Replimune Shares Initial Primary Analysis Results from CERPASS Clinical Trial in Advanced Cutaneous Squamous Cell Carcinoma and Presents New Data from IGNYTE Clinical Trial of RP1 in Anti-PD1 Failed Melanoma and Non-Melanoma Skin Cancers

December 5, 2023

RP1 in combination with cemiplimab demonstrated clinically meaningful improvements in complete response rate and duration of response compared to cemiplimab in the CERPASS clinical trial, but did not meet either of the two primary endpoints

Positive data update for full 140 patients in the IGNYTE clinical trial cohort of RP1 in anti-PD1 failed melanoma reinforces durable benefit; biologics license application (BLA) submission planned for 2H 2024

RP1 monotherapy data from ARTACUS clinical trial and new data from first 30 patients with anti-PD1 failed non-melanoma skin cancers in IGNYTE trial adds to growing body of evidence supporting the potential of RP1 in difficult to treat skin cancer settings

Portfolio reprioritization extends cash runway to early 2026

Company to host conference call and webcast today at 8:00 am ET

WOBURN, Mass. December 5, 2023 – Replimune Group, Inc. (NASDAQ: REPL), a clinical stage biotechnology company pioneering the development of a novel portfolio of oncolytic immunotherapies, today announced results from the primary analysis of the CERPASS trial evaluating RP1 in combination with cemiplimab for the treatment of locally advanced or metastatic cutaneous squamous cell carcinoma (CSCC) and provided initial data for all patients in the anti-PD1 failed melanoma cohort of the IGNYTE clinical trial. The company also shared a new data snapshot from the IGNYTE cohort of anti-PD1 failed non-melanoma skin cancer (NMSC) patients and data from the ARTACUS trial evaluating RP1 as monotherapy for skin cancer in patients who have had solid organ or hematopoietic cell transplants.

“Data from across our skin cancer program clearly show that RP1 is an active agent both as monotherapy and in combination with anti-PD1 therapy in multiple settings, giving us further confidence in the potential of RP1 to be an important treatment option for skin cancer patients,” said Philip Astley-Sparke, CEO of Replimune. “The overall data from the CERPASS study indicate that treatment with RP1 in combination with cemiplimab led to clinically meaningful activity with a higher rate of complete responses and favorable duration of response versus cemiplimab alone. Further, the positive data from the full 140 patient anti-PD1 failed melanoma cohort in the IGNYTE trial shows approximately 1 in 3 patients treated with RP1 in combination with nivolumab achieved a durable response which we believe is supportive of our planned submission of a BLA in 2H 2024 for this high unmet need patient population.”

Results from the CERPASS Trial in CSCC

The CERPASS clinical trial was a global, randomized study enrolling 211 patients randomized 2 to 1 to receive RP1 plus cemiplimab versus cemiplimab standard of care for patients with locally advanced or metastatic CSCC. The CERPASS study was conducted under a Master Clinical Trial Collaboration and Supply Agreement with Regeneron Pharmaceuticals.

The study did not meet either of the two primary endpoints of complete response rate (CRR) or overall response rate (ORR) as assessed by blinded independent central review. RP1 in combination with cemiplimab increased the CRR versus cemiplimab alone (38.1% vs. 25%, p=0.040), which was just short of the required threshold for statistical significance in this study ($p \leq 0.025$). Notably, among the 83 patients with locally advanced disease, the complete response rate in the RP1 plus cemiplimab group was 48.1% versus 22.6% in the cemiplimab only group. The ORR was comparable between the two study groups (52.5% for RP1 plus cemiplimab vs. 51.4% for cemiplimab alone, p=0.692). Importantly, RP1 in combination with cemiplimab also increased duration of response (DOR) as compared to cemiplimab alone (hazard ratio 0.45), however, these data are immature and further follow up is required. Of note, RP1 plus cemiplimab provided particularly meaningful clinical activity for many patients with difficult to treat, disfiguring tumors that typically have the greatest impact on quality of life, given their size and location.

There was also an imbalance in baseline tumor burden across the treatment groups which may have impacted the number of responses seen. A significantly greater number of patients with high baseline tumor burden (larger than 10 cm in total diameter) were treated in the RP1 plus cemiplimab group as compared to the cemiplimab alone group (23% of RP1 plus cemiplimab treated patients had high baseline tumor burden vs. 12.5% of cemiplimab only patients). In a pre-specified analysis, patients with total tumor burden less than or equal to 10 cm had a CRR of 43% in the RP1 plus cemiplimab group versus 27% in the cemiplimab only group. For those patients with tumor burden greater than 10 cm, CRR was 21.9% in the RP1 plus cemiplimab group versus 11.1% in the cemiplimab only group.

The trial will continue as planned to assess DOR, progression free survival (PFS) and overall survival (OS) with greater maturity.

Treatment-related adverse events with RP1 plus cemiplimab were predominantly additional transient Grade 1-2 “flu-like” symptoms

being seen as compared to cemiplimab alone, including fatigue, pyrexia, pruritis, nausea, hypothyroidism, chills, diarrhea, asthenia, infusion-related reaction, rash, rash maculo-popular, and vomiting. There was a range of Grade 3 events occurring in one patient each in the RP1 plus cemiplimab arm (16.5%), except for fatigue, rash maculo-popular, and immune-mediated hepatitis which occurred in 2 patients each. Grade 4 events were one each of immune-mediated myocarditis and myocarditis. There were no Grade 5 treatment-related adverse events.

Initial Data from All Patients in the IGNYTE Cohort of RP1 in Anti-PD1 Failed Melanoma
The registration directed anti-PD1 failed melanoma cohort from the IGNYTE clinical trial includes 140 patients and completed enrollment earlier this year. Data are also included for 16 patients from the initial cohort representing a total of 156 patients in this treatment setting.

