May 7, 2021

Oncolytics Biotech® Reports 2021 First Quarter Development Highlights and Financial Results

- AWARE-1 clinical data validate clinical development strategy by confirming pelareorep's anti-tumor mechanism of action known to be associated with improved patient outcomes and ability to synergize with checkpoint inhibitors

- Preclinical studies show that pelareorep's synergistic benefits extend across multiple classes of immunotherapeutic agents, including novel CAR T approaches in solid tumors

- Phase 2 BRACELET-1 clinical trial on track for full enrollment in Q4-2021

- Strong financial foundation with over $50 million in cash on hand and cash runway to Q4-2022

SAN DIEGO and CALGARY, AB, May 7, 2021 /PRNewswire/ -- Oncolytics Biotech® Inc. (NASDAQ: ONCY) (TSX: ONC) today announced its financial results and development highlights for the quarter ended March 31, 2021. All dollar amounts are expressed in Canadian currency unless otherwise noted.

"Our continued progress over the past several months has substantially de-risked our lead breast cancer program and validated our broader development strategy," said Dr. Matt Coffey, President and Chief Executive Officer of Oncolytics Biotech Inc. "Clinical data from our AWARE-1 trial show pelareorep alters tumor microenvironments by enabling the infiltration of anti-cancer T cells, shown to be associated with improved cancer patient outcomes, including survival, and demonstrates the synergy between pelareorep and checkpoint inhibitors. These findings support the overall survival benefit observed in our prior phase 2 breast cancer study and suggest that we can deliver additional benefits to patients with HR+/HER2- metastatic breast cancer by combining pelareorep with a checkpoint inhibitor. This hypothesis is currently being evaluated in the BRACELET-1 trial, which remains on track for full enrollment this year."

Dr. Coffey continued, "Alongside our clinical accomplishments, we also generated compelling preclinical data demonstrating pelareorep's potential to synergize with a broad array of immune-oncology (IO) agents such as CAR T cells and bispecific antibodies. These data suggest that pelareorep's clinically demonstrated ability to recruit T cells into tumors may significantly boost the effectiveness of various IO agents in solid cancers, an area where they have shown limited efficacy to date. Looking forward, we plan to pursue pelareorep's development as an enabling technology for multiple classes of IO agents through a partnership strategy, which should allow us to remain primarily focused internally on breast cancer and the execution of our stated clinical milestones."

First Quarter and Subsequent Highlights

Breast Cancer Program

Achieved primary endpoint in AWARE-1 study

An electronic poster at the American Association for Cancer Research (AACR) Annual Meeting 2021 included data from the twenty HR+/HER2- early-stage breast cancer patients included in AWARE-1's first two cohorts (link to PR; link to poster). Results from these patients, treated with pelareorep and letrozole without (cohort 1) or with (cohort 2) the PD-L1 inhibitor atezolizumab (Tecentriq®), showed pelareorep and letrozole treatment upregulated tumor PD-L1 expression, induced the generation and expansion of T cell clones, promoted tumor infiltration of CD8+ T cells, and increased CelTIL score, a measure of tumor cellularity and inflammation associated with favorable clinical outcomes. These desired outcomes were further enhanced by the addition of atezolizumab, demonstrating that pelareorep and atezolizumab synergistically combine to generate an anti-cancer immune response in the tumor and peripheral blood. Notably, the trial demonstrated dose-related activity of pelareorep led to the achievement of the primary endpoint, with six of ten patients achieving at least a 30% increase in CelTIL score following treatment in cohort 2. Together, these data support the results of a prior successful phase 2 trial (IND-213) that showed a near doubling of overall survival with pelareorep treatment in HR+/HER2- patients and the clinical rationale behind the phase 2 BRACELET-1 trial, which is evaluating the safety and efficacy of pelareorep and chemotherapy alone, and in combination with a PD-L1 inhibitor, in HR+/HER2- breast cancer patients.

