May 5, 2022

Oncolytics Biotech® Reports First Quarter 2022 Financial Results and Recent Operational Highlights

Anticipated Q4 2022 data readout from randomized phase 2 study in breast cancer is on track and expected to inform the design of a registrational trial

Clinical biomarker data demonstrates pelareorep's induced improvement in the prognosis of HR+/HER2- breast cancer patients by decreasing their risk of recurrence

Preclinical data demonstrating the synergistic anti-cancer activity of pelareorep combined with CAR T cell therapy in solid tumors published in Science Translational Medicine

$39.5 million in cash and cash equivalents expected to provide runway through key catalysts and into 2023

Management hosting conference call and webcast today at5:00 p.m. ET

SAN DIEGO, Calif and CALGARY, AB, May 5, 2022 /CNW/ -- Oncolytics Biotech® Inc. (NASDAQ: ONCY) (TSX: ONC) today announced recent operational highlights and financial results for the first quarter ended March 31, 2022. All dollar amounts are expressed in Canadian currency unless otherwise noted.

"Recent updates from multiple clinical trials have showcased pelareorep's wide-ranging therapeutic potential as well as the advantages of our corporate strategy," said Dr. Matt Coffey, President and Chief Executive Officer of Oncolytics Biotech Inc. "Our latest data in HR+/HER2- breast cancer show pelareorep driving changes in the tumor microenvironment that are known to be associated with improved patient outcomes and a decreased risk of recurrence. These results increase our understanding of pelareorep's mechanism of action and build upon our prior phase 2 data that showed pelareorep delivering a clinically meaningful and statistically significant survival benefit to HR+/HER2- breast cancer patients. They also further de-risk our lead program's upcoming randomized phase 2 data readout, which is expected to confirm and expand upon these prior findings and move us forward into

a registrational study."

Dr. Coffey continued, "Recent clinical and preclinical data also showed pelareorep safely combined with a range of drug classes and demonstrated its potential to enable the success of CAR T cell therapies against solid tumors. We believe our strategy has positioned us for sustained success, as its execution allowed us to generate proof-of-concept data in multiple indications while maintaining a strong balance sheet and a clear focus on our lead breast cancer program."

First Quarter and Subsequent Highlights

Breast Cancer Program

AWARE-1 data demonstrate pelareorep's ability to improve the prognosis of HR+/HER2- breast cancer patients and decrease their risk of recurrence

New clinical biomarker analyses from AWARE-1's first two cohorts presented at the European Society for Medical Oncology (ESMO) Breast Cancer Meeting evaluated changes in the tumor microenvironment (TME) following treatment with pelareorep and letrozole with (cohort 2) or without (cohort 1) the checkpoint inhibitor atezolizumab (link to PR). Gene expression analyses showed 100% of evaluable patients with a Risk of Recurrence Score (ROR-S) classified as "low" 21-days post-treatment vs. 55% with a "low" ROR-S prior to treatment. In both cohorts, the treatment regimen caused tumors to convert from the more aggressive luminal B classification to luminal A classification, which is associated with improved clinical outcomes. Collectively across both cohorts, the percentage of evaluable patients with a luminal A classification increased from 55% before treatment to 85% 21 days after treatment. Statistically significant increases in markers of tumor cell death and T cell activation were also observed with treatment. Altogether, these results reaffirm pelareorep's ability to improve the prognosis of breast cancer patients and decrease their risk of recurrence by remodeling the TME and stimulating anti-tumor immunity.

Partner Adlai Nortye advanced Chinese bridging trial of pelareorep-paclitaxel combination to final dosing cohort

The ongoing bridging trial is evaluating the safety, tolerability, and preliminary efficacy of pelareorep-paclitaxel combination therapy in Chinese patients with advanced or metastatic breast cancer. Initiation of the trial's final cohort followed the completion of the dose escalation evaluation periods of the first two cohorts, which indicated that the studied combination was well tolerated with no new safety signals observed. The dosing regimen for the trial's second cohort is equivalent to that administered in IND-213, while the regimen for the third cohort is equivalent to the regimen being administered in BRACELET-1, an ongoing phase 2 trial in HR+/HER2- breast cancer that is evaluating pelareorep plus paclitaxel with and without a checkpoint inhibitor. Completion of the bridging trial is expected to accelerate pelareorep's development in China, the world's second largest oncology market.

