Replimune Announces Presentation at the 2020 Society for Immunotherapy of Cancer (SITC) Annual Meeting

October 14, 2020

Initial safety and efficacy data from the single agent RP2 portion of the Phase 1 clinical trial of RP2 alone & in combination with Opdivo® (nivolumab) in patients with solid tumors

An update from the melanoma & non-melanoma skin cancer patients enrolled into the Phase 1/2 clinical trial of RP1 in combination with Opdivo® (nivolumab)

WOBURN, Mass., Oct. 14, 2020 (GLOBE NEWSWIRE) -- Replimune Group Inc. (NASDAQ: REPL), a biotechnology company developing oncolytic immuno-gene therapies derived from its Immulytic™ platform, announced that data with the Company's lead product candidate, RP1, along with initial single agent safety and efficacy data with RP2 in advanced solid tumors, will be presented at the Society for Immunotherapy of Cancer (SITC) annual meeting being held virtually from November 9-14, 2020.

The abstracts for these presentations appeared briefly and in error on the SITC website this morning, prior to their intended release on November 9th 2020, and as a result are provided in full below.

Details of Replimune's poster presentations:

Title: (647) Initial results of a phase 1 trial of RP2, a first in class, enhanced potency, anti-CTLA-4 antibody expressing, oncolytic HSV as single agent and combined with nivolumab in patients with solid tumors

Abstract Authors: Mark Middleton, Joseph J. Sacco, Kevin Harrington, Anna Olsson-Brown, Pablo Nenclares, Francesca Aroldi, Suzanne Thomas, Robert S. Coffin, etc.

Presentation times: Wednesday, Nov. 11 from 5:15–5:45 p.m. EST and Friday, Nov. 13 from 4:40–5:10 p.m. EST

Location: Virtual Poster Hall

Full abstract:

Background: RP2 is an enhanced potency oncolytic HSV-1 expressing granulocytemacrophage colony-stimulating factor (GM-CSF), a fusogenic protein (GALVGP R-), and an anti-cytotoxic T lymphocyte antigen 4 (CTLA-4) antibody-like molecule which is being tested in an open-label, multicenter, phase 1 study alone and combined with PD-1 blockade (NCT04336241).

Methods: The objectives were to assess initial safety and efficacy and determine the recommended phase 2 dose (RP2D) of RP2 alone and combined with nivolumab. Patients were to be treated using a 3+3 dose escalation at two dose levels of up to 10mL of RP2 Q2W up to 5 times (dose level 1: 10^5 PFU/mL then 4 doses of 106 PFU/mL; dose level 2: 10^6 PFU/mL then 4 doses of 10^7 PFU/mL). Following determination of the RP2D, additional HSV-1 seronegative patients were to be enrolled such that ≥3 had been dosed with RP2 at the RP2D, and a combination cohort of up to 30 patients dosed up to 8 times with RP2 at the RP2D combined with nivolumab (240mg Q2W for 4 months from the second RP2 dose, then 480 mg Q4W for 20 months) opened. Lesions were injected directly or under imaging guidance used for visceral lesions. Tumor biopsies were obtained for biomarker analysis. Viral shedding and antiHSV antibody titers were also monitored.

Results: Six HSV seropositive patients were enrolled in the dose-escalation phase with primarily Grade 1-2 adverse events, including febrile and other constitutional symptoms, local inflammation, and erythema observed. There were no DLTs requiring dose level expansion. The RP2D was selected as up to 10mL of 10^6 PFU/mL followed Q2W by multiple doses of 10^7 PFU/mL. Of the six patients treated with single agent RP2, three (50%) have ongoing partial responses. Objective responses (including in uninjected tumors) were observed in patients with uveal melanoma (prior ipilumumab/nivolumab; extensive liver metastases), mucoepidermoid carcinoma (prior carboplatin/paclitaxel, bicalutamide, ceralasertib), and esophageal cancer (prior durvalumab, M6620, capecitabine, oxaliplatin, cisplatin, chemoradiation; liver and abdominal node metastases). Enrollment is underway in HSV seronegative patients and in combination with nivolumab. Updated data including biomarker and biodistribution data will be presented.