Additional Immunotherapeutic Combinations and Opportunities

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

A preclinical study from the Mayo Clinic showed that loading chimeric antigen receptor (CAR) T cells with pelareorep vastly improved their persistence and efficacy in a murine solid tumor model, in stark contrast to prior preclinical studies that showed intratumoral infection with the VSV oncolytic virus weakened CAR T cells (link to PR; link to poster). The efficacy of pelareorep-loaded CAR T cell ("CAR/Pela") therapy was further enhanced by subsequently administering a single intravenous dose of pelareorep, which led to the generation of highly persistent CAR T cells, the inhibition of recurrent tumor growth, and ultimately tumor cures. These synergistic immune effects were notably specific to pelareorep, as intravenous boosting with VSV did not augment CAR/Pela therapy or prevent the growth of recurrent tumors. Collectively, these data demonstrate the potential of

pelareorep to broaden the applicability of CAR T cells to solid tumors, an area where CAR T cell efficacy is currently limited due to immunosuppressive tumor microenvironments that promote T cell exhaustion and exclusion.

Announced preclinical data highlighting pelareorep's ability to synergize with multiple classes of anti-cancer agents

Data presented in two electronic poster presentations at the AACR Annual Meeting 2021 showed that pelareorep enhanced the anti-tumor efficacy of the poly(ADP)-ribose polymerase 1 (PARP-1) inhibitor talazoparib and the cyclin-dependent kinase (CDK) 4/6 inhibitor palbociclib, which are both FDA approved for the treatment of breast cancer. The observed synergistic effects between pelareorep and both talazoparib and palbociclib were notably mediated through immunologic mechanisms rather than through the molecular pathways typically associated with PARP-1 and CDK 4/6 inhibition (link to PR; link to CDK4/6 poster; link to PARP-1 poster). Together, these results suggest that pelareorep may enhance the therapeutic potential of PARP-1 and CDK 4/6 inhibitors by expanding the mechanisms by which they exert anti-tumor effects.

Initiation of a preclinical research collaboration with Leiden University Medical Center (LUMC) and Oncode Institute to evaluate pelareorep-bispecific antibody combination therapies

Collaborative preclinical studies with LUMC will evaluate the combination of pelareorep-CD3-bispecific antibody combinations in breast and pancreatic tumor models. Pelareorep's clinically demonstrated ability to recruit T cells to solid tumors provides a strong rationale for these studies, as CD3-bispecific antibodies are designed to facilitate cancer-killing by simultaneously engaging both T cells and tumor tissue. Prior preclinical studies in breast and pancreatic cancer models also support this collaboration, as they have shown that the addition of pelareorep to CD3-bispecific antibody therapy results in cancer regression and prolonged survival.

Corporate Highlights

Hosted a key opinion leader webinar on AWARE-1 data, the immunotherapeutic effects of pelareorep in breast cancer, and its synergistic activity with CAR T cells in solid tumors

The webinar featured presentations by Key Opinion Leaders (KOLs) Aleix Prat, M.D., Ph.D. (Clínic Barcelona) and Richard Vile, Ph.D., (Mayo Clinic), as well as a corporate update by members of the Oncolytics management team. The formal presentations were followed by a question and answer session. A replay of the event can be accessed by clicking here.

Financial Highlights

- As of March 31, 2021, the Company reported $50.4 million in cash and cash equivalents. The Company raised gross proceeds of $25.8 million during the first quarter through issuing of common stock through its ATM facility.
- Operating expense for the first quarter of 2021 was $3.1 million, compared to $3.0 million in the first quarter of 2020.
- R&D expense for the first quarter of 2021 was $2.8 million, compared to $2.5 million in

the first quarter of 2020.
- Net cash used in operating activities for the first quarter of 2021 was $5.6 million, compared to $4.0 million for the first quarter of 2020.
- The net loss for the first quarter of 2021 was $6.4 million, compared to a net income of $0.4 million in the first quarter of 2020, which reflected a $4.2 million non-cash gain in fair value of warrant derivative. The basic and diluted loss per share was $0.13 in the first quarter of 2021, compared to a basic earnings and diluted loss per share of $0.01 and $0.04, respectively, in the first quarter of 2020.

