into 200 additional accounts within 6 to 9 months

Replimune®

Hospital (50%)
Integrated Oncologists and IRs

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®
MAYO CLINIC
BJC HealthCare
MOFFITT CANCER CENTER
KAISER PERMANENTE
BAPTIST HEALTH

Community (50%)
Referrals established with IR services*

TEXAS ONCOLOGY
More breakthroughs. More victories.®
HOA Hematology-Oncology Associates of CNY
HOG HIGHLANDS ONCOLOGY GROUP
TENNESSEE ONCOLOGY
FLORIDA CANCER SPECIALISTS & Research Institute
OKLAHOMA CANCER SPECIALISTS AND RESEARCH INSTITUTE

~70 patients have received RP1 via Compassionate Use or Expanded Access

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

U.S. Manufacturing Ready for Commercialization

State-of-the-art facility for end-to-end GMP manufacturing

Drug substance production

Fill-finish

Packaging & labeling

Commercial supply ready for market

Opportunities in Skin Cancers Beyond Melanoma

Expanding into Other Skin Cancers with a Novel Approach

Melanoma & Skin Cancers

RP1

- PD1-failed Melanoma (PDUFA pending)
- NMSC including PD-1 failed (e.g., CSCC, MCC, BCC)
- Angiosarcoma
- Solid Organ Transplant Skin Cancer (ARTACUS study)
- Neoadjuvant Skin Cancers (e.g., CSCC)

Monotherapy in Patients Unable to Receive Checkpoint Inhibitors

- Immunocompromised solid organ transplant (SOT) patients (ARTACUS study)
- Patients' ineligible for Immunotherapy or discontinue due to AE's (~8-13%)[1,2,3]

Early Disease and/or Surgery Sparing

- Neoadjuvant settings
  - Includes resectable & surgically ineligible due to tumor location (impact to QoL) e.g., low-risk CSCC
- High-risk patients for cancer prevention

Activity already demonstrated

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.

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

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Results from the ARTACUS Study

Confirmed Best overall response, n (%)	Intend To Treat Population (n=26)
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)**

- Optimal management of CSCC in SOT is not well established and significant unmet need remains[1,2]

Heart Transplant Patient Example

Migden, M. (2025, October 26) RP1 monotherapy in solid organ transplant recipients with locally advanced cutaneous squamous cell carcinoma (ARTACUS), Society for Melanoma Research 22nd International Congress, Amsterdam, Netherlands.

[1]Struckmeier AK, et al. Transplant Rev (Orlando). 2024;38:100882. [2]National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Squamous cell skin cancer. Version 1.2026. Accessed September 11, 202 https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf.

Complete Responses Observed in RP1 Monotherapy in Low Risk, Resectable Neoadjuvant cSCC

Confirmed BOR, n (%)	Clinical Response (n=12)	Pathological Response (n=12)
ORR	**12 (100)**	**12 (100)**
CR	**8 (67)** **No surgery needed**	**10 (83)***
PR	4 (33)	2 (17)

CR/cPR Patient Example

Baseline — **12 weeks** → **Pre Surgery**

"It's incredibly exciting, all but 2 lesions were composite CRs! Nobody had any AEs of any kind other than some local erythema or itching. A well tolerated, effective alternative to surgery for small SCCs!!!"

Principal Investigator, Dr Sherrif Ibrahim (Rochester)

Replimune data on file. Investigator supported trial: *A Phase 1b, single-center, open-label study, evaluating efficacy and safety of RP1 for the treatment of resectable cutaneous Squamous Cell Carcinoma;* *pCRs were confirmed by biopsy in 8 patients that did not undergo Surgery

Expanding the RPx Opportunity via Deep Injections

Broad Tumor Injectability with ~1,200 Deep RPx Injections Successfully Conducted

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Metastases in the liver/lung is common and difficult to treat*

ORR benefit observed & acceptable safety profile with RPx deep/ visceral injections

RP2 HCC/BTC Ph1 cohort enrolling

~800 lung & liver RPx injections completed

RP2 Uveal study (REVEAL) enrolling with injection of liver mets

Deep/visceral injections allow RPx expansion

*SEER 2021 Estimated Deaths. From SEER Cancer Stat Facts by indication; Riihimaki et al Cancer Med 2018; Yu et al Nat Med Jan 2021

Enhanced ORR with Deep/Visceral (± superficial) Injections with Acceptable Safety Demonstrated in the IGNYTE study

Efficacy by Injection Type by BICR using RECIST 1.1 (patient-level data)

Confirmed BOR, (%)	Superficial only (n=104)	Deep/visceral ± superficial (n=14)	Deep/visceral only (n=22)
ORR	**29.8**	**42.9**	**40.9**

Safety by Injection Location (most common TRAEs)

