Replimune Announces Positive Initial Data from the Anti-PD1 Failed Melanoma Cohort of the IGNYTE Clinical Trial & an RP2/3 Program Update

December 7, 2022

RP1 combined with nivolumab continues to demonstrate deep and durable responses in patients with anti-PD1 failed melanoma

Overall response rate (ORR) of 36% and complete response (CR) rate of 20%, with clinically meaningful activity across a broad range of anti-PD1 failed cutaneous melanoma settings observed, including in patients with high tumor burden and visceral disease

Update, including new data, provided on the RP2/3 program

Virtual investor event to be held today at 8:00 am ET

WOBURN, Mass., Dec. 07, 2022 (GLOBE NEWSWIRE) -- Replimune Group, Inc. (NASDAQ: REPL), a clinical stage biotechnology company pioneering the development of a novel class of tumor-directed oncolytic immunotherapies, today announced an initial data snapshot from the first 75 patients from the anti-PD1 failed cutaneous melanoma cohort of the IGNYTE clinical. The IGNYTE clinical trial is evaluating RP1 (vusolimogene oderparepvec) in combination with nivolumab, with the anti-PD1 failed melanoma cohort being conducted with registrational intent. The Company also provided new data from the ongoing Phase 1 clinical trials evaluating RP2 and RP3, as well as a detailed overview of its RP2/3 Phase 2 development plans. A virtual investor event will be held today at 8:00 a.m. ET to discuss the new data. The data from this update can be found in the presentation for today's investor event, linked here.

"We are pleased to be providing an initial data snapshot from the first 75 patients from the IGNYTE clinical trial being conducted with registrational intent for the treatment of anti-PD1 failed cutaneous melanoma," said Philip Astley-Sparke CEO of Replimune. "The data confirms the prior signal seen in anti-PD1 failed melanoma in a smaller earlier cohort of patients, with the data from the first 75 patients in the new cohort showing an overall 36% ORR, a 20% CR rate, and clinically meaningful activity across all sub-groups analyzed, including the most advanced Stage IVM1b/c patients. This highly encouraging data, taken together with the compelling and durable data with RP1 we have previously shared from our prior IGNYTE cohorts gives us high confidence we will be able to realize our ambition of establishing a broad skin cancer franchise with RP1. We plan to also further leverage our planned US commercial infrastructure with potential fast to market opportunities with RP2/3, and today announced a cost sharing collaboration with Roche in 3L CRC and 2L HCC."

Data Snapshot from the IGNYTE Clinical Trial Evaluating RP1 Combined with Nivolumab in anti-PD1 Failed Melanoma

IGNYTE is Replimune's multi-cohort clinical trial evaluating RP1 combined with nivolumab in multiple tumor type specific cohorts. The Company is today presenting new data from the first 75 patients from the 125 patient anti-PD1 failed melanoma cohort, which has registrational intent. The IGNYTE clinical trial is being conducted under a collaboration and supply agreement with Bristol-Myers Squibb, with the anti-PD1 failed melanoma cohort expected to complete enrollment by around the end of this year.

- The ORR in the first 75 patients from the anti-PD1 failed melanoma cohort was 36%, consistent with that observed in the prior Phase 2 cohort (N=16) presented in June 2022 where an ORR of 37.5% was seen. The complete response (CR) rate was 20.0%, compared to 12.5% shown in the prior 16 patients presented in June 2022. Further patients remain on study from the first 75 patients who have the opportunity for response, and current responses continue to deepen. The data demonstrates that RP1 combined with nivolumab shows clinically meaningful durable activity across the range of anti-PD1 failed cutaneous melanoma presentations, including in patients with moderate to high tumor burden, with 85% of responses ongoing.
- The data clearly demonstrate systemic activity, with both injected and in un-injected lesions responding, including in un-injected visceral disease. Most responses seen were in patients who did not respond to prior anti-PD1 therapy (i.e. did not previously achieve a PR or CR).
- Safety data with RP1 in combination with nivolumab assessed across all skin cancer patients treated with RP1 combined with nivolumab (N=187), including the new 75 patients, continues to demonstrate an attractive safety profile, with predominantly 'on target' Grade 1-2 side effects indicative of systemic immune activation.
- Overall, Replimune believes that RP1 in combination with nivolumab has the potential to become a go-to treatment option for melanoma patients after progressing on or after anti-PD1 therapy, including on adjuvant therapy or on or after a first- or second-line anti-PD1-containing regimen, including in combination with anti-CTLA-4.