Gastrointestinal Cancers Program

Successfully completed safety run-ins for the phase 1/2 GOBLET trial

The GOBLET trial is evaluating the safety and efficacy of pelareorep in combination with

Roche's anti-PD-L1 checkpoint inhibitor atezolizumab in patients with advanced or metastatic pancreatic, colorectal, and anal cancers. The three-patient safety run-ins for the trial's pancreatic cancer and third-line metastatic colorectal cancer (mCRC) cohorts have each been successfully completed following an independent review by the study's Data Safety Monitoring Board (DSMB), which noted no safety concerns. Following the DSMB reviews and authorization from the Paul Ehrlich Institute (PEI; Germany's medical regulatory body), all of the trial's four cohorts are now cleared for full enrollment.

In addition to providing data on the safety and efficacy of pelareorep-atezolizumab combinations, the GOBLET trial is designed to evaluate CEACAM6 and T cell clonality as predictive biomarkers of treatment response. Use of a predictive biomarker in future studies may increase their likelihood of success by ensuring selection of the most appropriate patients.

Additional Immunotherapeutic Opportunity

Preclinical data demonstrating the synergistic anti-cancer activity of pelareorep combined with chimeric antigen receptor (CAR) T cell therapy in solid tumors published in Science Translational Medicine

Though CAR T cells have generated long-term cures in patients with hematological malignancies[1], they have thus far had limited success against solid tumors due primarily to challenges posed by short-lived perseverance, immunosuppressive TMEs, and antigen escape. A peer-reviewed preclinical study published recently in *Science Translational Medicine* showed the persistence and anti-cancer activity of CAR T cells improved dramatically when these cells were loaded with pelareorep (link to PR, link to publication). Compared to either treatment alone, treatment with pelareorep-loaded CAR T cells led to statistically significant survival benefits in murine models of skin and brain cancer. In addition, boosting mice treated with pelareorep-loaded CAR T cells with a subsequent intravenous dose of pelareorep led to a further enhancement in efficacy and tumor cures in >80% of mice treated in each model. Mechanistic analyses indicated that the enhanced efficacy of this combination was due to pelareorep's ability to increase CAR T cell perseverance, reverse immunosuppressive TMEs, and reduce antigen escape. The reduction in antigen escape was linked to the creation of dual-specific CAR T cells that target both the tumor directly and pelareorep proteins within the tumor. Given that solid tumors represent the vast majority of cancer cases, these results demonstrate pelareorep's potential to significantly expand the commercial opportunity offered by CAR T cell therapies.

Financial Highlights

- As of March 31, 2022, the Company reported $39.5 million in cash and cash equivalents.
- Operating expense for the first quarter of 2022 was $2.6 million, compared to $3.1 million for the first quarter of 2021.
- R&D expense for the first quarter of 2022 was $3.7 million, compared to $2.8 million for the first quarter of 2021.
- The net loss for the first quarter of 2022 was $6.8 million, compared to a net loss of $6.4 million in the first quarter of 2021. The basic and diluted loss per share was $0.12 in the first quarter of 2022, compared to a basic and diluted loss per share of $0.13 in the first quarter of 2021.

- Net cash used in operating activities for the first quarter of 2022 was $6.3 million, compared to $5.6 million for the first quarter of 2021.

