Replimune Presents RP1 Data from the IGNYTE anti-PD1 Failed Melanoma Cohort and RP2 Data in Uveal Melanoma at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting

June 3, 2023

Updated data from ongoing IGNYTE anti-PD1 failed melanoma cohort shows RP1 combined with nivolumab continues to demonstrate deep and durable responses with a well-tolerated safety profile; no progression in responding patients since the data snapshot presented in December 2022

Overall response rate (ORR) of 37.4%, with clinically meaningful activity across the range of anti-PD1 failed cutaneous melanoma settings enrolled, including in patients with moderate-high tumor burden and visceral disease

RP2 demonstrated an acceptable benefit risk profile and meaningful antitumor activity in patients with uveal melanoma from the ongoing RP2 Phase 1 trial

WOBURN, Mass., June 03, 2023 (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 updated data from the first 75 patients in the anti-PD1 failed melanoma cohort of the IGNYTE clinical trial along with data from the ongoing Phase 1 trial of RP2 combined with nivolumab in patients with uveal melanoma are being presented at the ASCO annual meeting. The anti-PD1 failed melanoma cohort of the IGNYTE clinical trial evaluating RP1 (vusolimogene oderparepvec) in combination with nivolumab is registration-directed.

“We are excited to share further data from these ongoing clinical trials evaluating our novel tumor-directed oncolytic immunotherapies, RP1 and RP2,” said Robert Coffin, President and Chief Research & Development Officer of Replimune. “The IGNYTE data demonstrate RP1 combined with nivolumab provides deep and durable responses with clinically meaningful rates of response in each of the anti-PD1 failed settings enrolled, and further highlights the potent systemic activity in tumors which have not been injected with RP1. These data indicate that RP1 has the potential to become a valuable new treatment option for melanoma patients following progression on anti-PD1 therapy, where treatment options are currently limited. Additionally, the data from RP2 in combination with nivolumab in uveal melanoma demonstrates a promising signal in a challenging tumor type that predominantly metastasizes to the liver, which could unlock additional opportunities for our oncolytic immunotherapies.”

Updated Data from the IGNYTE Clinical Trial Cohort 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 anti-PD1 failed melanoma cohort is registration-directed and completed enrollment earlier in the year with 141 patients enrolled. These updated data include the first 75 patients from the anti-PD1 failed melanoma cohort combined with the 16 anti-PD1 failed melanoma patients from the prior all comers 30 patient melanoma cohort (n=91 in total). The IGNYTE clinical trial is being conducted under a collaboration and supply agreement with Bristol Myers Squibb.

- With a median follow up of 75.9 weeks, the updated data show an overall objective response rate (ORR) of 37.4% (37.5% in the 16 patients from the prior cohort, 37.3% in the 75 patients from the new cohort), with an ORR of at least 28.3% in all subgroups analyzed, including in patients:
    - Having failed anti-CTLA-4 therapy as well as anti-PD1 therapy (34.4% ORR, n=32)
    - With Stage IVM1b/c disease (28.3% ORR, n=46)
    - Who progressed *while on* prior adjuvant anti-PD1 therapy (50% ORR, n=32); patients who progressed *after stopping* adjuvant therapy were not eligible for the trial
    - With both primary refractory (36.0% ORR, n=50) and secondary refractory (42.1% ORR, n=38) disease
- The data show systemic activity, with both injected and in un-injected lesions responding with similar durability and kinetics, including in un-injected visceral disease.
- From when last reported in December 2022, all responding patients remain in response, further highlighting the duration of benefit; 85 percent of responses are ongoing with 71 percent of responders out over one year from starting therapy.
- Patients with up to >20cm of total disease responded, including patients with up to >10cm of uninjected disease.
- Updated analyses demonstrate activity in patients with PD-L1 negative tumors as well as those whose tumors were PD-L1

positive and with both BRAF wild type and BRAF mutant disease.

- Analysis of PFS and ORR for the population as a whole and broken down by prognostic and other factors was also provided. This demonstrated that PFS and OS are most strongly impacted by response to RP1 combined with nivolumab, but not impacted by whether all lesions were or were not injected with RP1. Other factors assessed (disease stage, prior treatment setting [adjuvant vs not adjuvant prior anti-PD1], prior anti-CTLA-4 or no prior anti-CTLA-4) had only a more modest impact on progression-free survival (PFS) and overall survival (OS).

- RP1 continues to be generally well tolerated with safety data showing predominantly 'on target' flu-like Grade 1-2 side effects indicative of systemic immune activation. Grade 3 treatment related events were rarely seen in the 91-patient group, with a range of Grade 3 events in one patient each, and two Grade 3 events of fatigue. There were two Grade 4 treatment related events (elevated lipase, and cytokine release syndrome) and no treatment related Grade 5 events.

The ORR data for this snapshot was investigator assessed. The primary endpoint is ORR for all patients in the cohort which will be assessed by central review.

The poster presented at ASCO can be found on our website under Presentations.

Updated Data from RP2 Combined with Nivolumab in Uveal Melanoma

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. Data in uveal melanoma patients from the Phase 1 clinical trial evaluating RP2 in combination with nivolumab was presented. The Company believes the data in uveal melanoma provides a proxy for the potential treatment of a range of intractable tumor types that metastasize to the liver. This trial is being conducted under a collaboration and supply agreement with Bristol Myers Squibb.

- Seventeen patients have been treated with RP2 as monotherapy (N=3) or in combination with nivolumab (N=14) 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, including for patients with liver and bone metastases, with the fourth patient having progressed at 15 months.

- The safety profile as monotherapy and in combination with nivolumab was generally well tolerated with no additive adverse events observed.

- The poster presented at ASCO can be found on our website under Presentations.

Additional Abstracts Being Presented at ASCO

Three additional trial-in-progress abstracts were presented at ASCO outlining Phase 2 development plans for RP2 and RP3.

- A Phase 2, open-label, multicenter study investigating efficacy and safety of RP3 oncolytic immunotherapy combined with other therapies in patients with locoregionally advanced or recurrent squamous cell carcinoma of the head and neck (SCCHN)

    - A two-cohort clinical trial will be conducted, with the first cohort of 100 patients with locally advanced disease being randomized to receive either standard of care (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.

- An open-label clinical trial of RP2 and RP3 oncolytic immunotherapy in combination with atezolizumab and bevacizumab for the treatment of patients with advanced colorectal carcinoma (CRC)

    - Two signal finding cohorts of 30 patients each will be enrolled in collaboration with Roche. The first cohort will enroll patients to be treated with atezolizumab combined with bevacizumab and RP2 and the second cohort with atezolizumab and bevacizumab and RP3. The Company 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.

- An open-label, multicenter study investigating RP3 oncolytic immunotherapy in combination with first- or second-line systemic atezolizumab and bevacizumab therapy in patients with locally advanced unresectable or metastatic hepatocellular carcinoma (HCC)

    - Two signal finding cohorts of 30 patients each will be enrolled in collaboration with Roche. The first cohort will enroll 1L HCC patients treated with SOC atezolizumab combined with bevacizumab and RP3, and the second cohort will

enroll HCC patients who have progressed on 1L immunotherapy (including atezolizumab/bevacizumab) and will be treated with atezolizumab combined with bevacizumab and RP3.

These clinical trials are currently in the trial set up phase and are expected to initiate around mid-year.

About IGNYTE
IGNYTE (NCT03767348) 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 include non-melanoma skin cancers which includes both naïve and anti-PD1 failed CSCC. This trial is being conducted under a collaboration and supply agreement with Bristol Myers Squibb.

About RP1
RP1 (vusolimogene oderparepvec) 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 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.

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