The data snapshot from the first 75 patients was investigator assessed as compared to the primary endpoint of ORR for all patients in the cohort which is to be assessed by central review.

"The rate, depth and durability of responses seen across a range of anti-PD1 failed melanoma settings with RP1 combined with nivolumab suggests broad utility of RP1 in this difficult to treat patient population," said Dr. Mark Middleton, Professor of Experimental Cancer Medicine, consultant Medical Oncologist at the Oxford Cancer Centre and Head of the Department of

Oncology at the University of Oxford, and Principal Investigator on the IGNYTE study. “Based on the growing body of clinical data with RP1, I believe it has the potential to become a new treatment paradigm across multiple skin cancers, including in melanoma patients who have failed anti-PD1 therapy. I look forward to seeing the primary analysis data from the full 125 patients in the anti-PD1 failed cohort from the IGNYTE clinical trial, and of the registration-directed CERPASS clinical trial in CSCC in 2023.”

RP2/3 Clinical Update and Development Plan

RP2 leverages the Company’s platform to express an anti-CTLA-4 antibody, in addition to the GALV-GP R- and GM-CSF expressed by RP1. RP3 further expresses CD40L and 4-1BBL in addition to anti-CTLA-4 and GALV-GP R-, but does not express GM-CSF, and is intended to induce a broad and potent anti-tumor immune response.

The Company is pursuing a Phase 2 development plan for RP2 and RP3 targeting tumor types in large and underserved markets, including where liver metastases are common, as well as patients with primary liver cancer, and patients with earlier disease where the objective of treatment would be to achieve a cure. This includes the development of RP2/3 in combination with the current standard of care (SOC), including immunotherapy, chemotherapy and radiation, and in settings following the current SOC.

RP2/3 Data Updates

- The Company is today presenting updated data in uveal melanoma patients from the Phase 1 clinical trial evaluating RP2 in combination with nivolumab which the Company believes provides a proxy for the treatment for a range of intractable tumor types that metastasize to the liver.
    - Seventeen patients have been treated with RP2 as monotherapy (N=4) or in combination with nivolumab (N=13) to date, with enrollment of uveal melanoma patients into this clinical trial now being complete.
    - Four of the 14 patients which are so far evaluable have responded to treatment (28.6%), including metastatic tumors in the liver and bone. The final three of 17 patients remain on treatment, but currently have insufficient follow-up data to determine response outcome as of the cut-off date. Three of the four responses are ongoing at 9, 12 and 21 months, with the fourth patient having progressed at 15 months.

- The Company is also presenting data from a Phase 1 clinical trial of RP3 in combination with nivolumab, in patients with soft tissue sarcomas.
    - Five patients have been treated with RP3 combined with nivolumab in patients with multiple soft tissue sarcomas including in leiyomyosacoma, osteosarcoma, chondrosarcoma, and epithelioid sarcomas who have all have failed standard of care (chemotherapy and other therapies). At the data cut-off date, 3 of 5 patients have sufficient follow up for response assessment, and all three are responding to therapy in settings with no viable alternative treatment option, indicating the potential utility of RP3 in treating this difficult to treat tumor type.

Overall, RP2/3 continues to demonstrate promising early signals that could unlock additional opportunities in hard to treat cancers.

RP2/3 Phase 2 Development Plans

The Company is today providing further details on its Phase 2 development plans with RP2/3, and is also separately announced a clinical collaboration with Roche in colorectal cancer (CRC) and hepatocellular carcinoma (HCC), which will both utilize Roche’s atezolizumab and bevacizumab.

Three Phase 2 clinical trials are to be conducted with RP2/3, each initiating in the first half of 2023.

- **Squamous cell carcinoma of the head and neck (SCCHN):** A two cohort clinical trial with RP3 will be conducted, with the first cohort of 100 patients with locally advanced disease being randomized to receive either SOC chemotherapy combined with radiation or RP3 combined with chemotherapy and radiation followed by adjuvant nivolumab therapy. The second, signal finding cohort, will enroll 30 patients with recurrent or metastatic SCCHN with low PDL1 levels (CPS<20) who will be treated with chemotherapy, nivolumab and RP3.

- **Hepatocellular carcinoma (HCC):** Two 30 patient signal finding cohorts of patients will be enrolled. The first cohort of patients will enroll 1L patients treated with SOC atezolizumab combined with bevacizumab and RP3, and the second cohort of patients who have progressed on 1L immunotherapy (including atezolizumab/bevacizumab) also to be treated with atezolizumab combined with bevacizumab and RP3.