Anticipated Milestones and Catalysts

- Announcement of final data from phase 2 NU 18I01 second-line pancreatic cancer study: H1 2021
- Dosing of the first patient in GOBLET study in gastrointestinal cancer: mid-2021
- Final biomarker data for AWARE-1 breast cancer study in the intended target population for a registrational study: H2 2021
- Completion of enrollment in BRACELET-1 metastatic breast cancer study: Q4 2021
- Interim safety update from IRENE study in triple-negative breast cancer: Q4 2021
- Interim safety data from phase 1 WINSHIP 4398-18 multiple myeloma study: Q4 2021

Oncolytics expects to provide updates on the timing of the following milestones over the coming months:

- Interim safety update from Phase 2 BRACELET-1 metastatic breast cancer study
- Phase 2 BRACELET-1 metastatic breast cancer study: final data

Update on COVID-19

Oncolytics continues to collaborate with its investigators to ensure the safety of patients and employees, as well as the productivity of its clinical programs. We expect these measures will allow us to build on the positive momentum of 2020, despite any COVID-19-related challenges that may arise. Moving forward, we plan to remain in contact with relevant stakeholders and keep the market apprised of any new information that may materially impact clinical timelines.

Accessing the Annual Corporate Update Presentation

The Annual Corporate Update, which will also discuss first quarter 2021 financial results, beginning immediately following the Annual General Meeting at approximately 12:10 p.m. Eastern Daylight Time, may be accessed via the AGM webcast link, https://web.lumiagm.com/158281614, as a guest or by dialing +1-888-231-8191 for callers in North America and +1-647-427-7450 for International callers. The live webcast of the corporate update section of the call will be accessible on the Investor Relations page of Oncolytics' website at https://ir.oncolyticsbiotech.com/events-presentations and will be archived for three months.

ONCOLYTICS BIOTECH INC.
INTERIM CONSOLIDATED STATEMENTS OF FINANCIAL POSITION
(unaudited)
(in Canadian dollars, except share amounts)

As at	March 31, 2021 $	December 31, 2020 $
Assets		
Current assets		
Cash and cash equivalents	**50,362,162**	31,219,574
Other receivables	**111,665**	89,661
Prepaid expenses	**2,881,730**	2,427,200
Total current assets	**53,355,557**	33,736,435
Non-current assets		
Property and equipment	**215,587**	236,664
Right-of-use assets	**609,297**	372,468
Total non-current assets	**824,884**	609,132
Total assets	**54,180,441**	34,345,567
Liabilities And Shareholders' Equity		
Current Liabilities		
Accounts payable and accrued liabilities	**1,918,638**	1,805,015
Other liabilities	**—**	123,985
Lease liabilities	**252,356**	248,885
Warrant derivative	**237,546**	531,228
Total current liabilities	**2,408,540**	2,709,113
Non-current liabilities		
Contract liability	**6,730,287**	6,730,287
Lease liabilities	**371,974**	153,174
Total non-current liabilities	**7,102,261**	6,883,461
Total liabilities	**9,510,801**	9,592,574
Commitments and contingencies		
Shareholders' equity		
Share capital Authorized: unlimited Issued: March 31, 2021 – 52,844,210 December 31, 2020 – 46,166,980	**382,963,397**	356,824,172
Warrants	**3,617,570**	3,617,570
Contributed surplus	**31,274,835**	31,022,356
Accumulated other comprehensive income	**359,913**	400,225
Accumulated deficit	**(373,546,075)**	(367,111,330)
Total shareholders' equity	**44,669,640**	24,752,993
Total liabilities and shareholder's equity	**54,180,441**	34,345,567

ONCOLYTICS BIOTECH INC.
INTERIM CONSOLIDATED STATEMENTS OF (LOSS) INCOME AND COMPREHENSIVE (LOSS) INCOME
(unaudited)
(in Canadian dollars, except share amounts)

