February 23, 2021

Oncolytics Biotech® Reports Preclinical Data Demonstrating the Synergistic Anti-cancer Activity of Pelareorep Combined with CAR T Cell Therapy in Solid Tumors

Mayo Clinic shows pelareorep vastly improved persistence and efficacy of CAR T cell therapy leading to cures in this model

Pelareorep's synergistic effects with CAR T therapy appear to be specific and were not observed with the oncolytic virus VSV

Results demonstrate the potential of pelareorep to broaden the applicability of CAR T cells to solid tumors

SAN DIEGO, Calif. and CALGARY, AB, Feb. 23, 2021 /PRNewswire/ -- Oncolytics Biotech® Inc. (NASDAQ: ONCY) (TSX: ONC) announced publication of an electronic poster at the CAR-TCR Summit Europe 2021 with data from a preclinical study evaluating pelareorep and chimeric antigen receptor (CAR) T cell combination therapy in solid tumors.

Newly published results show that loading CAR T cells with pelareorep vastly improved their persistence and efficacy in a murine solid tumor model, in stark contrast to preclinical studies using intratumoral infection with the VSV oncolytic virus that weakened CAR T cells. Efficacy of pelareorep-loaded CAR T cell ("CAR/Pela") therapy was further enhanced by boosting mice 8 days later with a single intravenous dose of pelareorep ("pelareorep boost"), generating highly persistent CAR T cells, inhibition of recurrent tumor growth, and ultimately tumor cures. These synergistic immune effects were specific to pelareorep, as intravenous boosting with VSV did not augment CAR/Pela therapy or prevent the growth of recurrent tumors. Survival data from the preclinical study are shown below:

Therapy	Survival Rate at End of Study
PBS (vehicle)	0% (0/7)
CAR T	14% (1/7)
Pelareorep	0% (0/7)
Pelareorep + Pelareorep boost	0% (0/7)
CAR/Pela	57% (4/7)
CAR/Pela + pelareorep boost	100% (7/7)
CAR/Pela + VSV boost	42% (3/7)

"These very exciting data demonstrate pelareorep's ability to overcome major shortcomings of CAR T cells," said Dr. Matt Coffey, President and Chief Executive Officer of Oncolytics Biotech Inc. "Despite commercial success in *hematological* cancers, CAR T therapies have limited efficacy against solid tumors due to immunosuppressive tumor microenvironments (TMEs) that promote T cell exhaustion and exclusion. Pelareorep's ability to reverse

immunosuppressive TMEs has been well documented in the clinic, and combining CAR T cells with pelareorep may enable their success against *solid* cancers. This would be a major advancement, as it would substantially broaden the applicability of CAR T cells to a variety of highly prevalent and difficult-to-treat indications."

Andrew de Guttadauro, President of Oncolytics Biotech U.S. and Global Head of Business Development, added, "While our primary focus is on advancing our lead breast cancer program to a registrational trial, we continue to evaluate additional opportunities to expand pelareorep's business development and partnership potential. In clinical studies, pelareorep recruited high concentrations of T cells to solid tumors, positioning it to synergistically interact with checkpoint inhibitors. In this newly published study, we show the synergistic benefits of pelareorep can be extended to additional cutting-edge immunotherapeutic agents. Based on these findings, we are specifically exploring a partnership strategy to further the development of pelareorep as an enabling technology for CAR T cells and additional immunotherapies that require immune effector cell infiltration in solid tumors."

The electronic poster titled "*Combination Therapy with Oncolytic Viruses and CAR T Cells*," was developed in collaboration with researchers from the Mayo Clinic, Duke University, and Oncolytics. It is available on the *Posters & Publications* page of Oncolytics' website (LINK).

