Abstract: TPS9597

# An open-label, multicenter, phase 1b/2 study of RP1, a first-in-class, enhanced-potency oncolytic virus in solid organ transplant recipients with advanced cutaneous malignancies (ARTACUS)

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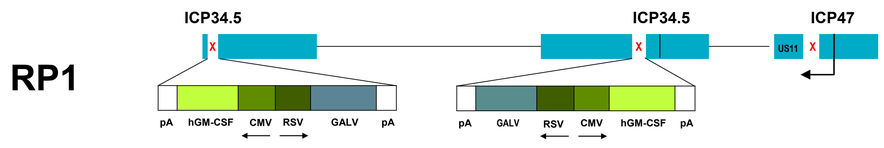
## Background

- Solid organ transplantation (SOT) has emerged as an important lifesaving procedure for patients with end-organ diseases characterized by dysfunction or specific organ function failure
- For SOT recipients, transplant rejection is a major complication and commits patients to lifelong immunosuppressive therapy to prevent rejection
- The chronic immunosuppression required to prevent rejection of a transplanted organ impairs immune surveillance, allowing tumors to proliferate unchecked, and increases the risk of a wide range of cutaneous tumors
- Nonmelanoma skin cancer (NMSC) is the most common posttransplant malignancy in SOT recipients [1]
- Cutaneous squamous cell carcinoma (CSCC) and basal cell carcinoma (BCC) account for >90% of all cases of NMSC [2]
- CSCC is associated with a higher mortality rate than breast or colon cancer in SOT recipients [3]
- The management of locally advanced and metastatic CSCC to skin, soft tissue, or lymph nodes in SOT patients is not established, but generally follows therapeutic approaches used in non-SOT patients. This includes localized radiation therapy, systemic chemotherapy, and targeted therapy
- Withdrawal of immunosuppressive therapy may be required for the management of CSCC, but may be associated with high rates of graft failure
- Thus, there is a high unmet need for a safe and effective treatment for SOT recipients who experience cutaneous malignancies that also protects patients from allograft rejection
- RP1 is an oncolytic virus (herpes simplex virus-1 [HSV-1]) that expresses a fusogenic glycoprotein (GALV-GP R-) and granulocyte macrophage colony stimulating factor (GM-CSF) [4]




- In preclinical studies, RP1 induced immunogenic tumor cell death and provided potent systemic antitumor activity [4]; clinical data in combination with an anti-PD1 antibody has demonstrated a high rate of deep and durable responses in non-SOT patients with advanced skin cancers [5]

### Objective

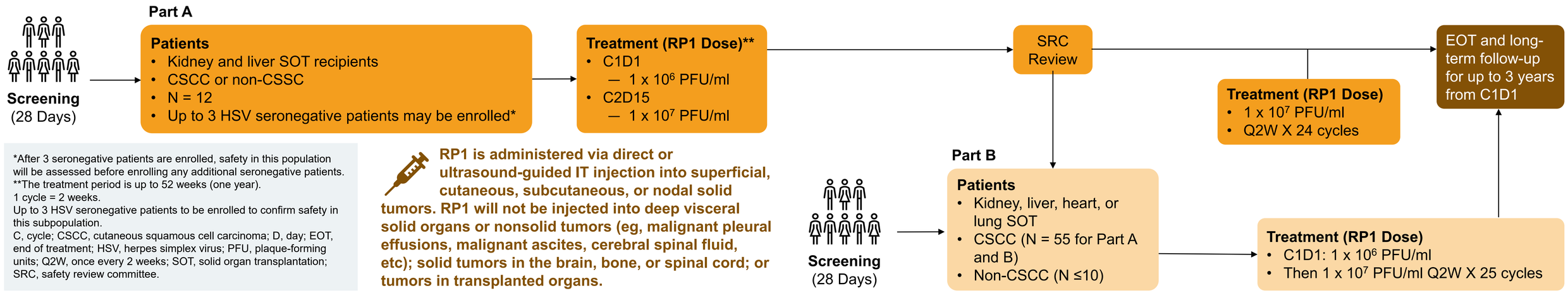
To assess the safety and efficacy of single agent RP1 in organ transplant recipients (kidney, liver, heart, and lung) with skin cancers, with focus on CSCC

