Replimune to Present New Biomarker & Pre-clinical Data for Lead Oncolytic Immunotherapy Programs at the 2021 American Association for Cancer Research Annual Meeting

April 12, 2021

Data confirms potent anti-tumor activity & activation of robust systemic immune responses by RP1 and RP2

- *Increased infiltration of CD8+ T cells and PD-L1 expression for patients dosed with RP1 in combination with Opdivo® (nivolumab) and single agent RP2 in human biomarker samples*
- *Pre-clinical evidence of innate immune activation mediated by GALV-GP R- expression*
- *Gene expression profiling supportive of broad immune activation in both humans & mice*
- *Further pre-clinical demonstration of potent lytic activity in tumors*

WOBURN, Mass., April 12, 2021 (GLOBE NEWSWIRE) -- Replimune Group, Inc. (Nasdaq: REPL), a biotechnology company developing oncolytic immuno-gene therapies derived from its Immulytic® platform, today announced additional data supporting the multiple mechanisms of action for its lead programs, RP1 and RP2, during two presentations at the American Association for Cancer Research (AACR) Annual Meeting 2021 being held virtually April 10-15, 2021 and May 17-21, 2021.

"We developed Replimune's Immulytic platform with the intention of developing therapies with both enhanced tumor killing potency and with an enhanced ability to initiate a systemic anti-tumor immune response. This pre-clinical and clinical biomarker data provides further evidence that these objectives are being achieved, and that RP1 and RP2 are able to initiate a potent systemic immune response against a patient's cancer," said Robert Coffin, PhD, President and Chief Research and Development Officer, Replimune.

Details of the presentations are as follows:

Abstract Title: Clinical biomarker studies with two fusion-enhanced versions of oncolytic HSV (RP1 and RP2) alone and in combination with nivolumab in cancer patients indicate potent immune activation – Abstract #: LB180

- In patients dosed with RP1 in combination with nivolumab or single agent RP2 alone and in combination with nivolumab, immunohistochemistry for CD8 and PD-L1 from paired tumor biopsies demonstrated robust and increased infiltration of CD8+ T cells and PD-L1 expression across different tumor types, including reversal of T cell exclusion following prior combined treatment with ipilimumab and nivolumab in melanoma.
- A significant increase in the expression levels of genes associated with innate and adaptive immune activation and genes previously reported to be associated with responsiveness to anti-PD1 therapy was demonstrated.
- In patients dosed with RP2 monotherapy, an increase in CD8+ T cell infiltration as well as robust changes in expression of key tumor and immune cell signalling pathway genes was observed.
- Peripheral blood T cell receptor (TCR) sequencing indicated the expansion of existing T cell clones and generation of new T cell clones.
- Increased CD8+ T cell infiltration and PD-L1 expression, coupled with changes in TCR clonal expansion in PBMC samples, suggest systemic immune activation.

This presentation is now available for on-demand viewing on the AACR Annual Meeting 2021 website linked here and also posted to the presentations section of the Replimune website and linked here.

RP1 is Replimune's lead Immulytic product candidate and is based on a proprietary new strain of herpes simplex virus (HSV) engineered to maximize tumor killing potency, the immunogenicity of tumor cell death and the activation of a systemic anti-tumor immune response through the expression of a GALV-GP R- fusogenic protein and GM-CSF. RP2 is a derivative of RP1 that expresses an anti-CTLA-4 antibody-like molecule 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.

Abstract Title: Immunomodulatory effects of a novel, enhanced potency gibbon ape leukemia virus (GALV) fusogenic membrane glycoprotein-expressing herpes simplex virus platform with increased efficacy combined with anti PD-1 therapy – Abstract #1917

This poster presentation is a collaboration between Replimune and The Institute of Cancer Research, London, UK.

- In a histological examination of tumors injected with RP1 or RP2, large areas of necrosis in syngeneic mouse tumours were observed, even in a model where GALV-GP R- is not functional. In models where GALV-GP R- is functional, including in human xenograft tumors in nude mice (which have no adaptive immune system, but retain innate, e.g. NK cell mediated, immune function), GALV-GP R- was observed to give anti-tumor activity in both injected and in uninjected tumors, whereas

a virus without GALV-GP R- only exhibited anti-tumor activity in injected tumors. These effects in uninjected tumors were presumed to result from enhanced innate immune activation mediated by GALV-GP R-.
- RP1 increased PD-L1 expression, particularly on neutrophils, and increased CD3 T cell infiltration in injected and contralateral tumors.
- Profound effects on the gene expression profile were also seen in both injected and contralateral tumors which are consistent with potent and broad immune activation. These were significantly greater than that seen with single agent anti-PD1, and were further enhanced when RP1 was combined with anti-PD1.

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"RP1 and RP2 represent attractive potential treatment modalities with the ability to self-amplify, kill through multiple mechanisms and promote anti-tumour immune responses," said Professor Kevin Harrington, PhD, Professor in Biological Cancer Therapies at The Institute of Cancer Research, London, and Consultant Clinical Oncologist at The Royal Marsden NHS Foundation Trust in the UK. "These data show that RP1 increases PD-L1 expression, increases CD3 T cell infiltration in injected and contralateral tumors, and has profound effects on the gene expression profile in both injected and non-injected tumors which are consistent with potent and broad immune activation. These benefits are then further enhanced by treatment with anti-PD1 creating the potential for an attractive treatment option for patients with difficult to treat tumor types who are currently underserved."

Opdivo® is a registered trademark of Bristol Myers Squibb.

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 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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