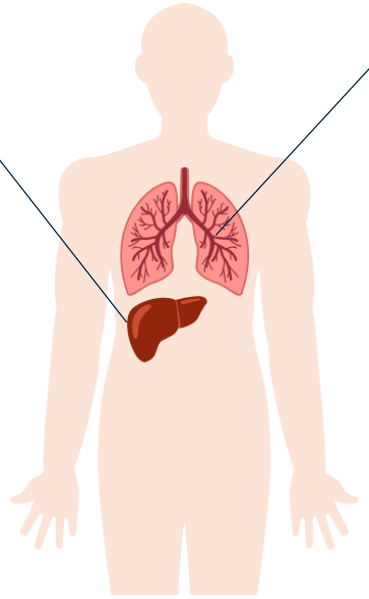
Preferred term (%)	Superficial only (n = 104)		Deep/visceral ± superficial (n = 36)	
	All grades	Grades 3/4	All grades	Grades 3/4
Total	89.4	**14.4**	91.7	**8.3**
Fatigue	31.7	**1.0**	36.1	**0**
Pyrexia	29.8	**0**	33.3	**0**
Chills	28.8	**0**	41.7	**0**
Nausea	21.2	**0**	25.0	**0**
Diarrhea	13.5	**1.0**	16.7	**0**
Vomiting	13.5	**0**	13.9	**0**
Headache	12.5	**0**	13.9	**0**
Influenza-like illness	12.5	**0**	33.3	**0**
Injection-site pain	12.5	**0**	22.2	**0**

In GK et al. ASCO 2025. Abstract 9547. Poster 20. Analysis from IGNYTE RP1 + Nivo (Anti-PD-1 failed melanoma)

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

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

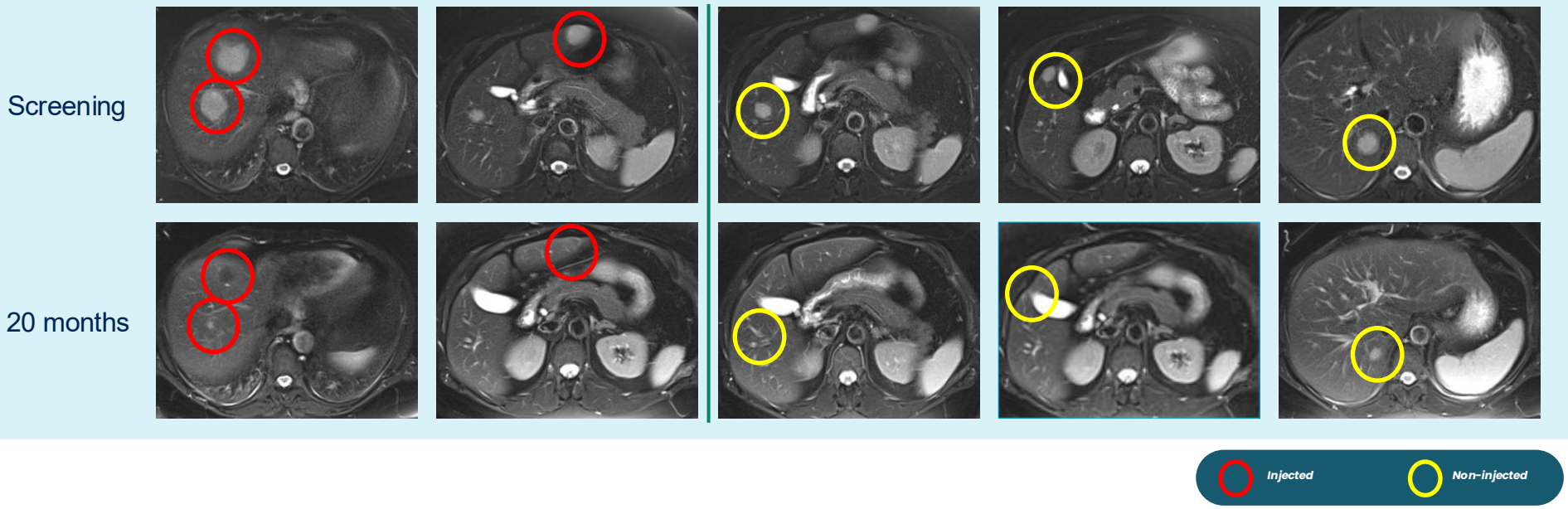
- Osteosarcoma (75-85%)
- Prostate cancer (46%)
- Renal cell carcinoma (45.2%)
- Hepatocellular carcinoma (39.5%)
- Breast cancer (21-32%)
- Colorectal cancer (31.7%)

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

Metastatic Uveal Melanoma: ~70% of Patients Have Liver Metastases

Phase 1 Study Confirmed BOR, n (%)	RP2 monotherapy (n = 3)	RP2 + nivolumab (n = 14)	Total (N = 17)
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)**

Patient 4403-0017: PR



- Total **of 47 liver lesion injections** (**12/17 pts**)
- **3 prior LOT***
- mDOR **11.5 months**
- **Responses observed regardless of HLA**
- 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; Sacco J. et al. ASCO 2024.

