

Edinburgh, U.K. 4th March 2020

NuCana Receives Positive Opinion for Orphan Drug Designation in the European Union for Acelarin (NUC-1031) for the Treatment of Patients with Biliary Tract Cancer

EDINBURGH, United Kingdom, March 4, 2020 (GLOBE NEWSWIRE) – NuCana plc (NASDAQ: NCNA) announced that the European Medicines Agency's (EMA) Committee for Orphan Medicinal Products (COMP) has issued a positive opinion for orphan drug designation of Acelarin for the treatment of patients with biliary tract cancer. Acelarin, in combination with cisplatin, is currently being evaluated in a global Phase III study (NuTide:121) for the first-line treatment of patients with biliary tract cancer.

"The receipt of a positive opinion for our orphan drug application in the European Union marks another important milestone in Acelarin's development," said Hugh S. Griffith, NuCana's Chief Executive Officer. "Acelarin in combination with cisplatin has achieved an approximate doubling in response rates when compared to the historical results achieved with the standard of care, gemcitabine plus cisplatin. NuTide:121 has the potential to establish Acelarin plus cisplatin as the first approved medicines for the treatment of patients with biliary tract cancer."

Orphan Drug Designation in the European Union (EU) is available to companies developing products for life-threatening or chronically debilitating conditions that affect fewer than five in 10,000 people in the region. This designation creates regulatory and financial incentives for NuCana, including reduced fees from the EMA during the development phase and a 10-year market exclusivity period in the EU following marketing authorization.

NuCana previously received Orphan Drug Designation for Acelarin from the FDA's Office of Orphan Products for the treatment of patients with biliary tract cancer.

About the NuTide:121 Study

NuTide:121 is a global, multi-center, randomized Phase III study that is enrolling up to 828 patients in approximately 120 sites across North America, Europe, Asia and Australia. Patients are being randomized 1:1 and treated with either a combination of Acelarin (725 mg/m²) plus cisplatin (25 mg/m²) or the current standard of care regimen, gemcitabine (1,000 mg/m²) plus cisplatin (25 mg/m²).

The primary objectives of NuTide:121 are Overall Survival (OS) and Objective Response Rate (ORR). Three interim analyses, including two designed to support accelerated approval, are planned as part of the Phase III study protocol, in addition to the final analysis. Based on discussions with the FDA and subject to any further regulatory guidance, the Company believes that a statistically significant improvement in ORR at either of the first two interim analyses, supported by positive trends in other endpoints, could potentially allow for an accelerated approval of a new drug application (NDA) for Acelarin. Accelerated approval requires a confirmatory clinical study to verify the drug's clinical benefit. If accelerated approval were to occur, NuTide:121 would continue and the Company anticipates that data from subsequent analyses could provide the confirmatory data to support full (regular) approval.

More information about this study may be found [here](#).

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About Biliary Tract Cancer

Biliary tract cancer, including cholangiocarcinoma, gallbladder and ampullary carcinoma, is cancer originating in the bile duct, a vessel that transports bile from the liver to the gallbladder and small intestine. Approximately 178,000 new cases of biliary tract cancer are diagnosed each year worldwide, with more than 18,000 of those diagnoses in the United States. There are currently no agents approved for the treatment of biliary tract cancer; however, the worldwide standard of care in biliary tract cancer patients with locally advanced or metastatic disease is the combination of gemcitabine and cisplatin. Patients receiving this regimen have a median overall survival of 11.7 months.

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 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; 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

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"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, 2018 filed with the Securities and Exchange Commission ("SEC") on March 7, 2019, 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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