- **Colorectal cancer (CRC):** Two 30 patient 3L signal finding cohorts of patients will be enrolled. The first cohort will be treated with atezolizumab combined with bevacizumab and RP2 and the second cohort with RP3 combined with atezolizumab and bevacizumab. Replimune believes that data with both RP2 and RP3 in CRC will allow the comparative efficacy of RP2 and RP3 to be evaluated in a particularly difficult to treat patient population.

Investor event and webcast information

Replimune will host a virtual investor event today, Wednesday, December 7, 2022 at 8:00 a.m. ET. The webcast and slides will be accessible live under “Events & Presentations” on the Investors page of the Company’s website at www.replimune.com or by clicking here. A replay of the event will be available on Replimune’s website.

About IGNYTE
IGNYTE is Replimune's multi-cohort Phase 1/2 trial of RP1 plus nivolumab. There are 3 tumor specific cohorts currently enrolling in this clinical trial including a 125-patient cohort in anti-PD1 failed cutaneous melanoma with registrational intent. This cohort was initiated after completing enrollment in a prior Phase 2 cohort in the same clinical trial of approximately 30 patients with melanoma. The additional cohorts are in non-melanoma skin cancers which includes both naïve and anti-PD1 failed CSCC, and in anti-PD1 failed microsatellite instability high, or MSI-H/dMMR tumors. This trial is being conducted under a collaboration and supply agreement with Bristol-Myers Squibb.

About RP1
RP1 is Replimune's lead product candidate and is based on a proprietary new strain of herpes simplex virus engineered and genetically armed with a fusogenic protein (GALV-GP R-) and GM-CSF to maximize tumor killing potency, the immunogenicity of tumor cell death, and the activation of a systemic anti-tumor immune response.

About RP2 & RP3
RP2 and RP3 are derivatives of RP1 that express additional immune-activating proteins. RP2 expresses an anti-CTLA-4 antibody-like molecule and RP3 additionally expresses the immune co-stimulatory pathway activating proteins CD40L and 4-1BBL, but does not express GM-CSF. RP2 and RP3 are intended to provide targeted and potent delivery of these proteins to the sites of immune response initiation in the tumor and draining lymph nodes, with the goal of focusing systemic immune-based efficacy on tumors and limiting off-target toxicity.

About Replimune
Replimune Group, Inc., headquartered in Woburn, MA, was founded in 2015 with the mission to transform cancer treatment by pioneering the development of novel tumor-directed oncolytic immunotherapies. Replimune's proprietary RPx platform is based on a potent HSV-1 backbone with payloads added to maximize immunogenic cell death and the induction of a systemic anti-tumor immune response. The RPx platform has a unique dual local and systemic mechanism of action (MOA) consisting of direct selective virus-mediated killing of the tumor resulting in the release of tumor derived antigens and altering of the tumor microenvironment (TME) to ignite a strong and durable systemic response. This MOA is expected to be synergistic with most established and experimental cancer treatment modalities, and, with an attractive safety profile the RPx platform has the versatility to be developed alone or combined with a variety of other treatment options. For more information, please visit www.replimune.com.

Forward Looking Statements
This press release contains 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 our expectations about our cash runway, the design and advancement of our clinical trials, the timing and sufficiency of our clinical trial outcomes to support potential approval of any of our product candidates, our goals to develop and commercialize our product candidates, patient enrollments in our existing and planned clinical trials and the timing thereof, and other statements identified by words such as "could," "expects," "intends," "may," "plans," "potential," "should," "will," "would," or similar expressions and the negatives of those terms. Forward-looking statements are not promises or guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in such forward-looking statements. These factors include risks related to our limited operating history, our ability to generate positive clinical trial results for our product candidates, the costs and timing of operating our in-house manufacturing facility, the timing and scope of regulatory approvals, changes in laws and regulations to which we are subject, competitive pressures, our ability to identify additional product candidates, political and global macro factors including the impact of the coronavirus as a global pandemic and related public health issues, and other risks as may be detailed from time to time in our Annual Reports on Form 10-K and 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.

Investor Inquiries
Chris Brinzey
Westwicke, an ICR Company
339.970.2843
chris.brinzey@westwicke.com

Media Inquiries
Lissette Steele
Verge Scientific Communications
202.930.4762 x 409
lsteele@vergescientific.com