In the RP1 plus nivolumab group (n=156), the ORR was 31.4% with a CR rate of 12% showing activity consistent with the prior snapshot of 91 anti-PD1 failed melanoma patients. As of this report, there are 5 patients still on study with the opportunity for response. In the full population, almost half of patients failed combination therapy with ipilimumab plus nivolumab as compared to the earlier snapshot where approximately a third were ipilimumab and nivolumab failures. Approximately 50% of patients experienced clinical benefit, defined as CR, PR, or stable disease (SD). Of responders, 100% are ongoing at more than six months with 78% of responses still ongoing as of November 6, 2023. Responses reported for this snapshot were investigator-assessed. RP1 combined with nivolumab continues to be well-tolerated, with mainly Grade 1-2 “on target” side effects, observed.

In this cohort, responses were seen across disease stages, including complete responses in patients with stage IVM1b/c disease. Responses are highly durable with median DOR greater than 24 months, and often deepening over time. Preliminary OS data are promising. The primary analysis by independent central review will be triggered once all patients have had at least 12 months of follow up in March 2024.

Treatment-related adverse events associated with RP1 in combination with nivolumab in this cohort were predominantly Grade 1-2 constitutional type events (> 5% of patients), including fatigue, chills, pyrexia, nausea, influenza-like illness, pruritis, diarrhea, injection site pain, vomiting, headache, rash, myalgia, asthenia, decreased appetite, and injection site reaction, with a low incidence of Grade 3-5 events. Grade 4 events were one each of lipase increased, cytokine release syndrome, myocarditis and hepatic cytosis and the Grade 5 treatment-related adverse event was one event of immune mediated myocarditis, which was attributed to nivolumab and is an expected immune mediated adverse event for nivolumab.

IGNYTE Regulatory Update
The company recently participated in a Type C meeting with the U.S. Food and Drug Administration (FDA). During the discussion, the FDA acknowledged that the anti-PD1 failed melanoma population is one of unmet need. The FDA agreed with an anti-PD1 failed melanoma confirmatory study design concept consisting of a 2-arm randomized trial with physician’s choice of treatment as a comparator arm in the study population. Full protocol development is currently underway. The proposed Phase 3 confirmatory trial should be initiated by the time of an application under the accelerated approval pathway. After following all patients for at least 12 months and pending central review by RECIST v1.1, BLA submission for RP1 in combination with nivolumab is planned for 2H 2024.

Data Overview from Phase 1/2 ARTACUS Clinical Trial of RP1 Monotherapy
As previously presented, treatment with RP1 monotherapy in the Phase 1/2 ARTACUS clinical trial in skin cancer patients who have had solid organ or hematopoietic cell transplants led to an ORR of 34.8% (8 of 23 evaluable patients, including 5 CRs and 3 partial responses). These patients are generally not eligible for anti-PD1 therapy which could precipitate transplant rejection. Most responses were ongoing as of the data cutoff date of September 18, 2023. There was no evidence of allograft rejection. RP1 monotherapy was well tolerated, and the safety profile was similar to that observed in non-immunocompromised patients with advanced skin cancers.

Initial Data Snapshot from the IGNYTE Cohort of RP1 in Anti-PD1 Failed NMSC
The NMSC data reported from the IGNYTE trial is from the first 30 patients enrolled in the cohort, all with at least 6 months of follow up, including patients with CSCC, MCC, basal cell carcinoma, and angiosarcoma. The data show that treatment with RP1 in combination with nivolumab led to an ORR of 30% (9 of 30 patients) which is consistent with data from the anti-PD1 failed melanoma cohort with approximately a third of patients responding and 60% demonstrating clinical benefit. The combination of RP1 and nivolumab was well tolerated in this patient population with a safety profile consistent with the overall experience seen with this treatment regimen to date in skin cancer.

Portfolio Update
As previously shared, the company presented strong data with RP2 in uveal melanoma during a plenary session at the 20th International Congress of the Society for Melanoma Research in November. Based on the data in this population, planning is underway for a randomized controlled clinical trial of RP2 in second line (2L) uveal melanoma with the company intending to investigate other rare cancer opportunities as target indications.

To focus on near term priority studies, including the RP1 Phase 3 confirmatory study in anti-PD1 failed melanoma and the RP2 registrational study in uveal melanoma, RP2/3 development in squamous cell carcinoma of the head and neck (SCCHN) and colorectal cancer (CRC) is being discontinued. The 2L hepatocellular carcinoma (HCC) trial will continue with RP2 only. At this time, development of RP3 will be discontinued.

As of September 30, 2023, cash and investments total $496.8M. We expect that the reprioritization of the portfolio will extend the

cash runway into early 2026.

Conference Call Details
Replimune will host a conference call and webcast today at 8:00 a.m. ET. Listeners can register for the conference call via this link. Analysts wishing to participate in the question and answer session should use this link. The webcast and slides of the presentation can be accessed in the Investors section of Replimune's website at www.replimune.com. A replay of the webcast will be available on Replimune's investor website approximately two hours after the call's conclusion. Those who plan on participating are advised to join 15 minutes prior to the start time.

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 a novel portfolio of 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 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 to ignite a strong and durable systemic response. This MOA is 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 our expectations about our cash runway, 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 and the likelihood of the benefit of our product candidates to patients, patient enrollments in our existing and planned clinical trials and the timing thereof, our belief that RP1 can be an important treatment option for skin cancer patients, the timing of a submission of a BLA for our IGNYTE cohort, if any, 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 and related public health issues, the affects of the discontinuation of certain of our trials and our development of RP3, 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