Conclusions: The Phase 1 clinical data supports the safety and efficacy of single agent P2, including demonstration of uninjected tumor response in patients with difficult to treat advanced cancers. This data supports the hypothesis that anti-CTLA-4 delivered intra-tumorally through oncolytic virus replication, with accompanying antigen release and presentation, can provide potent anti-tumor effects.

Title: (650) An Open-label, multicenter, Phase 1/2 clinical trial of RP1, an enhanced potency oncolytic HSV, combined with nivolumab: Updated results from the skin cancer cohorts

Abstract Authors: Mark R. Middleton, Francesca Aroldi, Joseph J. Sacco, Mohammed M. Milhem, Brendan D. Curti, Ari M. Vanderwalde, Scott Baum, Adel Samson, Anna C. Pavlick, Jason Alan Chesney, Jiaxin Niu, Terence Duane Rhodes, Tawnya Lynn Bowles, Robert Conry, Anna Olsson-Brown, Douglas Earl Laux, Praveen Bommareddy, Alex Deterding, Robert S. Coffin, Kevin Harrington

Presentation times: Thursday, Nov. 12 from 4:50–5:20 p.m. EST and Saturday, Nov. 14 from 1–1:30 p.m. EST

Location: Virtual Poster Hall

Full abstract:

Background: RP1 is an enhanced potency oncolytic HSV encoding a fusogenic protein (GALV-GP R-) and GM-CSF which has previously demonstrated tolerable safety and tumor regression alone and with nivolumab in patients with a number of tumor types. Updated data from the phase 1 expansion with nivolumab, melanoma phase 2 (enrollment complete) and non-melanoma skin cancer (NMSC; enrollment ongoing) cohorts will be presented (NCT03767348). Enrollment of a further 125 patient anti-PD1 refractory cutaneous melanoma cohort; and activation of a cohort of anti-PD1 refractory NSCLC is underway.

Methods: Stage IIIb-IV melanoma patients for whom anti-PD-1 was indicated or who were refractory to prior anti-PD-1 alone or in combination with anti-CTLA-4, were enrolled. NMSC patients were anti-PD1 naïve. Patients received ≤8 doses of RP1 (≤10 mL/visit Q2W; first dose 10^6 PFU/mL then 10^7 PFU/mL) with nivolumab (240 mg IV Q2W for 4 months then 480 mg IV Q4W up to 2 years) from the second RP1 dose.

Results: As of 24th June 2020, 36 melanoma and 16 NMSC patients had been enrolled with follow up of <1-17 months. Of the melanoma patients, 16 previously antiPD1 treated cutaneous (8 also prior anti-CTLA-4), 8 anti-PD1 naïve cutaneous, 6 mucosal, and 6 uveal. Of the NMSC patients, 10 had squamous cell (CSCC), 3 had a basal cell, 1 had Merkel cell carcinomas, and 2 had angiosarcoma. Treatment emergent adverse events (TEAEs) remain consistent with phase 1, with RP1 side effects generally of Grade 1/2 constitutional-type symptoms, with no exacerbation of the side effects expected for nivolumab. At the data cut-off, 5 previously anti-PD1 treated (4 also anti-CTLA-4) cutaneous melanoma patients, 4 anti-PD1 naïve cutaneous melanoma patients, two mucosal melanoma patients (one anti-PD1 refractory) and one uveal melanoma patient (ipi/nivo refractory) have achieved response (WHO criteria for uveal). For NMSC, for the 13 patients with >8 weeks follow up, one of two angiosarcoma patients and seven of eight CSCC patients (5 CR) have achieved response (CSCC ORR 87.5%; CR rate 62.5%, including of uninjected visceral disease). Tumor biopsies in patients continue to routinely show immune activation, including robust recruitment of CD8+ T cells, reversal of T cell exclusion, and increased PD-L1 expression. Treatment remains ongoing, and current data will be presented.

Conclusions: RP1 and nivolumab have continued to be well tolerated, with continued promising anti-tumor activity in patients with skin cancers, including those with anti-PD1 refractory and other difficult to treat melanomas, and in patients with CSCC.

As well as during the official presentation times, the posters will also be available for virtual viewing throughout the conference via the SITC annual meeting website, and will be made available on the Company's website at www.replimune.com.

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. 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 advancement of our clinical trials, our plans to initiate new clinical trials, 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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