Oncorus Announces Publication of Preclinical Data Demonstrating Potent Systemic Antitumor Activity of its Clinical Stage Oncolytic Herpes Simplex Viral Immunotherapy Product Candidate ONCR-177

January 20, 2021

-- Preclinical findings show that ONCR-177's systemic antitumor immunity is driven by its five complementary immunomodulatory transgene payloads and retention of γ34.5 --

-- Complete and durable tumor regression and protective antitumor memory observed in multiple syngeneic tumor models --

-- Preclinical safety data and preliminary readout from the ongoing Phase 1 study support Oncorus' proprietary safety strategies --

CAMBRIDGE, Mass. , Jan. 20, 2021 (GLOBE NEWSWIRE) -- Oncorus, Inc. (Nasdaq: ONCR), a clinical stage biopharmaceutical company developing next-generation, systemically active viral immunotherapies to transform outcomes for cancer patients, announced today the recent publication of preclinical data supporting the clinical development of its lead oncolytic Herpes Simplex Virus (oHSV) clinical candidate, ONCR-177. In the paper, entitled, "ONCR-177, an Oncolytic HSV-1 Designed to Potently Activate Systemic Antitumor Immunity" (Haines, et al., 2020), published online in the journal *Cancer Immunology Research*, ONCR-177 demonstrated potent and durable antitumor activity in multiple immune-competent tumor models. The preclinical findings demonstrate that the activity of ONCR-177, an intratumorally administered viral immunotherapy engineered for systemic activity currently in a Phase 1 study, is driven by Oncorus' unique combination of five complementary immunomodulatory transgene payloads in addition to its retention of γ34.5. A herpes simplex virus 1 (HSV-1) gene, γ34.5 allows the virus to replicate in the presence of host antiviral immune responses. ONCR-177's safety strategies and their ability to enhance oHSV tolerability without impeding potency were previously characterized in a paper published by Oncorus in September 2020 in *Molecular Therapy* on ONCR-159, the unarmed version of ONCR-177, (Kennedy et al., 2020) titled, "Design of an Interferon-Resistant Oncolytic HSV-1 Incorporating Redundant Safety Modalities for Improved Tolerability."

"We are pleased to share these encouraging preclinical findings, which supported our advancement of ONCR-177 into clinical development last year. These data give important insight into how our proprietary engineering of ONCR-177 may enable systemic activity without compromising safety, and position us to advance our mission to realize the full potential of this therapeutic class for cancer patients," said Theodore (Ted) Ashburn, M.D., Ph.D., President and Chief Executive Officer at Oncorus. "We believe viral immunotherapies as a class are a proven modality and represent the most promising approach in development today to activate multiple arms of the immune system and improve outcomes for cancer patients."

Oncorus is conducting a Phase 1 study to evaluate the safety and tolerability of ONCR-177 as well as to evaluate preliminary antitumor activity in patients with solid tumors (NCT04348916) as a monotherapy and in combination with Merck's anti-PD-1 therapy, KEYTRUDA ® (pembrolizumab) via a clinical trial collaboration and supply agreement signed with Merck in July 2020. Oncorus expects to report initial interim data from the monotherapy dose escalation part of this trial in the second half of 2021 with addition data readouts through the second half of 2022.

Christophe Quéva, Ph.D., Oncorus' Chief Scientific Officer and Senior Vice President, Research, commented, "We have designed our proprietary oHSV Platform to safely maximize the impact of viral immunotherapies to foster the development of a potent systemic antitumor activity. With our Phase 1 study of ONCR-177 now well underway, we look forward to the potential of these preclinical findings translating into improving patient outcomes."

In addition to ONCR-177, Oncorus plans to nominate a second intratumorally administered oHSV clinical candidate to specifically target cancers of the central nervous system, including glioblastoma multiforme, in the second half of 2021 (ONCR-GBM). In the first half of 2021, Oncorus plans to nominate intravenously administered Synthetic Coxsackievirus A21 and Synthetic Seneca Valley Virus clinical candidates from its Synthetic Virus Platform for difficult-to-inject tumors such as those of the lung.

Preclinical Data Highlights

Highlights from Oncorus' preclinical data described in these papers include:

- The murine version of ONCR-177 (mONCR-171) demonstrated durable complete tumor regressions and abscopal activity in four syngeneic tumor models: A20, MC38, CT26 and B16F10N1.
- Durable survival was achieved in both A20 and CT26 models versus the unarmed version of ONCR-177 (i.e., ONCR-159), specifically demonstrating the impact that ONCR-177's arming strategy has in driving systemic activity in these *in vivo* models of cancer. Re-challenge experiments in long term responders to mONCR-171 demonstrated that tumor antigen-specific protective memory responses were achieved.
- The retention of a gene coding for γ34.5 demonstrated more robust replication in the presence of interferon-γ versus viruses that do not contain this gene. Of note, ONCR-159, which also retains γ34.5 expression, demonstrated statistically significant improvement in an *in vivo* bi-lateral CT26 model of survival.
- The addition of systemic anti-PD-1 augmented the activity of mONCR-171, particularly for un-injected tumors, suggesting that utilizing systemic anti-PD-1 immunotherapy may augment the systemic antitumor effect of ONCR-177.

- Directional viral promoters, CAG and MND, were shown to elicit strong transgene expression in injected tumors. Furthermore, the addition of the five complementary immunomodulatory transgenes and other modifications in ONCR-177 remain potently oncolytic *in vitro* in cancer cell lines. The oncolytic activity of ONCR-177 is on par with what has been reported for talimogene laherparepvec (IMLYGIC®), which is commonly referred to as “T-VEC”. [1]

- *In vivo* biodistribution analyses suggest that viral DNA and transgene expression were relegated primarily to the injected tumor. As previously disclosed, no dose limiting toxicities were observed in the first four patients dosed with ONCR-177 suggesting that the safety strategies incorporated into ONCR-177 are working as intended.