Anticipated Milestones and Catalysts

- Completion of enrollment in phase 2 BRACELET-1 metastatic breast cancer study: Q2 2022
- GOBLET pancreatic cohort update: Q3 2022
- Top-line data from phase 2 BRACELET-1 metastatic breast cancer study: Q4 2022

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

- Interim safety update from BRACELET-1 metastatic breast cancer study

Webcast and Conference Call

Management will host a conference call for analysts and institutional investors at 5:00 p.m. ET today, May 5, 2022. To access the call, please dial (888) 664-6383 (North America) or (416) 764-8650 (International) and, if needed, provide confirmation number 6952-6976. A live webcast of the call will also be available by clicking here or on the Investor Relations page of Oncolytics' website (LINK) and will be archived for three months. A dial in replay will be available for one week and can be accessed by dialing (888) 390-0541 (North America) or (416) 764-8677 (International) and using replay code: 526-976#.

ONCOLYTICS BIOTECH INC.
CONDENSED INTERIM CONSOLIDATED STATEMENTS OF FINANCIAL POSITION
(unaudited)

(in Canadian dollars, except share amounts)

As at	March 31, 2022	December 31, 2021
Assets		
Current assets		
Cash and cash equivalents	**$ 39,483,022**	$ 41,262,044
Other receivables	**102,217**	866,055
Prepaid expenses	**3,950,332**	2,775,800
Total current assets	**43,535,571**	44,903,899
Property and equipment	**403,153**	392,041
Right-of-use assets	**507,556**	584,251
Total assets	**$ 44,446,280**	$ 45,880,191
Liabilities And Shareholders' Equity		
Current Liabilities		
Accounts payable and accrued liabilities	**$ 2,048,476**	$ 1,987,870
Other liabilities	**—**	352,279
Lease liabilities	**307,480**	293,672
Warrant derivative	**68,231**	56,017
Total current liabilities	**2,424,187**	2,689,838
Contract liability	**6,730,287**	6,730,287
Lease liabilities	**276,640**	361,081
Total liabilities	**9,431,114**	9,781,206
Commitments and contingencies		
Shareholders' equity		
Share capital		
Authorized: unlimited Issued: March 31, 2022 – 57,501,688 December 31, 2021 – 55,043,789	**396,504,249**	391,348,183
Warrants	**3,617,570**	3,617,570
Contributed surplus	**34,746,749**	34,161,103
Accumulated other comprehensive income	**340,728**	387,738
Accumulated deficit	**(400,194,130)**	(393,415,609)
Total shareholders' equity	**35,015,166**	36,098,985
Total liabilities and shareholder's equity	**$ 44,446,280**	$ 45,880,191

ONCOLYTICS BIOTECH INC.
CONDENSED INTERIM CONSOLIDATED STATEMENTS OF LOSS AND COMPREHENSIVE LOSS
(unaudited)

(in Canadian dollars, except share amounts)

For the three months ended March 31,	2022	2021
Expenses		
Research and development	**$ 3,707,996**	$ 2,759,014
Operating	**2,602,090**	3,141,890
Loss before the following	**(6,310,086)**	(5,900,904)
Change in fair value of warrant derivative	**(13,019)**	(164,780)
Foreign exchange loss	**(474,120)**	(390,554)
Interest income, net	**18,704**	21,493
Net loss	**(6,778,521)**	(6,434,745)
Other comprehensive loss items that may be reclassified to net loss		
Translation adjustment	**(47,010)**	(40,312)
Net comprehensive loss	**$ (6,825,531)**	$ (6,475,057)
Basic and diluted loss per common share	**$ (0.12)**	$ (0.13)
Weighted average number of shares (basic and diluted)	**56,576,462**	49,666,585

ONCOLYTICS BIOTECH INC.
CONDENSED 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, 2020	$ 356,824,172	$ 3,617,570	$ 31,022,356	$ 400,225	$ (367,111,330)	$ 24,752,993
Net loss and other comprehensive loss	—	—	—	(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
As at December 31, 2021	$ 391,348,183	$ 3,617,570	$ 34,161,103	$ 387,738	$ (393,415,609)	$ 36,098,985
Net loss and other comprehensive income	—	—	—	(47,010)	(6,778,521)	(6,825,531)
Issued pursuant to stock option plan	19,570	—	(7,487)	—	—	12,083
Issued pursuant to incentive share award plan	45,848	—	(45,848)	—	—	—
Issued pursuant to "At the Market" Agreement	5,267,058	—	—	—	—	5,267,058
Share-based compensation	—	—	638,981	—	—	638,981
Share issue costs	(176,410)	—	—	—	—	(176,410)
As at March 31, 2022	**$ 396,504,249**	**$ 3,617,570**	**$ 34,746,749**	**$ 340,728**	**$ (400,194,130)**	**$ 35,015,166**

