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# pharma TECH OUTLOOK

IMMUNOTHERAPY EDITION

MATT COFFEY, PRESIDENT & CEO

## A NEW PARADIGM IN IMMUNO-ONCOLOGY THERAPY

## ONCOLYTICS BIOTECH

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COVER STORY

# ONCOLYTICS BIOTECH

## A NEW PARADIGM IN IMMUNO-ONCOLOGY THERAPY

pharma TECH OUTLOOK TOP 10 IMMUNOTHERAPY COMPANIES - 2020

BY STACEY SMITH

Viruses are the most common biological entity on our planet—a drop of seawater, for instance, can contain more than ten million of them. The etymological meaning for 'virus' comes from the Latin word 'venom,' which translates into poison. Viruses have long been dreaded due to their ability to cause widespread, deadly outbreaks such as the Spanish Flu, H1N1/Swine Flu, Ebola, and now COVID-19. Not all viruses, however, can be deemed to be pathogens. Some viruses, known as oncolytic viruses (OVs), for example, can be used as cancer therapies. The idea that viruses can be used to treat cancer has been around since the beginning of the 20th century. Only recently, however,

ANDREW DE GUTTADAURO, GLOBAL HEAD OF BUSINESS DEVELOPMENT

MATT COFFEY, PRESIDENT & CEO

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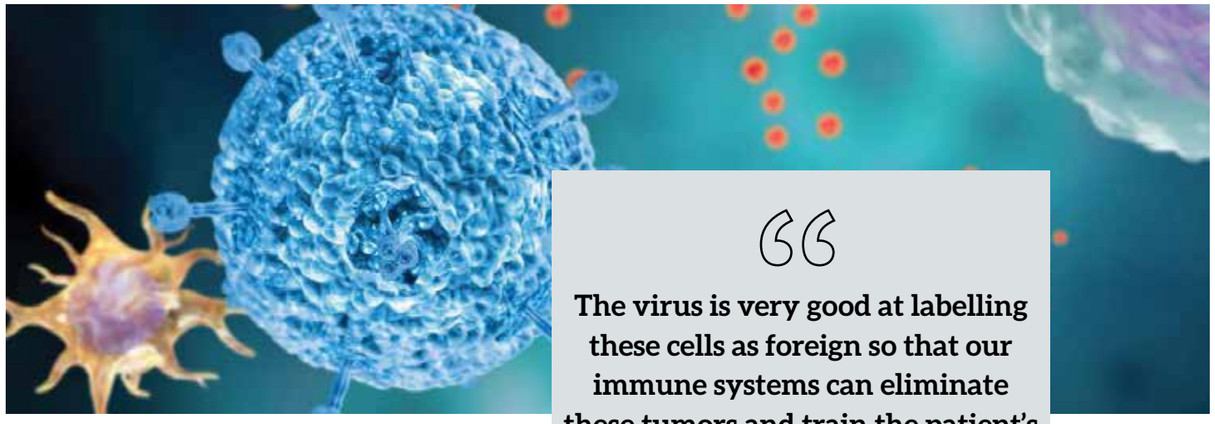
KIRK LOOK, CFO

has the field of oncology shifted to a point where OVs are poised to become key therapeutics in the fight against cancer. This shift has been brought about by the emergence of cancer immunotherapy, which attempts to exploit a patient's natural anti-tumor immune response. By selectively replicating and lysing tumor cells, but not healthy cells, OVs can further promote anti-tumor immunity and thus, when combined with existing immunotherapeutic agents, increase their effectiveness.

On the cusp of revolutionizing immuno-oncology, and advancing OV therapy, is Oncolytics Biotech. The company is developing an intravenously delivered immuno-oncolytic virus called "pelareorep" to treat solid tumors and haematological malignancies. Pelareorep is a non-pathogenic, proprietary isolate of the unmodified reovirus that uniquely induces selective tumor lysis and promotes an inflamed tumor phenotype through innate and adaptive immune responses.

As opposed to harmful cytotoxic agents or radiotherapy, we're stimulating the patient's own immune system to be the most effective way of eliminating the cancer," explains Andrew de Guttadauro, Global Head of Business Development.

