Oncorus Presents Preclinical Data Supporting ONCR-719, an armed HSV-1 Vector engineered to use the Epidermal Growth Factor Receptor (EGFR/EGFRvIII) for viral entry in Glioblastoma, at the 2022 Society for Neuro-Oncology Annual Meeting

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- **ONCR-719** is uniquely engineered to use the Epidermal Growth Factor Receptor (EGFR/EGFRvIII) for viral entry, which is highly expressed in glioblastoma multiforme (GBM); data show that the canonical entry receptor for HSV-1, NECTIN-1, is only minimally expressed in human GBM tumors.

- **ONCR-719** expresses four immunomodulatory payloads, including IL-12, an anti-PD-1 nanobody, 15-hydroxyprostaglandin dehydrogenase (HPGD), and a novel macrophage-modulating Fc-enhanced antibody to reverse GBM’s immunosuppressed tumor microenvironment.

- **ONCR-719** is derived from a potent HSV-1 strain that is engineered with fusogenic mutations to enhance viral spread and oncolysis and with Oncorus’ clinically validated microRNA attenuation strategy for safety.

ANDOVER, Mass., Nov. 18, 2022 (GLOBE NEWSWIRE) -- Oncorus, Inc. (Nasdaq: ONCR), a viral immunotherapy company focused on driving innovation to transform outcomes for cancer patients, today announced the presentation of preclinical data for ONCR-719 in a poster at the 2022 Society for Neuro-Oncology (SNO) Annual Meeting, taking place November 17-20, 2022 in Tampa, Florida.

ONCR-719 is a novel, armed oncolytic HSV-1 vector engineered with targeted entry via EGFR/EGFRvIII and expresses four immunomodulatory payloads designed to reverse GBM’s immunosuppressive tumor microenvironment. In addition, ONCR-719 is derived from a potent HSV-1 isolate to drive oncolysis, is engineered with fusogenic mutations to enhance viral spread, and uses Oncorus’ clinically validated microRNA attenuation strategy to inhibit viral replication in healthy cells.

Highlights from the preclinical poster describing ONCR-719, previously known as ONCR-GBM, include:

- Minimal expression of HSV-1 virus entry receptor, NECTIN-1, on human GBM samples suggests targeted oncolytic viruses are required to effectively treat human GBM tumors.
- ONCR-719 has been engineered to enter tumor cells using either EGFR/EGFRvIII or NECTIN-1 as an entry receptor, thereby increasing virus tropism for GBM tumors.
- EGFR-targeting and engineered fusogenic mutations in ONCR-719 enhance virus spread and tumor immunogenicity by driving syncytia formation in human GBM tumor cell lines.
- ONCR-719 is engineered to include IL-12, an anti-PD-1 nanobody, 15-hydroxyprostaglandin dehydrogenase (HPGD), and a novel macrophage modulating-Fc enhanced antibody. These payloads confer enhanced T cell recruitment and activation and target the immune suppressive macrophages and myeloid cells in the tumor microenvironment. Multiple payloads or transgenes were screened using in vivo orthotopic GBM models to identify immune-modulatory payloads to target the GBM microenvironment.
- Together, EGFR/EGFRvIII targeting, oncolytic potency, and incorporation of rationally designed payloads within ONCR-719 leads to enhanced anti-tumor efficacy and complete responses in preclinical orthotopic GBM models.
- ONCR-719 is engineered for safety in the central nervous system using multiple CNS-specific microRNA targets. Oncorus’ clinically proven strategy to limit viral replication in healthy cells. When injected intracranially in an HSV-1 sensitive mouse, ONCR-719 demonstrates a greater than 50,000-fold tolerability window compared to the unattenuated strain.