ONCOLYTICS BIOTECH INC.
CONDENSED INTERIM CONSOLIDATED STATEMENTS OF CASH FLOWS
(unaudited)

(in Canadian dollars)

For the three months ended March 31,	2022	2021
Operating Activities		
Net loss for the period	**$ (6,778,521)**	$ (6,434,745)
Depreciation - property and equipment	**23,952**	20,550
Depreciation - right-of-use-assets	**73,612**	86,184
Share-based compensation	**638,981**	658,076
Interest expense on lease liabilities	**23,774**	13,809
Unrealized foreign exchange loss	**409,863**	519,368
Change in fair value of warrant derivative	**13,019**	164,780
Net change in non-cash working capital	**(656,805)**	(596,479)
Cash used in operating activities	**(6,252,125)**	(5,568,457)
Investing Activities		
Acquisition of property and equipment	**(35,521)**	—
Cash used in investing activities	**(35,521)**	—
Financing Activities		
Proceeds from exercise of stock options	**12,083**	189,350
Proceeds from exercise of warrant derivative	**—**	230,946
Proceeds from "At the Market" equity distribution agreement	**5,090,648**	24,857,662
Payment of lease liabilities	**(88,836)**	(111,673)
Cash provided by financing activities	**5,013,895**	25,166,285
(Decrease) increase in cash	**(1,273,751)**	19,597,828
Cash and cash equivalents, beginning of period	**41,262,044**	31,219,574
Impact of foreign exchange on cash and cash equivalents	**(505,271)**	(455,240)
Cash and cash equivalents, end of period	**$ 39,483,022**	$ 50,362,162

References

1. Melenhorst, J.J., Chen, G.M., Wang, M. *et al.* Decade-long leukaemia remissions with persistence of CD4^{+} CAR T cells. *Nature* (2022). https://doi.org/10.1038/s41586-021-04390-6

About Oncolytics Biotech Inc.

Oncolytics is a biotechnology company developing pelareorep, an intravenously delivered immunotherapeutic agent. This compound induces anti-cancer immune responses 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 oncology treatments. Oncolytics is currently conducting and planning clinical trials evaluating pelareorep in combination with checkpoint inhibitors and targeted therapies in solid and hematological malignancies as it advances towards a registration study in metastatic breast cancer. For further information, please visit: www.oncolyticsbiotech.com.

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 Oncolytics' belief as to the potential and benefits of pelareorep as a cancer therapeutic; Oncolytics' expectations as to the purpose, design, outcomes and benefits of its current or pending clinical trials involving pelareorep; Oncolytics' beliefs as to pelareorep's wide-ranging therapeutic and the advantages of its corporate strategy; Oncolytics' beliefs that the latest data in HR+/HER2- breast cancer further de-risk its upcoming randomized phase 2 data

readout and its expectation that the data readout will confirm and expand upon its prior findings; Oncolytics' belief that its strategy has positioned it for sustained success; Oncolytics' expectations the completion of its Nortye Adlai's bridging trial will accelerate pelareorep's development in China; Oncolytics' belief that use of a predictive biomarker in future studies may increase the likelihood of success of the studies; Oncolytics' belief that pelareorep has the potential to significantly expand the potential opportunity offered by CAR T therapies; Oncolytics anticipated milestones and catalysts, including completion of enrollment in phase 2 BRACELET-1 metastatic breast cancer study in Q2 2022; GOBLET pancreatic cohort update in Q3 2022; top-line data from phase 2 BRACELET-1 metastatic breast cancer study in Q4 2022; and its plans to release an interim safety update from BRACELET-1 metastatic breast cancer study; our plans to advance towards a registration study in metastatic breast cancer; 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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