Edinburgh, U.K. 15th May 2020

# NuCana to Present Two Abstracts at the American Association for Cancer Research (AACR) Annual Meeting 2020

## Non-Clinical Findings Suggest that Acelarin and NUC-3373 May Induce an Immune Response Against Cancer Cells

## Acelarin (NUC-1031) Releases DAMPs and Upregulates PD-L1 Expression in Lung Cancer Cells

## NUC-3373 Induces Endoplasmic Reticulum Stress and Release of DAMPs in Colorectal Cancer Cells

Edinburgh, United Kingdom, May 15, 2020 (GLOBE NEWSWIRE) – NuCana plc (NASDAQ:NCNA) today announced that two abstracts describing non-clinical studies related to the mechanisms of action of its proprietary ProTides, Acelarin (NUC-1031) and NUC-3373, were selected for poster presentations at the AACR Annual Meeting 2020 on June 22-24, 2020.

In prior non-clinical studies, Acelarin has shown an ability to cause cancer-cell death via DNA damage. These new *in vitro* data presented at AACR suggest that Acelarin may also have a potential immunomodulatory role. Acelarin was found to cause the release of Damage Associated Molecular Patterns, or DAMPs, and increase the expression of PD-L1 on cancer cells. The findings indicate that Acelarin produces changes in the cancer cells and the tumor microenvironment that could alter the recognition by the immune system, thus potentially making Acelarin an attractive combination partner for immune checkpoint inhibitors.

In the second AACR abstract, an additional novel mode of action was identified for NUC-3373, NuCana's ProTide transformation of the active anti-cancer metabolite of 5-fluorouracil (5-FU), a very widely used anti-cancer drug. NUC-3373 was found to be a potent inhibitor of thymidylate synthase, which results in DNA damage of cancer cells. The recent *in vitro* studies have shown NUC-3373 is able to not only damage DNA, but also induce endoplasmic reticulum stress, and the subsequent release of DAMPs. Thus, in addition to being effective DNA damaging agents in cancer cells, these data suggest that both NUC-3373 and Acelarin may have the potential to alter tumor biology and enhance the activity of immune checkpoint inhibitors.

Hugh S. Griffith, NuCana's Chief Executive Officer, said: "These findings reveal new and exciting modes of action of our ProTides and help to explain why they appear to be such potent anti-cancer agents."

Acelarin is currently being evaluated in a global Phase III study in combination with cisplatin as a first-line treatment for patients with advanced biliary tract cancer. NUC-3373 is in a Phase Ib clinical study in patients with advanced colorectal cancer in combination with other agents with which 5-FU is typically combined and a Phase I clinical study in patients with advanced solid tumors. NuCana's third ProTide, NUC-7738, a transformation of a novel nucleoside analog, 3'-deoxyadenosine, is in a Phase I study in patients with advanced solid tumors.

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Details of NuCana's e-poster presentations on June 22-24, 2020: AACR Virtual Annual Meeting II are as follows:

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| **Abstract Title:** | NUC-1031 causes release of DAMPs and upregulates PD-L1 expression in lung cancer cells |
| **Poster Number:** | 1840 |
| **Poster Session Title:** | Mechanisms of Drug Action 2 |
| **Abstract Title:** | NUC-3373 induces ER stress and the release of damage-associated molecular patterns in colorectal cancer cells |
| **Poster Number:** | 1848 |
| **Poster Session Title:** | Mechanisms of Drug Action 2 |

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

## About NuCana plc

NuCana is a clinical-stage biopharmaceutical company focused on significantly improving treatment outcomes for cancer patients 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. Our most advanced ProTide candidates, 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 currently being evaluated in four clinical studies, including a Phase III study for patients with biliary tract cancer, a Phase Ib study for patients with biliary tract cancer, a Phase II study for patients with platinum-resistant ovarian cancer and a Phase III study for patients with metastatic pancreatic cancer for which enrollment has been suspended. NUC-3373 is currently in a Phase I study for the potential treatment of a wide range of advanced solid tumors and a Phase Ib study for patients with previously treated 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

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statements concerning the Company's planned, ongoing and completed non-clinical and 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, ongoing and completed non-clinical and clinical studies; the impact of COVID-19 on its non-clinical studies, clinical studies, business, financial condition and results of operations; 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, 2019 filed with the Securities and Exchange Commission ("SEC") on March 10, 2020, 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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