“Oncolytic viruses are well-positioned to treat this aggressive form of brain cancer. We are excited to share ONCR-719 as a cutting-edge preclinical candidate that is engineered to improve outcomes and can stimulate a productive and durable anti-tumor immune response across multiple mouse models following a single intratumoral injection,” said Theodore (Ted) Ashburn, M.D., Ph.D., President and Chief Executive Officer of Oncorus. “Most notably, we’ve enabled the virus to use EGFR for entry, which is expressed at high levels in GBM. Underscoring the importance of this advance is our data showing that the canonical entry receptor for HSV, NECTIN-1, is only minimally expressed in GBM cells, which arguably makes using EGFR for entry an essential capability for such an agent. By utilizing our clinically proven microRNA attenuation strategy, ONCR-719 is engineered to protect healthy brain tissue while replicating at its full potential in tumor cells.”

“GBM is the most common type of primary brain tumor in adults; it’s a devastating disease that has a great unmet need with a 5-year overall survival of approximately 7 percent,” said Tooba Cheema, Ph.D., Senior Director, Translational Medicine and ONCR-719 Program Leader at Oncorus. “We engineered ONCR-719 to overcome the common impediment that this treatment class faces, limited spread of virus in the highly immunosuppressive GBM tumor microenvironment. We are pleased with the results demonstrated in preclinical models and look forward to seeing how our innovations translate into improved outcomes for GBM patients.”

ONCR-719 is the company’s second candidate from its HSV Platform and is developed from a clinical isolate of HSV-1 selected for oncolytic potency.
across cancer cell lines. Further development of ONCR-719 is dependent on a strategic partnership or additional financing.

About Oncorus

At Oncorus, we are focused on driving innovation to deliver next-generation viral immunotherapies to stimulate the immune system and transform outcomes for cancer patients. We are advancing a portfolio of intratumorally (iTu) and intravenously (IV) administered viral immunotherapies for multiple indications with significant unmet need based on our Herpes Simplex Virus (HSV) and self-amplifying viral RNA/LNP Platforms.

Designed as a next-generation viral immunotherapy, our HSV Platform improves upon key characteristics of this therapeutic class to enhance systemic activity with immune stimulating payloads. Our lead HSV program, ONCR-177, currently in the clinic, is designed to be directly administered into a tumor, resulting in high local concentrations of therapeutic agent and its five encoded transgenes, as well as low systemic exposure to the therapy, which could limit systemic toxicities. Our pioneering self-amplifying vRNA/LNP Platform, highlighted by our product candidates ONCR-021 and ONCR-788, involves a highly innovative, novel combination of RNA and LNP-based modalities designed to realize the potential of RNA medicines for cancer.

Please visit 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 the utility and potential of Oncorus’ HSV Platform and the engineering of ONCR-719, including its ability to reverse GBM’s immunosuppressed tumor microenvironment, enhance viral spread and oncolysis, inhibit viral replication in certain healthy cells and increase virus tropism for GBM tumors; the ability of oncolytic viruses to treat aggressive brain cancer; ONCR-719’s ability to improve patient safety and efficacy outcomes; and Oncorus’ ability to progress ONCR-719 into the clinic. The words “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “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: Oncorus’ ability to successfully demonstrate the safety, tolerability and efficacy of its product candidates and obtain regulatory approval thereof; the adequacy of Oncorus’ existing capital resources and availability of financing on commercially reasonable terms; Oncorus’ ability to obtain the requisite components for its product candidates manufactured in accordance with regulatory requirements; the expansion of Oncorus’ in-house manufacturing capabilities; the impact of COVID-19 on Oncorus’ operations and the timing and anticipated results of its ongoing and planned clinical trials; the accuracy of the Oncorus’ estimates regarding expenses, future revenue, capital requirements and needs for additional financing; 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’ Annual Report on Form 10-K for the year ended December 31, 2021, filed with the Securities and Exchange Commission (“SEC”) on March 9, 2022, and Oncorus’ Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022, June 30, 2022 and September 30, 2022, filed with the SEC on May 4, 2022, August 4, 2022 and November 2, 2022, respectively, as well as discussions of potential risks, uncertainties, and other important factors in the other filings that Oncorus makes with the SEC 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, except as required by law. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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