RP2 Liver Mets/Liver-focused Studies are Well Underway

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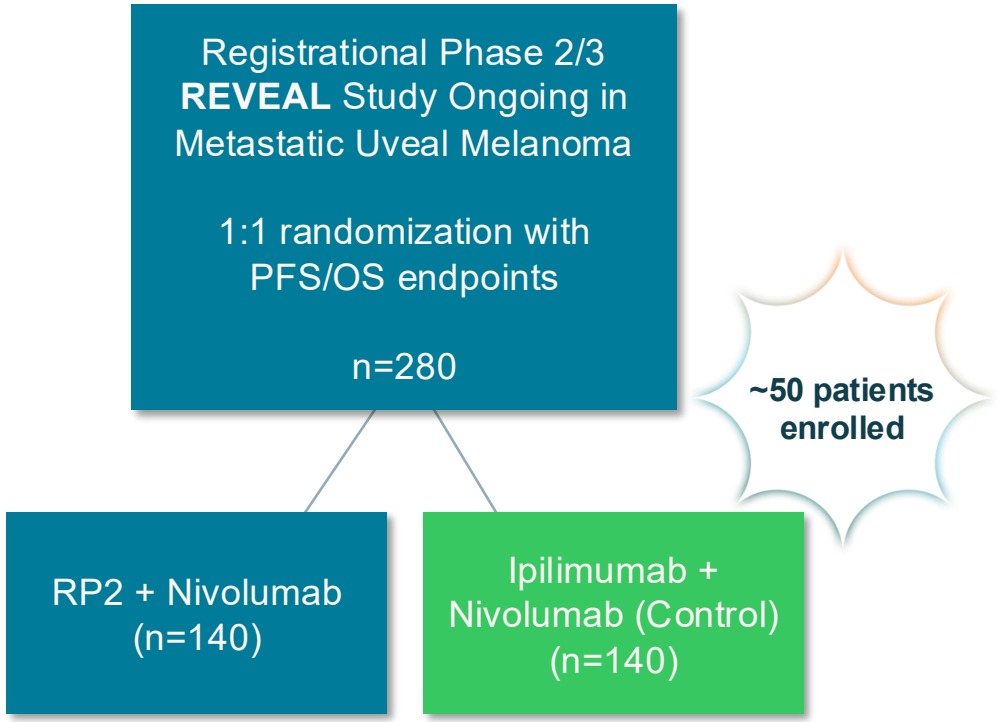
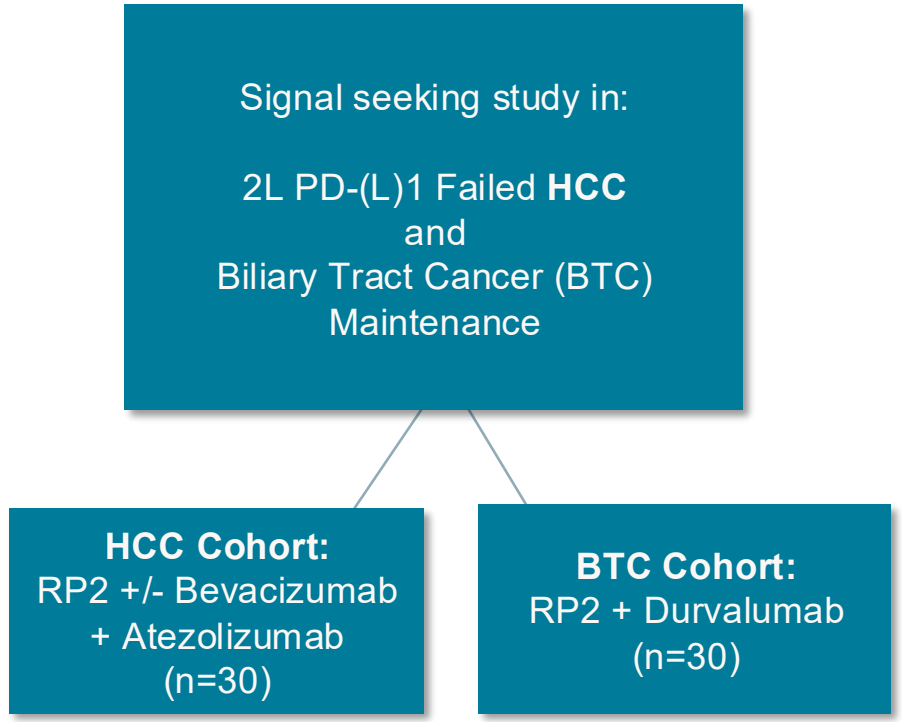
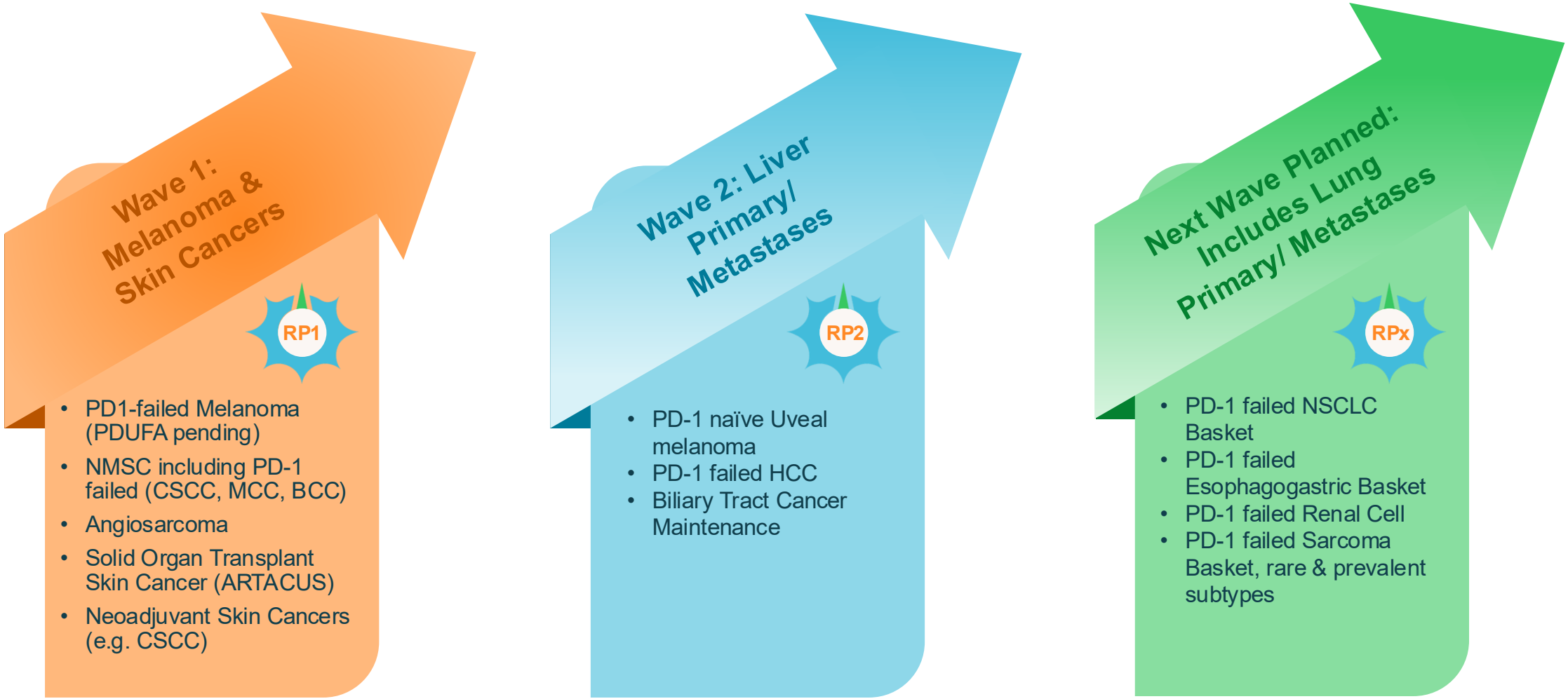


- Global trial with ~50 sites, ex-US expansion initiated
- Phase 2/3 transition at 90 patients with 6-month follow-up expected in Q1 2027
- PFS analysis basis for potential accelerated approval



- First patients enrolled in BTC cohort in Q4 2025
- Preliminary HCC data expected Q4 2026

RPx Beyond Skin Cancers: Potential to Reach Up to ~130K Patients in the U.S.



Source: CancerMPact® Patient Metrics, Oracle (formerly known as Kantar Health; available from www.cancermpact.com, accessed on 9/9/25) and Replimune analysis
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Corporate Highlights

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Near-term PDUFA Date for RP1 in Anti-PD-1 Failed Melanoma

7 Ongoing Clinical Trials with RP1 and RP2 to Support RPx Expansion

In-house U.S. based Manufacturing Facility with RP1 Launch Supply Produced

Poised for Commercial Launch Success – >150 Accounts Ready on Day 1

Broad Market Opportunity in High Unmet Need Cancers

Cash of $269.2M as of 12/31/25 (unaudited)

Thank You

Replimune®