Edinburgh, U.K. 10th April 2021

NuCana Announces Five Poster Presentations at the American Association for Cancer Research (AACR) Annual Meeting 2021

- NUC-3373 Shows Encouraging Efficacy Signals and a Favorable Safety Profile in Patients with Advanced Colorectal Cancer
- NUC-3373 Promotes Natural Killer Cell Activation by Colorectal Cancer Cells
- NUC-7738 Demonstrates Anti-Cancer Activity, Prolonged Stable Disease and a Favorable Tolerability Profile in Patients with Advanced Solid Tumors
- NUC-7738 Generates High and Prolonged Intracellular Levels of the Active Anti-Cancer Metabolite 3'-dATP
- Acelarin Induces Persistent DNA Damage in Biliary Tract Cancer Cells

Edinburgh, United Kingdom, April 10, 2021 (GLOBE NEWSWIRE) – NuCana plc (NASDAQ: NCNA) announced the presentation of five posters at the American Association for Cancer Research (AACR) Annual Meeting 2021 being held virtually April 9 to 14, 2021. Data from all three of NuCana's ProTides in clinical development were presented. Summaries of the posters are described below.

NUC-3373

NuCana presented two posters on NUC-3373, its ProTide transformation of the active anti-cancer metabolite of 5-fluorouracil (5-FU), a very widely used anti-cancer drug. NUC-3373 has been designed to overcome the main challenges associated with 5-FU and capecitabine, including cancer-resistance mechanisms, the generation of toxic metabolites and unfavorable pharmacokinetic profile.

Poster Title: NUC-3373, a targeted inhibitor of thymidylate synthase, in patients with advanced colorectal cancer

This poster describes further encouraging interim data from 38 patients with metastatic colorectal cancer. In this difficult-to-treat group, who had received a median of four prior lines of therapy, NUC-3373, with or without leucovorin, demonstrated a 62% disease control rate (defined as stable disease lasting more than 8 weeks) in the efficacy-evaluable population. Three patients experienced reductions in their target lesions of 40%, 28% and 15% and several patients achieved a longer progression-free survival on NUC-3373 than they had on their prior therapy. NUC-3373 also continues to demonstrate a favorable safety profile with no FBAL or FUTP-associated Grade 3 or 4 toxicities, such as hand-foot syndrome, GI or hematological adverse events.

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Poster Title: NUC-3373-induced DAMPs release in CRC cells promotes natural killer cell activation

The second NUC-3373 poster showed that NUC-3373-treated colon cancer cells are able to activate a natural killer (NK) cell response. NUC-3373 was shown to induce the release of damage associated molecular patterns (DAMPs) which may restore NK cell-mediated immune responses by reducing inhibitory signals. Thus, NUC-3373 has the potential to evoke immunogenic cell death and may enhance the clinical utility of immunotherapy agents.

NUC-7738

NuCana presented two posters on NUC-7738, a ProTide transformation of a novel nucleoside analog, 3'-deoxyadenosine or 3'-dA. NUC-7738, which has several potential anti-cancer mechanisms of action, is being evaluated in a Phase I study in patients with advanced solid tumors who have exhausted all standard therapies.

Poster Title: NUC-7738, a novel ProTide transformation of 3'-deoxyadenosine, in patients with advanced solid tumors

The first poster describes additional interim data from the ongoing Phase I study. These data demonstrate NUC-7738's encouraging anti-cancer activity and favorable tolerability profile. Three case studies were described detailing patients who achieved tumor reductions and prolonged stable disease on NUC-7738.

Poster Title: From bench to bedside: Using ProTide chemistry to transform 3'-deoxyadenosine into the novel anti-cancer agent NUC-7738

The second poster describes how NUC-7738 was designed to overcome the key cancer resistance mechanisms which have prevented the clinical development of 3'-dA. NUC-7738 was shown to efficiently generate high and prolonged intracellular levels of the active anti-cancer metabolite, 3'-dATP, and to cause cell death by activation of apoptotic pathways, as well as through inhibition of NFκB nuclear translocation.

Acelarin

Poster Title: NUC-1031 causes incorporation of fluorinated deoxycytidine into DNA, inducing persistent damage in biliary tract cancer cells

NuCana presented a poster that further demonstrated Acelarin's activity in biliary tract cancer cells. Specifically, the poster described how Acelarin (NUC-1031) is converted to the active anti-cancer metabolite (dFdCTP) and demonstrated that it is incorporated into DNA, inducing persistent double-strand breaks. This leads to cell cycle arrest and DNA damage resulting in apoptosis in biliary tract cancer cells.

Abstracts and full session details can be found at www.aacr.org

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About NuCana

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 robust pipeline includes three ProTides in clinical development. Acelarin and NUC-3373, are new chemical entities derived from the nucleoside analogs gemcitabine and 5-fluorouracil, respectively, two widely used chemotherapy agents. Acelarin is in a Phase III study for patients with advanced biliary tract cancer and a Phase III study for patients with metastatic pancreatic cancer for which enrollment has been suspended. NUC-3373 is in a Phase I study for the potential treatment of a wide range of patients with advanced solid tumors and a Phase Ib study for patients with metastatic colorectal cancer. Our third ProTide, NUC-7738, is a transformation of a novel nucleoside analog (3'-deoxyadenosine) and is in a Phase I 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 Acelarin, 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

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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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