Edinburgh, U.K. 26th October 2022

NuCana Presents Positive Data on NUC-3373 at the 34th EORTC-NCI-AACR Annual Meeting 2022

NUC-3373 Potentiates Immunogenic Activity in Lung Cancer Cells

Pembrolizumab Activity Increased by NUC-3373 in Lung Cancer Cells

NuCana has Initiated the NuTide:303 Study of NUC-3373 in Combination with Pembrolizumab or Docetaxel

Barcelona, Spain, October 26, 2022 (GLOBE NEWSWIRE) – NuCana plc (NASDAQ: NCNA) announced non-clinical data from two poster presentations at the 34th EORTC-NCI-AACR Annual Meeting being held from October 26 to 28, 2022.

Abstract 185: **NUC-3373 is a potent TS inhibitor and induces DNA damage in NSCLC cancer cells regardless of histological subtype**

Pemetrexed is an important therapeutic option for first-and second-line adenocarcinoma lung cancers, but is not recommended in squamous lung cancer due to higher levels of thymidylate synthase (TS) expression. NUC-3373 was shown to be a more potent inhibitor of TS than both pemetrexed and 5-FU. NUC-3373 generated high intracellular levels of the anti-cancer metabolite FUDR-MP, resulting in TS inhibition, and the DNA-targeting metabolite, FUDR-TP. This resulted in extensive DNA damage in both adenocarcinoma and squamous carcinoma cell lines. These data highlight that NUC-3373 may be an effective treatment for non-small cell lung cancer (NSCLC) regardless of histological subtype and basal TS expression.

Abstract 128: **NUC-3373 induces DAMPs from NSCLC cells potentiating a favorable immunogenic microenvironment**

NUC-3373 causes NSCLC cells to release damage associated molecular patterns (DAMPs), molecular signals that activate immune cells leading to immunogenic cell death (ICD). NUC-3373 also enhanced the cell surface expression of the transmembrane protein PD-L1 in lung cancer cell lines, highlighting a potential role for NUC-3373 to enhance immunotherapy efficacy. The addition of pembrolizumab, an anti-PD-1 antibody, to NUC-3373 in a co-culture system where NSCLC cells were incubated alongside human-derived immune cells also enhanced ICD, highlighting a potential role for NUC-3373 as an attractive combination partner for immune checkpoint inhibitors in NSCLC.

Hugh S. Griffith, NuCana's Founder and Chief Executive Officer, said: "These data are highly supportive of our strategy to combine NUC-3373 with pembrolizumab and to investigate NUC-3373 in patients with NSCLC. We have initiated the NuTide:303 study evaluating NUC-3373 in combination with either pembrolizumab in patients with advanced solid tumors or in combination with docetaxel in patients with non-small cell lung cancer. We have also initiated a randomized study in second-line CRC patients comparing NUFIRI plus bevacizumab to FOLFIRI plus bevacizumab, the global standard of care, and we look forward to sharing data from both of these studies in 2023."

Cont'd

Edinburgh, U.K. 26th October 2022

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, they have significant shortcomings that limit their efficacy and they are often poorly tolerated. Utilizing our proprietary technology, we are developing new medicines, ProTides, designed to overcome the key limitations of nucleoside analogs 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. NUC-3373, in combination with other agents, is in a Phase 1b/2 study in patients with metastatic colorectal cancer. NuCana has also initiated a randomized Phase 2 study of NUC-3373, in combination with other agents, for the second-line treatment of patients with advanced colorectal cancer. In addition, NuCana has initiated a Phase 1b/2 modular study of NUC-3373 in combination with other agents, including a PD-1 inhibitor, in patients with advanced solid tumors to identify additional indications for development. NUC-7738 is a transformation of 3'-deoxyadenosine, a novel anti-cancer nucleoside analog. NUC-7738 is in the Phase 2 part of a Phase 1/2 study in patients with advanced solid tumors which is evaluating NUC-7738 as a monotherapy and in combination with a PD-1 inhibitor.

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 and non-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, 2021 filed with the Securities and Exchange Commission ("SEC") on April 27, 2022, and subsequent reports that

Cont'd

Edinburgh, U.K. 26th October 2022

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.

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