Replimune Provides Data Update from its RP1 (vusolimogene oderparepvec) and RP2 Programs and Announces Plans to Expand the Development of RP2/3 Beyond Phase 1

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High rate of complete responses in RP1 skin cancer cohorts underscore the potential for profound patient benefit and supports the ongoing registration directed development programs

RP2 data confirms the signal with RP1 in anti-PD1 failed melanoma, uveal melanoma and in treating patients whose cancer has metastasized to the liver

Announces plans to initiate broad Phase 2 development of RP2 and/or RP3 in tumor types that commonly metastasize to the liver

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

WOBURN, Mass., June 03, 2021 (GLOBE NEWSWIRE) -- Replimune Group, Inc. (NASDAQ: REPL), a biotechnology company developing oncolytic immuno-gene therapies derived from its Immulytic® platform, today announced updated interim data from the Phase 2 skin cancer cohorts combining RP1 (vusolimogene oderparepvec) with Opdivo®* (nivolumab) and data from RP2 alone and in combination with Opdivo that continues to provide strong support for development in its lead indications. Additionally, Replimune announced plans to initiate a Phase 2 clinical trial program in tumor types that metastasize to the liver. A virtual investor event will be held today at 8:00 a.m. ET to discuss the updated data.

“As our data matures there are some clear themes emerging,” said Philip Astley-Sparke CEO of Replimune. “In our longest-running clinical trial of RP1 combined with Opdivo in melanoma and in non-melanoma skin cancers including cutaneous squamous cell carcinoma (CSCC), we are seeing a clear trend that partial responses tend to convert to complete responses over time, providing many patients with the potential for a cure while also having a transformative long-term impact on quality of life. Our updated data further support our two registration-directed studies in skin cancers. We look forward to seeing if we can replicate the data we have seen with RP1 in skin cancers in anti-PD1/L1 failed non-small cell lung cancer (NSCLC), where we recently dosed our first patient. The signal with RP1 in patients who have failed anti-PD1 is continuing with RP2 and reinforces the potential utility of our platform for treating patients who have failed prior immune checkpoint therapy. Finally, the signal with RP1 indicating the potential to treat patients with liver metastases, who in general have a very poor prognosis, has been further confirmed with RP2, where we are now planning to move into Phase 2 development with RP2/3 in tumor types that commonly metastasize to the liver, including colon cancer, lung cancer and breast cancer.”

Updated clinical data from the Phase 2 cohort with RP1 in combination with Opdivo in patients with CSCC and other non-melanoma skin cancers continues to support the CERPASS registration-directed clinical trial of RP1 in combination with Libtayo®* (cemiplimab) in CSCC

The data continues to demonstrate that RP1 in combination with Opdivo is well tolerated and that it drives deep and durable responses in patients with CSCC with the number of complete responses (CRs), a dual independent primary endpoint in the CERPASS study, continuing to increase. At the current data cut off (n=15), seven of the nine responses are complete responses with a current CR rate of 46% and overall response rate (ORR) of 60%. Another potentially eighth complete response will require biopsy confirmation. The Company believes this data provides clear differentiation versus anti-PD1 therapy alone and provides strong validation of Replimune’s current registration-directed clinical development plan, with the initial readout of the CERPASS study expected in 2022.

Updated clinical data evaluating RP1 in combination with Opdivo in anti-PD1 failed melanoma patients continues to strongly support the Company’s registration-directed cohort in the IGNYTE clinical trial

Sixteen anti-PD1 failed cutaneous melanoma patients were enrolled into the previously reported 30 patient cohort in melanoma (which included anti-PD1 naïve cutaneous melanoma, mucosal and uveal melanoma, in addition to anti-PD1 failed cutaneous melanoma). The status of the anti-PD1 failed melanoma patients is as follows:

- Five of these patients have so far met the formal criteria for response; four of which had previously failed both anti-PD1 and anti-CTLA-4 therapies, with a current ORR of 31%.
- Of two further patients on study one remains a surgical complete response at 18 months from the start of treatment (classified as stable disease according to the study protocol) and the second patient with local progression following an extended period of stable disease has reinitiated RP1 treatment and is responding to therapy.

Despite improvements in therapy, many melanoma patients treated with anti-PD1 therapy have primary resistance or acquire resistance to immune checkpoint blockade following initial response. The clear activity of RP1 in combination with Opdivo in anti-PD1 failed patients, including in patients with extensive visceral disease, represents a new potential therapeutic option for

these patients. Based on the initial data with RP1 in melanoma, the Company initiated a registration-directed 125-patient cohort of anti-PD1 failed melanoma which is expected to read out in 2022. The signal with RP1 in anti-PD1 failed melanoma indicating that the Replimune series of product candidates may provide an effective therapy for these patients has also been further confirmed with RP2 (see below), although there are no current plans to independently develop RP2 in cutaneous melanoma.

Based on the emerging data indicating that RP1 can be safely administered to tumors in the lung and the evidence of clinical activity in patients with lung metastases from other tumor types, including in patients with anti-PD1 failed disease, the Company has commenced dosing into a 30 patient cohort of patients with anti-PD1/L1 failed NSCLC.