For the three-month period ending March 31,	2021 $	2020 $

Expenses		
Research and development	**2,759,014**	2,529,646
Operating	**3,141,890**	2,993,388
Loss before the following	**(5,900,904)**	(5,523,034)
Change in fair value of warrant derivative	**(164,780)**	4,151,982
Foreign exchange (loss) gain	**(390,554)**	1,704,805
Interest income, net	**21,493**	65,909
Net (loss) income	**(6,434,745)**	399,662
Other comprehensive (loss) income items that may be reclassified to net loss		
Translation adjustment	**(40,312)**	295,212
Net comprehensive (loss) income	**(6,475,057)**	694,874
(Loss) earnings per common share		
Basic	**(0.13)**	0.01
Diluted	**(0.13)**	(0.04)

ONCOLYTICS BIOTECH INC.
INTERIM CONSOLIDATED STATEMENTS OF CHANGES IN EQUITY
(unaudited)
(in Canadian dollars)

	Share Capital $	Warrants $	Contributed Surplus $	Accumulated Other Comprehensive Income $	Accumulated Deficit $	Total $
As at December 31, 2019	311,077,859	3,617,570	29,338,849	464,101	(344,606,273)	(107,894)
Net loss and other comprehensive loss	—	—	—	295,212	399,662	694,874
Issued pursuant to stock option plan	134,985	—	(49,835)	—	—	85,150
Issued pursuant to incentive share award plan	209,475	—	(209,475)	—	—	—
Issued pursuant to "At the Market" Agreement	17,529,109	—	—	—	—	17,529,109
Issued pursuant to warrant derivative exercised	5,529,266	—	—	—	—	5,529,266
Share-based compensation	—	—	392,805	—	—	392,805
Share issue costs	(691,297)	—	—	—	—	(691,297)
As at March 31, 2020	333,789,397	3,617,570	29,472,344	759,313	(344,206,611)	23,432,013

As at December 31, 2020	356,824,172	3,617,570	31,022,356	400,225	(367,111,330)	24,752,993
Net loss and other comprehensive income	—	—	—	(40,312)	(6,434,745)	(6,475,057)
Issued pursuant to stock option plan	302,908	—	(113,558)	—	—	189,350
Issued pursuant to incentive share award plan	292,039	—	(292,039)	—	—	—
Issued pursuant to "At the Market" Agreement	25,831,909	—	—	—	—	25,831,909
Issued pursuant to warrant derivative exercised	686,616	—	—	—	—	686,616
Share-based compensation	—	—	658,076	—	—	658,076
Share issue costs	(974,247)	—	—	—	—	(974,247)
As at March 31, 2021	**382,963,397**	**3,617,570**	**31,274,835**	**359,913**	**(373,546,075)**	**44,669,640**

ONCOLYTICS BIOTECH INC.
INTERIM CONSOLIDATED STATEMENTS OF CASH FLOWS
(unaudited)
(in Canadian dollars)

For the three-month period ending March 31,	**2021 $**	**2020 $**
Operating Activities		
Net loss for the period	**(6,434,745)**	399,662
Depreciation - property and equipment	**20,550**	23,045
Depreciation - right-of-use-assets	**86,184**	91,023
Share-based compensation	**658,076**	392,805
Interest expense on lease liabilities	**13,809**	18,209
Unrealized foreign exchange loss (gain)	**519,368**	(1,427,756)
Change in fair value of warrant derivative	**164,780**	(4,151,982)
Net change in non-cash working capital	**(596,479)**	699,737
Cash used in operating activities	**(5,568,457)**	(3,955,257)
Investing Activities		
Acquisition of property and equipment	**—**	(10,715)
Cash used in investing activities	**—**	(10,715)
Financing Activities		
Proceeds from exercise of stock options	**189,350**	85,150
Proceeds from exercise of warrant derivative	**230,946**	1,433,142
Proceeds from "At the Market" equity distribution agreement	**24,857,662**	16,837,813
Payment of lease liabilities	**(111,673)**	(113,474)