Pelareorep has demonstrated the ability to localize to both primary and metastatic tumors. Much like monoclonal antibodies, and other similar biologic therapies, pelareorep acts systemically and, therefore, can be delivered via simple, intravenous delivery (IV). Upon IV delivery, the virus escapes neutralization in part by binding to peripheral blood mononuclear cells (PBMCs). After binding to PBMCs, the virus is handed off to tumor targets. Once at the tumor, the virus promotes an inflammatory immune response which upregulates the expression of immune checkpoints and causes T and NK cells to infiltrate the tumor and attack the cancer cells. By priming the tumor in this manner, pelareorep can increase the percentage of patients who respond to checkpoint



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## A Non-Toxic, Safe and Efficient Treatment of Breast Cancer

Tumors can grow due to the lack of an immune response to the cancer cell. Tumor cells evade an immune response through key receptors called "checkpoints" that tell the immune system 'do not attack me.' Approved immunotherapies, including checkpoint inhibitors, are designed to block this pathway, thereby enabling the immune system to recognize and kill the cancer. Depending on the tumor type, as few as 1 in 5 patients will respond to checkpoint blockade. Responses are limited when tumors do not have the critical elements required for checkpoint blockade to work, such as T-cells, an inflamed tumor, and expression of checkpoints. "We want to increase the number of responders to more than one in five, as well as expand the range of tumors eligible for checkpoint blockade treatment. inhibitors and open up new indications where checkpoint blockade has been ineffective.

"The virus is very good at labelling these cells as foreign so that our immune systems can eliminate these tumors and train the patient's immune system to eliminate the disease from the body," commented Dr. Matt Coffey, President and CEO of Oncolytics. Two essential safety features of pelareorep are its inability to replicate in non-cancer cells and to be actively cleared by the immune system. The virus can selectively replicate only in permissive cancer cells located in the primary tumor and metastatic sites in response to defective cell signalling pathways, a high level of genomic mutations, and cellular stress from chemo or radiation therapy.

Upon virus replication, cancer cells lyse/die and release new virus particles to infect nearby cancer cells. Also, the binding of pelareorep to PBMCs promotes immune cell activation, further facilitating an anti-cancer immune response by activating innate and adaptive immune systems, converting immune-unresponsive 'cold tumors' into immune-responsive 'hot tumors.' Following cancer cell death by the virus, tumor and viral antigens are taken up by antigen-presenting cells (APCs). The APCs in our bodies process and present antigens to T-cells, thus training the adaptive immune system to recognize and kill cancer cells. An adaptive immune response allows for existing cancer cells to be eliminated, constant cancer cell surveillance, relapse prevention, and increased overall survival. "In an earlier study of the virus in breast cancer, when combined with paclitaxel, results demonstrated a doubling in the overall survival of hormone receptor positive (HR+)/HER2 receptor negative (HER2-) metastatic breast cancer patients from 10 to almost 21 months," further adds Coffey.

## Accelerating the Future of Cancer Treatment

According to the American Cancer Institute, in 2019, an estimated 268,600 new cases of invasive breast cancer were diagnosed among women with Luminal A - HR+/HER2 - being the most common type of breast cancer. Approximately 1 in 8 women (13 percent) will be diagnosed with invasive breast cancer in their lifetime, and 1 in 39 women (3 percent) will die from breast cancer. Breast cancer survival rates vary greatly worldwide—the lower survival rates prevalent in less developed countries can be explained mainly by the lack of early detection programs, resulting in a high proportion of women presenting with late-stage disease, as well as by the lack of adequate diagnosis and treatment facilities. To positively impact the statistics and increase survival rates, Oncolytics is currently researching pelareorep's efficacy with other immunotherapy combinations, including Bavencio®, Keytruda®, Opdivo®, and Tecentriq®. The firm is continually seeking collaboration and partnership opportunities, particularly with checkpoint inhibitors and other immuno-oncology drugs that will enable them to advance pelareorep in either the adjuvant or metastatic settings. Based on its Clinical Development Plan, Oncolytics has already forged partnerships and collaborations with several market leaders such as Pfizer, Roche, Bristol-Myers Squibb, and Merck KGaA. The firm has approximately 400 patents issued globally, including approximately 50 in the U.S. and 20 in Canada. With the planning of a phase 3 registrational trial expected in 2021, pelareorep is currently being manufactured at commercial scale under a commercial supply agreement with Merck Millipore Sigma. "We are expecting insights from multiple phase 2 studies over the next 12-18 months then completing the phase 3 trial with the opportunity to be a commercial company after that," Kirk Look, CFO at Oncolytics, concludes. Ph

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## Oncolytics Biotech


*The annual listing of 10 companies that are at the forefront of providing Immunotherapy solutions and transforming businesses*