Replimune Presents Late-Breaking Abstract Featuring Data from IGNYTE Clinical Trial of RP1 Combined with Nivolumab in Anti-PD1 Failed Melanoma at the 39th Annual Meeting of the Society for Immunotherapy of Cancer (SITC 2024)

November 9, 2024

Oral presentation highlighting IGNYTE primary analysis data shows anti-tumor activity across all subgroups with injected and non-injected lesions responding with similar frequency, depth, duration, and kinetics

Initial biomarker data shows increase in tumor CD8+ T cell and PD-L1 expression after dosing along with an increase in gene signatures associated with CD8+ T cells and inflammatory cytokines, highlighting the potential of RP1 plus nivolumab to generate a potent anti-tumor immune response

WOBURN, Mass., Nov. 09, 2024 (GLOBE NEWSWIRE) -- Replimune Group, Inc. (NASDAQ: REPL), a clinical stage biotechnology company pioneering the development of novel oncolytic immunotherapies, today announced that the primary analysis data from the IGNYTE clinical trial, including initial biomarker analyses, was presented as a late-breaking abstract during an oral session at the 39th Annual Meeting of the Society for Immunotherapy of Cancer (SITC 2024) in Houston, Texas. In addition, data from the ARTACUS clinical trial evaluating RP1 monotherapy in solid organ transplant patients with advanced cutaneous malignancies was also shared in an encore poster presentation during the meeting.

“The initial biomarker analyses included in the SITC presentation which demonstrate increases in tumor CD8+ T cell infiltration and PD-L1 expression along with the induction of an immune inflammatory gene signature after treatment, further support the intended mechanism of RP1 in combination with nivolumab, including its ability to induce a systemic response after progression on prior anti-PD1 therapy,” said Kostas Xynos, MD, PhD, MBA, Chief Medical Officer of Replimune. “We believe that the systemic activity of RP1 and nivolumab is in particular demonstrated by the similar level of responses seen in both injected and non-injected lesions, including hard to treat visceral lesions, and by the durability of the responses seen.”

IGNYTE Clinical Trial Data at SITC
The IGNYTE clinical trial cohort in anti-PD-1 failed melanoma included 140 patients who received RP1 plus nivolumab after confirmed progression while being treated for at least 8 weeks with anti-PD-1 based therapy, with or without anti-CTLA-4. The primary analysis by blinded independent central review was triggered once all patients had been followed for at least 12 months. The median follow-up at the time of the primary analysis was 15.4 months (0.5-47.6 months).

Data from the IGNYTE trial presented at SITC 2024 show:

- One-third of patients experienced a confirmed response, with an overall response rate (ORR) of 33.6% by modified RECIST (mRECIST) v1.1 criteria, the primary endpoint in the trial protocol, and 32.9% by RECIST v1.1 criteria, an additional analysis requested by the FDA. The complete response (CR) rate by mRECIST v1.1 was 15%. In patients who had prior anti-PD1 and anti-CTLA-4, the ORR was 27.7% and for those who had primary resistance to anti-PD1, the ORR was 35.9% by mRECIST v1.1.
- The median duration of response from response initiation was 21.6 months.
- Most injected and non-injected lesions (85%) in responders had a 30% or greater reduction in size. RP1 plus nivolumab induced deep responses in non-injected lesions in visceral organs, including those distant from the injection site.
- Median overall survival for the trial has not been reached, however, one-, two-, and three-year survival rates were 75.3%, 63.3%, and 54.8%, respectively. 12-month progression free survival (PFS) was 32.8% and median PFS was 3.7 months.

Initial biomarker data included in the SITC presentation show:

- Tumor inflammation signature (TIS) and nano string analysis revealed an increase in the expression of genes associated with CD8+ T cells and inflammatory cytokines. These markers highlight the potential of RP1 plus nivolumab to generate a potent anti-tumor immune response. TIS is an investigational use only assay consisting of 18 genes that assesses the presence of an adaptive immune response, and which is associated with responsiveness to anti-PD1 therapy[1].
- Immunohistochemistry (IHC) images demonstrate that RP1 plus nivolumab may stimulate tumors to a more immune inflamed state, further highlighting the potential of RP1 plus nivolumab to reverse mechanisms of resistance to anti-PD1 therapy.

As previously reported, RP1 combined with nivolumab continues to be well-tolerated. Treatment-related adverse events associated with RP1 in combination with nivolumab were predominantly Grade 1-2 constitutional type events (> 5% of patients), including fatigue, chills, pyrexia, nausea, influenza-like illness, injection-site pain, diarrhea, vomiting, headache, pruritis, asthenia, arthralgia, myalgia, decreased appetite, and rash, with a low incidence (12.8% of patients) of Grade 3-4 events, which were predominantly Grade 3. Grade 4 events were one each of lipase increased, cytokine release syndrome, myocarditis, hepatic cytolysis, and

splenic rupture. There were no Grade 5 events.

The presentation is available on the Company website under **Events and Presentations**.

The IGNYTE-3 confirmatory phase 3 trial evaluating RP1 plus nivolumab versus physician's choice in patients with advanced melanoma who have progressed on anti-PD1 and anti-CTLA-4 or who are not candidates for anti-CTLA-4 therapy is currently recruiting. For additional information, visit https://replimune.com/clinical-trials/ignyte-3/.

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 oncolytic immunotherapies. Replimune's proprietary RPx platform is based on a potent HSV-1 backbone intended to maximize immunogenic cell death and the induction of a systemic anti-tumor immune response. The RPx platform is designed to have a unique dual local and systemic activity consisting of direct selective virus-mediated killing of the tumor resulting in the release of tumor derived antigens and altering of the tumor microenvironment to ignite a strong and durable systemic response. The RPx product candidates are expected to be synergistic with most established and experimental cancer treatment modalities, leading to 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, the availability of combination therapies needed to conduct our clinical trials, 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 the Russian-Ukrainian and Israel-Hamas political and military conflicts, 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
ICR Westwicke
339.970.2843
chris.brinzey@westwicke.com

Media Inquiries
Arleen Goldenberg
Replimune
917.548.1582
media@replimune.com