About CAR T cells and CAR T therapy

The CAR T process begins when blood is drawn from a patient and their T cells are separated so they can be genetically engineered to produce chimeric antigen receptors (CARs). These receptors enable the T cells to recognize and attach to a specific protein or antigen on tumor cells. Once the engineering process is complete, a laboratory can increase the number of CAR T cells into the hundreds of millions. Finally, the CAR T cells will be infused back into the patient where, ideally, the engineered cells further multiply, and recognize and kill cancer cells. Historically, solid tumors have been considered beyond the reach of CAR T therapy due to their tumor microenvironment, which is detrimental to CAR T cell entry and activity, amongst other challenges.[1]

About Pelareorep

Pelareorep is a non-pathogenic, proprietary isolate of the unmodified reovirus: a first-in-class intravenously delivered immuno-oncolytic virus for the treatment of solid tumors and hematological malignancies. The compound induces selective tumor lysis and promotes an inflamed tumor phenotype through innate and adaptive immune responses to treat a variety of cancers and has been demonstrated to be able to escape neutralizing antibodies found in patients.

About Oncolytics Biotech Inc.

Oncolytics is a biotechnology company developing pelareorep, an intravenously delivered immuno-oncolytic virus. The compound induces selective tumor lysis and promotes an inflamed tumor phenotype -- turning "cold" tumors "hot" -- through innate and adaptive immune responses to treat a variety of cancers.

Pelareorep has demonstrated synergies with immune checkpoint inhibitors and may also be synergistic with other approved immuno-oncology agents. Oncolytics is currently conducting

and planning additional studies of pelareorep in combination with checkpoint inhibitors and targeted therapies in solid and hematological malignancies, as it prepares for a phase 3 registration study in metastatic breast cancer. For further information, please visit: www.oncolyticsbiotech.com.

References:

1. National Cancer Institute. CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. Updated July 31, 2019. Accessed February 18, 2021. https://www.cancer.gov/about-cancer/treatment/research/car-t-cells

This press release contains forward-looking statements, within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended and forward-looking information under applicable Canadian securities laws (such forward-looking statements and forward-looking information are collectively referred to herein as "forward-looking statements"). Forward-looking statements, including the Company's belief as to the potential and mode of action of pelareorep as a cancer therapeutic, potential commercial opportunities for pelareorep; the Company's primary focus on advancing its lead breast cancer program to a registrational trial; the Company's evaluation and pursuit of business development and partnership potential opportunities; and other statements related to anticipated developments in the Company's business and technologies involve known and unknown risks and uncertainties, which could cause the Company's actual results to differ materially from those in the forward-looking statements. In any forward-looking statement in which Oncolytics expresses an expectation or belief as to future results, such expectations or beliefs are expressed in good faith and are believed to have a reasonable basis, but there can be no assurance that the statement or expectation or belief will be achieved. Such forward-looking statements involve known and unknown risks and uncertainties, which could cause Oncolytics' actual results to differ materially from those in the forward-looking statements. Such risks and uncertainties include, among others, the availability of funds and resources to pursue research and development projects, the efficacy of pelareorep as a cancer treatment, the success and timely completion of clinical studies and trials, Oncolytics' ability to successfully commercialize pelareorep, uncertainties related to the research and development of pharmaceuticals, uncertainties related to the regulatory process and general changes to the economic environment. In particular, we may be impacted by business interruptions resulting from COVID-19 coronavirus, including operating, manufacturing supply chain, clinical trial and project development delays and disruptions, labour shortages, travel and shipping disruption and shutdowns (including as a result of government regulation and prevention measures). It is unknown whether and how Oncolytics may be affected if the COVID-19 pandemic persists for an extended period of time. We may incur expenses or delays relating to such events outside of our control, which could have a material adverse impact on our business, operating results and financial condition. Investors should consult Oncolytics' quarterly and annual filings with the Canadian and U.S. securities commissions for additional information on risks and uncertainties relating to the forward-looking statements. Investors are cautioned against placing undue reliance on forward-looking statements. The Company does not undertake any obligation to update these forward-looking statements, except as required by applicable laws.

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