Cash provided by financing activities	**25,166,285**	18,242,631
Increase in cash	**19,597,828**	14,276,659
Cash and cash equivalents, beginning of period	**31,219,574**	14,148,021
Impact of foreign exchange on cash and cash equivalents	**(455,240)**	2,142,800
Cash and cash equivalents, end of period	**50,362,162**	30,567,480

About AWARE-1

AWARE-1 is an open label window-of-opportunity study in early-stage breast cancer enrolling 38 patients into five cohorts:

- Cohort 1 (n=10), HR+ / HER2- (pelareorep + letrozole)
- Cohort 2 (n=10), HR+ / HER2- (pelareorep + letrozole + atezolizumab)
- Cohort 3 (n=6), TNBC (pelareorep + atezolizumab)
- Cohort 4 (n=6), HR+ / HER2+ (pelareorep + trastuzumab + atezolizumab)
- Cohort 5 (n=6), HR- / HER2+ (pelareorep + trastuzumab + atezolizumab)

The study combines pelareorep, without or with atezolizumab, and the standard of care therapy according to breast cancer subtype. Tumor tissue is collected from patients as part of their initial breast cancer diagnosis, again on day three following initial treatment, and finally at three weeks following treatment, on the day of their mastectomy. Data generated from this study are intended to confirm that pelareorep is acting as a novel immunotherapy, to evaluate potential synergy between pelareorep and checkpoint blockade, and to provide comprehensive biomarker data by breast cancer subtype. The primary endpoint of the study is overall CelTIL score (a measurement of cellularity and tumor-infiltrating lymphocytes). Secondary endpoints for the study include CelTIL by breast cancer subtype, safety, and tumor and blood-based biomarkers.

For more information about the AWARE-1 study, refer to https://clinicaltrials.gov/ct2/show/NCT04102618.

Tecentriq® (atezolizumab) is a registered trademark of Genentech, a member of the Roche Group.

About BRACELET-1

The BRACELET-1(BReast cAnCEr with the Oncolytic Reovirus PeLareorEp in CombinaTion with anti- PD-L1 and Paclitaxel) study is an open-label, phase 2, randomized study in patients with HR+/HER2-, endocrine-refractory metastatic breast cancer being conducted under a co-development agreement with Merck KGaA, Darmstadt, Germany and Pfizer. PrECOG LLC, a leading cancer research network, is managing the study. The study will take place at 20 trial sites and enroll 45 patients randomized into three cohorts. A three-patient safety run-in will be conducted with patients receiving pelareorep, paclitaxel, and avelumab prior to randomization. The three cohorts will be treated as follows:

- Cohort 1 (n=15): paclitaxel
- Cohort 2 (n=15): paclitaxel + pelareorep
- Cohort 3 (n=18): paclitaxel + pelareorep + avelumab (Bavencio®)

Patients in cohort 1 will receive paclitaxel on days 1, 8, and 15 of a 28-day cycle. Patients in cohort 2 will receive the same paclitaxel regimen as cohort 1, plus pelareorep on days 1, 2, 8, 9, 15 and 16 of the 28-day cycle. Patients in cohort 3 will receive the same combination and dosing regimen as cohort 2, plus avelumab on days 3 and 17 of the 28-day cycle. The primary endpoint of the study is overall response rate. Exploratory endpoints include peripheral and tumor T cell clonality, inflammatory markers, and safety and tolerability assessments.

For more information about the BRACELET-1 study, refer to https://clinicaltrials.gov/ct2/show/NCT04215146.

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 contained in this press release include statements regarding the mode of action, potential and benefits of pelareorep as a cancer therapeutic; expectations as to the purpose, design, outcomes and benefits of its current or pending clinical trials involving pelareorep; expectations as to the enrollment in its various clinical studies; expectations regarding Oncolytics' cash runway; beliefs regarding Oncolytics being positioned for sustained growth; plans to pursue pelareorep's development through a partnership strategy and the anticipated benefits therefrom; Oncolytics upcoming catalysts and milestones and Oncolytics' expectations in relation thereto; our management of our business during the ongoing COVID-19 pandemic; the timing and content of our annual corporation presentation; and other statements related to anticipated developments in Oncolytics' business and technologies. 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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