About ONCR-177

ONCR-177, Oncorus’ lead viral immunotherapy candidate, is designed to mount a multidimensional attack on cancer. It induces immunogenic cancer cell death and ignites innate and adaptive immunity to drive a lasting and systemic anti-tumor response.

Five Complementary Immunomodulatory Transgene Payloads to Recruit Multiple Arms of Immune System

ONCR-177 is armed with five complementary transgenes with strong clinical and preclinical validation, IL-12, FLT3LG, CCL4, anti-PD-1 and anti-CLTA-4, which were selected by Oncorus to comprehensively drive the Cancer-Immunity Cycle[2] at multiple nodes:

- IL-12 is known to activate and expand CD8, CD4 T_{H1} and natural killer (NK) cells.
- FLT3LG is well understood to expand antigen cross-presenting classical dendritic cells, and CCL4 is known facilitate dendritic and CD8 T cell recruitment.

- ONCR-177’s local expression of antagonists to PD-1 (via a proprietary PD-1 nanobody) and CTLA-4 (using the ipilimumab sequence) is intended to counteract compensatory upregulation of key immune checkpoints.

γ34.5 Retention to Enable Resistance to Host Antiviral Immune Responses and Additional Innovations

ONCR-177 also retains a copy of γ34.5 to enable resistance to host antiviral interferon responses. γ34.5 is known to play a more central role in inhibition of antiviral response than US11.[3] Furthermore, ONCR-177 contains a gB:N/T mutation in a surface fusion protein shown to broaden tropism beyond Herpesvirus entry mediator (HVEM) and nectin-1 to include nectins-2, 3 and 4 and enhance infectivity.[4] Lastly, ONCR-177 contains inactivating null mutations in ICP47 intended to improve antigen presentation.[5]

Orthogonal Safety Strategies to Enable Selective Attenuation and Retention of γ34.5

Oncorus’ oHSV platform incorporates two complementary and proprietary approaches to limit viral replication in normal tissues. First, Oncorus’ microRNA attenuation strategy leverages the known differential expression of certain microRNA in tumors versus normal tissues to allow unencumbered viral replication in tumor cells, while preventing replication in healthy tissues. This microRNA attenuation strategy allows ONCR-177 to retain the ability to express the gene encoding for γ34.5, a feature unique among oHSV-based therapies such as T-VEC and others in development today. In addition, ONCR-177 also has engineered proprietary mutations into UL37 to eliminate the virus’ ability to transport, replicate and establish latency inside neurons.[6]

About Oncorus

At Oncorus, we are focused on driving innovation to deliver next-generation, systemically active viral immunotherapies to transform outcomes for cancer patients. We are advancing a portfolio of intratumorally and intravenously administered viral immunotherapies for multiple indications with significant unmet needs based on our oncolytic Herpes Simplex Virus (oHSV) Platform and Synthetic Virus Platform. Designed to deliver next-generation viral immunotherapy impact, our oHSV Platform improves upon key characteristics of this therapeutic class to enhance potency without sacrificing safety, including greater capacity to encode transgenes to drive systemic immunostimulatory activity, retention of full replication competency to enable high tumor-killing potency, and orthogonal safety strategies to restrict viral activity in tumor cells. Oncorus’ lead oHSV program, ONCR-177, is designed to be directly administered into a tumor, resulting in high local concentrations of the therapeutic agent, as well as low systemic exposure to the therapy, which we believe could potentially limit systemic toxicities. Please visit us at www.oncorus.com to learn more.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements regarding: expectations with respect to Oncorus’ ability to advance its clinical and preclinical pipelines, including statements regarding the clinical development of ONCR-177 and timing and anticipated data read-outs for the ongoing Phase 1 clinical trial; Oncorus’ expectations regarding upcoming milestones for its other potential product candidates, including the timing for nomination of clinical candidates from its two Synthetic Virus Platform development programs and its second oHSV Platform clinical candidate; and the therapeutic potential and clinical benefits of Oncorus’ existing and potential product candidates. The words "may," “might,” "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," “expect,” "estimate," “seek,” "predict," “future,” "project," "potential," "continue," "target" and similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks associated with: the impact of COVID-19 on Oncorus’ operations and the timing and anticipated results of its ongoing and planned preclinical studies and clinical trials; the risk that the preliminary results of preclinical studies or clinical trials may not be predictive of future results in connection with future clinical trials; Oncorus’ ability to successfully demonstrate the safety and efficacy of ONCR-177 and obtain regulatory approval and that Oncorus’ other preclinical or clinical programs do not advance or result in approved products on a timely or cost effective basis or at all; and Oncorus’ ability to obtain, maintain and protect its intellectual property. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Oncorus’ Quarterly Report on Form 10-Q for the

quarter ended September 30, 2020, which was filed with the Securities and Exchange Commission on November 12, 2020, as well as discussions of potential risks, uncertainties, and other important factors in the other filings that Oncorus makes with the Securities and Exchange Commission from time to time. These documents are available under the "SEC filings" page of the Investors section of Oncorus' website at http://investors.oncorus.com.

Any forward-looking statements represent Oncorus' views only as of the date of this press release and should not be relied upon as representing its views as of any subsequent date. Oncorus explicitly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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[1] Moesta, et al, *Cancer Research* 2017
[2] Chen and Mellman, *Immunity* 2013
[3] Mulvey et al., *J. Virol.* 2004 and Peters et al., *J. Virol.* 2018
[4] Uchida, *J. Virol.* 2010
[5] Twumasi-Boateng, *Nat. Rev. Cancer* 2018
[6] Richards et al., *PLoS Pathog.* 2017