Edinburgh, U.K. 25th October 2019

NuCana Announces FDA Clearance to Commence Phase III Study of Acelarin (NUC-1031) for the First-Line Treatment of Patients with Biliary Tract Cancer

Global NuTide:121 Study will Enroll up to 828 Patients and Compare Acelarin plus Cisplatin to Gemcitabine plus Cisplatin

Primary Endpoints of Overall Survival and Objective Response Rate

Three Interim Analyses, Including Two Designed to Support Accelerated Approval

Edinburgh, United Kingdom, October 25, 2019 (GLOBE NEWSWIRE) – NuCana plc (NASDAQ: NCNA) announced that the US Food and Drug Administration (FDA) has cleared the Investigational New Drug Application (IND) for its Phase III study (NuTide:121) of the investigational drug Acelarin in combination with cisplatin for patients with previously untreated locally advanced or metastatic biliary tract cancer.

"We are pleased to have received clearance of our IND from the FDA," said Hugh S. Griffith, NuCana's Founder and Chief Executive Officer. "We are also excited by NuTide:121's potential, if successful, to support both accelerated and full approval. Regulatory clearance to begin the study in other countries has also been received and we look forward to enrolling the first patients in the coming weeks."

Mr. Griffith continued: "We believe our investigational drug product Acelarin in combination with cisplatin has the potential to significantly improve the survival outcomes of patients with advanced biliary tract cancer. In the Phase Ib ABC-08 study, we observed an approximate doubling of the response rate with Acelarin plus cisplatin compared to previously reported data for gemcitabine plus cisplatin. Our goal is to establish Acelarin in combination with cisplatin as the global standard of care for the first-line treatment of patients with advanced biliary tract cancer, if Acelarin is approved for marketing."

NuTide:121 will be a global, multi-center, randomized Phase III study that will enroll up to 828 patients in approximately 120 sites across North America, Europe, Asia and Australia. Patients will be randomized 1:1 and treated with either a combination of Acelarin (725 mg/m^2) plus cisplatin (25 mg/m^2) or the current standard of care regimen, gemcitabine (1,000 mg/m^2) plus cisplatin (25 mg/m^2).

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.

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Edinburgh, U.K. 25th October 2019

Dr. Jennifer J. Knox, Professor of Medicine at the University of Toronto, Clinician Investigator at the Princess Margaret Cancer Centre and Chief Investigator of NuTide:121 stated: "I am very excited to be leading the NuTide:121 study. I believe Acelarin plus cisplatin may represent an important advance in the treatment of biliary tract cancer, a devastating disease for which there is a significant need for more effective medicines."

Dr. Juan Valle, Professor and Honorary Consultant in Medical Oncology at the University of Manchester and The Christie, Manchester, United Kingdom was Chief Investigator of the ABC-02 study that established gemcitabine plus cisplatin as the current standard of care for the first-line treatment of patients with advanced biliary tract cancer. Professor Valle said: "As Co-Chief Investigator of the ABC-08 Phase Ib Study, I was encouraged by the efficacy signals observed with Acelarin plus cisplatin, so I am enthusiastic about further investigating Acelarin in combination with cisplatin in NuTide:121, the largest study ever conducted in patients with advanced biliary tract cancer."

NuTide:121 Statistical Analysis Plan (SAP)

Three interim efficacy analyses, including two designed to support accelerated approval of Acelarin in the United States, are currently planned in addition to the final analysis.

The first interim analysis will evaluate the ORR primary endpoint and will be performed 22 weeks after 418 patients with measurable disease at baseline have been randomized. A statistically significant difference in ORR at this analysis would require the Acelarin plus cisplatin arm to have an ORR at least 14% higher than that of the gemcitabine plus cisplatin arm.

The second interim analysis will evaluate the ORR and OS primary endpoints. It will be performed 28 weeks after 644 patients with measurable disease at baseline have been randomized. A statistically significant difference in ORR at this analysis would require the Acelarin plus cisplatin arm to have an ORR approximately 9% higher than that of the gemcitabine plus cisplatin arm. If a statistically significant difference in ORR is detected, OS will also be analyzed at this analysis and a difference in median OS of approximately 3.4 months in favor of Acelarin plus cisplatin would be deemed a statistically significant improvement in OS.

The third interim analysis will evaluate the OS primary endpoint and will take place after 541 events have been observed. A statistically significant difference for OS in favor of Acelarin plus cisplatin would be achieved with an improvement in median OS of approximately 2.6 months.

The final analysis will evaluate the OS primary endpoint. It will take place after 637 events have been observed. A statistically significant difference for OS in favor of Acelarin plus cisplatin would be achieved with an improvement in median OS of approximately 2.2 months.

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Edinburgh, U.K. 25th October 2019

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 three clinical studies, including a Phase Ib study for patients with biliary tract cancer, a Phase II study for patients with 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 advanced colorectal cancer. Our third ProTide, NUC-7738, is a transformation of a novel nucleoside analog (3'-deoxyadenosine or cordycepin) 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 NuTide:121 clinical study; the protocol, statistical analysis plan and expected interim and final analyses from the NuTide:121 study; the Company's expectations and plans with respect to the potential regulatory pathway for Acelarin, including any potential for accelerated approval; 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 "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

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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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