Edinburgh, U.K. 8th March 2022

NuCana Announces Upcoming Presentations on NUC-3373 at the American Association for Cancer Research (AACR) Annual Meeting 2022

Checkpoint Inhibitor Nivolumab Activity Enhanced by NUC-3373 in vitro

NUC-3373 Shown to be a More Efficient DNA Damaging Agent in Cancer Cells than 5-FU

NUC-3373 Did Not Generate Metabolites Associated with 5-FU Dose-Limiting Toxicities

Edinburgh, United Kingdom, March 8, 2022 (GLOBE NEWSWIRE) - NuCana plc (NASDAQ: NCNA) announced the release of two abstracts to be presented as posters at the American Association of Cancer Research (AACR) Annual Meeting being held from April 8 to 13, 2022.

Abstract 4992: **NUC-3373 Potentiates Immune-Mediated Cytotoxicity of CRC Cells**

NUC-3373 causes colorectal cancer (CRC) cell lines to release damage associated molecular patterns (DAMPs), molecular signals that can activate immune cells leading to immunogenic cell death (ICD). The addition of nivolumab, an anti-PD-1 antibody, to NUC-3373 enhanced tumor cell death in a model where cancer cells were incubated alongside human-derived immune cells, highlighting NUC-3373's potential as an attractive combination partner for checkpoint inhibitors.

Abstract 1835: **NUC-3373 Targets the DNA-Directed Pathway More Effectively than 5-FU**

NUC-3373 and 5-FU exert their anti-cancer effects through the metabolite, FUDR-MP (or FdUMP), which inhibits thymidylate synthase (TS), a critical enzyme for cancer cell growth and survival. Pre-clinical and clinical data show that NUC-3373 generates far higher levels of FUDR-MP than 5-FU and is more effective at inhibiting TS activity. Data indicate that NUC-3373 also induces anti-cancer activity via the DNA-targeting metabolite, FdUTP. Furthermore, NUC-3373 avoids the RNA damage associated with 5-FU's dose-limiting toxicities of diarrhea, myelosuppression and mucositis.

Through a more targeted, DNA-directed pathway, NUC-3373 may provide, if approved, a potentially more effective, safer and convenient therapeutic option than 5-FU for patients with cancer.

Hugh S. Griffith, NuCana's Founder and Chief Executive Officer said: "We believe these data demonstrate NUC-3373's advantages over 5-FU and are highly supportive of our clinical development strategy. Our Phase 1/2 study of NUC-3373 in patients with colorectal cancer (NuTide:302) continues to generate data which will support our Phase 3 study for NUC-3373 in second-line colorectal cancer patients. In addition, NUC-3373 is entering a Phase 1/2 study (NuTide:303) in patients with solid tumors to identify additional indications for development, including in combination with checkpoint inhibitors."

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About NuCana plc

NuCana is a clinical-stage biopharmaceutical company focused on significantly improving treatment outcomes for patients with cancer by applying our ProTide technology to transform some of the most widely prescribed chemotherapy agents, nucleoside analogs, into more effective and safer medicines. While these conventional agents remain part of the standard of care for the treatment of many solid and hematological tumors, their efficacy is limited by cancer cell resistance mechanisms and they are often poorly tolerated. Utilizing our proprietary technology, we are developing new medicines, ProTides, designed to overcome key cancer resistance mechanisms and generate much higher concentrations of anti-cancer metabolites in cancer cells. NuCana's pipeline includes NUC-3373 and NUC-7738. NUC-3373 is a new chemical entity derived from the nucleoside analog 5-fluorouracil, a widely used chemotherapy agent and is in a Phase 1b/2 study in patients with metastatic colorectal cancer. NUC-7738, is a transformation of a novel anti-cancer nucleoside analog (3'-deoxyadenosine) and is in a Phase 1/2 study for patients with advanced solid tumors.

Forward-Looking Statements

This press release may contain "forward-looking" statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are based on the beliefs and assumptions and on information currently available to management of NuCana plc (the "Company"). All statements other than statements of historical fact contained in this press release are forward-looking statements, including statements concerning the Company's planned and ongoing clinical studies for the Company's product candidates and the potential advantages of those product candidates, including NUC-3373 and NUC-7738; the initiation, enrollment, timing, progress, release of data from and results of those planned and ongoing clinical studies; the Company's goals with respect to the development, regulatory pathway and potential use, if approved, of each of its product candidates; and the utility of prior non-clinical and clinical data in determining future clinical results. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "plans," "anticipates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other comparable terminology. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause the Company's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These risks and uncertainties include, but are not limited to, the risks and uncertainties set forth in the "Risk Factors" section of the Company's Annual Report on Form 20-F for the year ended December 31, 2020 filed with the Securities and Exchange Commission ("SEC") on March 4, 2021, and subsequent reports that the Company files with the SEC. Forward-looking statements represent the Company's beliefs and assumptions only as of the date of this press release. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, the Company assumes no obligation to publicly update any forward-looking statements for any reason after the date of this press release to conform any of the forward-looking statements to actual results or to changes in its expectations.

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For more information, please contact:

NuCana plc
Hugh S. Griffith
Chief Executive Officer
T: +44 131-357-1111
E: info@nucana.com

ICR Westwicke
Chris Brinzey
T: +1 339-970-2843
E: chris.brinzey@westwicke.com

RooneyPartners
Marion Janic
T: +1 212-223-4017
E: mjanic@rooneyco.com