Updated RP2 monotherapy data continues to show compelling durability of response and new data in combination with Opdivo provides initial additional evidence of the clinical utility of RP2 in patients with hard-to-treat cancers

RP2 leverages Replimune's platform to express an anti-CTLA-4 antibody, in addition to GALV-GP R- and GM-CSF expressed by RP1. After fully enrolling patients in the RP2 monotherapy cohort (n=9) in the Phase 1 clinical trial with RP2, 27 of the target number of 30 patients have now been enrolled in the cohort evaluating RP2 in combination with Opdivo. With limited follow up available, initial data shows:

- The data with RP2 combined with Opdivo in anti-PD1 failed cutaneous melanoma has further confirmed the signal previously seen with RP1 in this setting. Of the nine anti-PD1 failed cutaneous melanoma patients enrolled, four have so far achieved a partial response.
- The signal in uveal melanoma with RP1 combined with Opdivo and with single-agent RP2 has been further confirmed with RP2 combined with Opdivo, with clear evidence of anti-tumor activity.
- Signals of activity with RP2 combined with Opdivo have also been seen in patients with other tumor types beyond melanoma and uveal melanoma, including a partial response in anti-PD1 failed squamous cell head and neck cancer. RP2 single-agent activity had also previously been reported in a patient with anti-PD1 failed esophageal cancer and in a patient with salivary gland cancer where partial and complete responses respectively remain ongoing at 18 and 15 months from treatment initiation.

Replimune plans to conduct clinical trials with RP2/3 in patients with liver metastases from a range of tumor types

- Based on the observation of clinical responses in patients with liver metastases following treatment with both RP1 and with RP2, and the fact that treating liver metastases is a considerable unmet need in patients with advanced cancer, Replimune plans to initiate a clinical development program with RP2 and/or RP3 specifically in patients with liver metastases from various cancer types.
- The intended program includes:
    - Expanding the Phase 1/2 study with RP2 to provide further signal confirmation for the treatment of patients with liver metastases from various cancer types.
    - Plans to initiate a Phase 2 clinical trial program with RP2 and/or RP3 with cohorts of patients with liver metastases from a range of solid tumor types in the first half of 2022.
- Details of the clinical trial design will be announced at a later time and is intended to include a range of tumor types where metastasis to the liver are common. This includes highly prevalent tumors such as colorectal and other gastrointestinal cancers, lung cancer and breast cancer.
- Whether RP2 or RP3 is used for particular tumor types will depend on the clinical data as it continues to emerge.

"Patients with liver metastases across tumor types have a poorer prognosis than those without, and their treatment presents a considerable clinical challenge. Liver metastases across tumor types are also associated with systemic resistance to immune checkpoint blockade," commented Professor Mark Middleton, Professor of Experimental Cancer Medicine in the Department of Oncology, consultant Medical Oncologist at the Oxford Cancer and Haematology Centre and Head of the Department of Oncology at the University of Oxford, who will also present the latest data with RP1 and RP2 at today's investor event. "Treatment of patients with liver metastases with RP1 or RP2, including patients with anti-PD1/L1 failed disease, has resulted in durable and systemic clinical benefit and offers the potential to provide a new standard of care for this large patient group."

The data from this clinical update and an overview of the rationale and development strategy for patients with liver metastases can be found in the presentation for today's investor event, linked here.

Investor event and webcast information

Replimune will host a virtual investor event today, Thursday, June 3, 2021 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 CERPASS

CERPASS is Replimune's registration-directed randomized, global Phase 2 clinical study to compare the effects of Libtayo® (cemiplimab) alone versus a combination of Libtayo and Replimune's investigational oncolytic immunotherapy RP1. The clinical trial will enroll 180 patients with locally advanced or metastatic cutaneous squamous cell carcinoma (CSCC) who are naïve to anti-PD1 therapy. The trial will evaluate complete response (CR) rate and overall response rate (ORR) as its two primary efficacy endpoints as assessed by independent review, as well as duration of response, progression-free survival (PFS), and overall survival (OS) as its secondary endpoints. The study is being run under a clinical trial collaboration agreement with Regeneron in

which the costs of the trial are shared and full commercial rights retained by Replimune. Libtayo is being jointly developed by Regeneron and Sanofi.

About IGNYTE
IGNYTE is Replimune's multi-cohort Phase 1/2 trial of RP1 plus Opdivo® (nivolumab). There are 4 tumor specific cohorts currently enrolling in this trial including a 125-patient extension cohort of RP1 combined with Opdivo in anti-PD-1 failed cutaneous melanoma. This cohort was initiated after completing enrollment in a prior Phase 2 cohort in the same trial of approximately 30 patients with melanoma. The additional thirty patient cohorts are studying RP1 in combination with Opdivo in non-melanoma skin cancers which includes both naïve and anti-PD-1 failed CSCC, in microsatellite instability high, or MSI-H/dMMR tumor types and anti-PD-1 failed non-small cell lung cancer, or NSCLC. This trial is being done under a collaboration and supply agreement with Bristol Myer Squibb.

About RP1
RP1 (vusolimogene oderparepvec) is Replimune's lead Immulytic® product candidate and is based on a proprietary new strain of herpes simplex virus engineered 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 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. RP2 and RP3 are intended to provide targeted and potent delivery 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 to develop the next generation of oncolytic immune-gene therapies for the treatment of cancer. Replimune is developing novel, proprietary therapeutics intended to improve the direct cancer-killing effects of selective virus replication and the potency of the immune response to the tumor antigens released. Replimune's Immulytic® platform is designed to maximize systemic immune activation, in particular to tumor neoantigens, through robust viral-mediated immunogenic tumor cell killing and the delivery of optimal combinations of immune-activating proteins to the tumor and draining lymph nodes. The approach is expected to be highly synergistic with immune checkpoint blockade and other approaches to cancer treatment across a broad range of cancers. Replimune intends to progress these therapies rapidly through clinical development in combination with other immuno-oncology products with complementary mechanisms of action as well as in standalone indications. 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 the design, initiation and advancement of our clinical trials, the 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, the potential impact of COVID-19 on our operations and milestones, 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.

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*Opdivo® is a trademark of Bristol-Myers Squibb Company; Libtayo® is a trademark of Regeneron Pharmaceuticals

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