## Methods

### Study Design

- This is a Phase 1b/2, multicenter, open-label study evaluating the efficacy and safety of RP1 monotherapy for the treatment of locally advanced or metastatic cutaneous malignancies (to skin, soft tissue, or lymph nodes) in up to 65 evaluable SOT patients
- The study has two parts (Parts A and B); patients in both parts will receive RP1 via direct or ultrasound-guided intratumoral (IT) injection into superficial, cutaneous, subcutaneous, or nodal solid tumors to assess the safety and tolerability of RP1 treatment
- The primary efficacy population in Parts A and B (combined) is up to 55 SOT patients with CSCC. The enrollment of SOT patients with CSCC will determine study duration
- Up to 10 additional SOT patients with non-CSCC skin cancers may enroll concurrently with the 55 CSCC patients to explore preliminary safety and efficacy of RP1 in this patient population

## Trial Design




*After 3 seronegative patients are enrolled, safety in this population will be assessed before enrolling any additional seronegative patients.
**The treatment period is up to 52 weeks (one year).
1 cycle = 2 weeks.
Up to 3 HSV seronegative patients to be enrolled to confirm safety in this subpopulation.
C, cycle; CSCC, cutaneous squamous cell carcinoma; D, day; EOT, end of treatment; HSV, herpes simplex virus; PFU, plaque-forming units; Q2W, once every 2 weeks; SOT, solid organ transplantation; SRC, safety review committee.

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

## Key Eligibility Criteria

### Inclusion

- SOT patients with recurrent, locally advanced, or metastatic cutaneous malignancies including CSCC, BCC, Merkel cell carcinoma, and melanoma
- Patients must have progressed following local resection, prior radiation, or topical or systemic therapies. One prior line of systemic therapy is allowed in up to 30% of patients enrolled in either Parts A or B
- Documentation that the patient's allograft is stable
- At least one measurable tumor of ≥1 cm in longest diameter or ≥1.5 cm in shortest diameter for lymph nodes and injectable lesions that, in aggregate, comprise ≥1 cm in longest diameter
- Eastern Cooperative Oncology Group Performance Status ≤1 and adequate hepatic, renal, and hematologic function

### Exclusion

- Prior treatment with an oncolytic therapy. Active significant herpetic infections or prior complications of HSV-1 infection
- A history of transplant-related viral infections such as BK virus (BKV), Epstein-Barr virus, or cytomegalovirus within 3 months of study entry. Patients with BKV may be eligible if the BKV viral load is <1 x $10^7$ copies/ml by urine polymerase chain reaction or ≤4 log IU/ml by BKV plasma testing
- Patients with an autoimmune disease that requires systemic immunosuppressive treatment beyond immunosuppressive medications required for maintenance of allograft rejection prevention
- Patients with a history of any positive test result for hepatitis B or hepatitis C virus, indicating the presence of the virus
- Patients with hematologic malignancy (stable chronic lymphocytic leukemia not on active treatment is permitted)

## Key Endpoints

### Primary

- Safety and tolerability
- Objective response rate by investigator review

### Secondary

- Duration of response, complete response rate, disease control rate, progression-free survival, 1-year and 2-year overall survival rate by investigator review
- Quality of life score using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30

### Exploratory

- Biodistribution and viral shedding of RP1
- Activation of tumor infiltrating lymphocytes
- Expression levels of programmed death-ligand 1 and tumor mutation burden

ARTACUS is now recruiting SOT recipient patients. To learn more about enrolling your patient, contact clinicaltrials@replimune.com or +1 (781) 222 9570.

Additional information can be obtained by visiting clinicaltrials.gov (NCT04349436).

### Acknowledgements

The authors would like to thank the patients for their participation in the trial. Authors would also like to acknowledge the contribution of Taylor Jew for his contribution to the study. Editorial support was provided by Lauren Hanlon, PhD, of AlphaBioCom, LLC (King of Prussia, PA, USA).

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### Study Sponsor

The study is sponsored by Replimune Inc., Woburn, MA, USA.



**Presented at the 2022 American Society of Clinical Oncology (ASCO) meeting, June 3–7, 2022; Chicago, IL, USA**