Edinburgh, U.K. 16th September 2021

NuCana Announces Four Poster Presentations at the ESMO Congress 2021

- NUC-3373 Continues to Demonstrate Encouraging Efficacy Signals and a Favorable Safety Profile in Patients with Advanced Colorectal Cancer
- NUC-3373 Phase 1 Study Demonstrated Encouraging Efficacy Signals and a Favorable Safety Profile in Patients with Advanced Solid Tumors and Established the Recommended Monotherapy Phase 2 Dose
- NUC-7738 Continues to Show Anti-cancer Activity and Prolonged Disease Control with a Favorable Tolerability and Pharmacokinetic Profile in Patients with Advanced Solid Tumors

Edinburgh, United Kingdom, September 16, 2021 (GLOBE NEWSWIRE) – NuCana plc (NASDAQ: NCNA), announced the presentation of four posters at the European Society for Medical Oncology (ESMO) Congress 2021. The Company presented additional data from the ongoing Phase 1b/2 study of NUC-3373 in combination with standard therapies in patients with advanced colorectal cancer (NuTide:302), final data from the Phase 1 study of NUC-3373 in patients with advanced solid tumors (NuTide:301), and additional interim data from the Phase 1 study of NUC-7738 in patients with advanced solid tumors. The Company also presented a trials-in-progress poster describing the ongoing Phase 3 study of Acelarin plus cisplatin in patients with advanced biliary tract cancer.

"The posters being presented during ESMO continue to support the potential of our ProTide platform to transform both existing as well as novel nucleoside analogues into more effective and safer medicines for patients with cancer," said Hugh S. Griffith, NuCana's Founder and Chief Executive Officer. "Looking ahead to the remainder of 2021 and first half of 2022, we have multiple milestones that we plan to announce. These include announcing the outcome of the first interim analysis in the Phase 3 NuTide:121 study of Acelarin plus cisplatin in patients with biliary tract cancer, initiating a registrational study for NUC-3373 in patients with colorectal cancer, and initiating and announcing data from a Phase 2 study of NUC-7738 in patients with advanced solid tumors."

Details of NuCana's e-poster presentations during the ESMO Congress 2021 being held September 16-21, 2021 are as follows:

NUC-3373

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

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Poster Title: A Phase Ib study of NUC-3373, a targeted inhibitor of thymidylate synthase, in combination with standard therapies in patients with advanced colorectal cancer (NuTide:302)

This poster describes encouraging interim data from 38 patients with metastatic colorectal cancer. In this difficult-to-treat group, with patients having received a median of four prior lines of therapy, NUC-3373, with or without leucovorin, demonstrated encouraging signs of efficacy. In addition to several patients achieving a longer progression-free survival on NUC-3373 than they had on their prior therapy, tumor reductions were observed in three patients: one who experienced a 40% reduction in their target lesion and two others with 28% and 15% reductions, respectively, in overall tumor burden. NUC-3373 also demonstrated a favorable safety profile in this patient population with no FBAL or FUTP-associated Grade 3 or 4 toxicities, such as hand-foot syndrome, diarrhea or neutropenia.

Based on these encouraging interim results, NuTide:302 has been expanded to a Phase 1b/2 study and now allows enrollment of less heavily pre-treated patients, including second-line colorectal cancer patients. A registrational study of NUC-3373 in second-line colorectal cancer patients is also planned.

Poster Title: Final results of a first-in-human study of the ProTide thymidylate synthase inhibitor NUC-3373, in patients with advanced solid tumours (NuTide:301)

This poster highlights final results from the NuTide:301 study in patients with advanced solid tumors. NUC-3373 showed a favorable safety profile and encouraging anti-cancer activity, including in patients previously treated with 5-FU. Additionally, three patients achieved stable disease lasting at least 9 months. NUC-3373 demonstrated an attractive pharmacokinetic profile with a long plasma half-life of between 6 and 14 hours compared to 8 to 14 minutes for 5-FU. Furthermore, NUC-3373 generated approximately 300 times higher levels of the active anti-cancer metabolite, FUDR-MP, than 5-FU. The recommended Phase 2 monotherapy dose of NUC-3373 was established at 2,500mg/m^2.

NUC-7738

NUC-7738, a ProTide transformation of a novel anti-cancer nucleoside analog, 3'-deoxyadenosine, has multiple potential anti-cancer mechanisms of action and is being evaluated in a Phase 1 study in patients with advanced solid tumors who have exhausted all standard therapies.

Poster Title: A first-in-human study of NUC-7738, a ProTide transformation of 3'-deoxyadenosine, in patients with advanced solid tumors (NuTide:701)

This poster describes interim data from the ongoing Phase 1 study (NuTide:701) and the data demonstrate NUC-7738's encouraging anti-cancer activity in multiple tumor-types. NUC-7738 has been well tolerated with no Grade 3 or 4 treatment-related adverse events and no dose-limiting toxicities. The ProTide generated high levels of the key anti-cancer metabolite, 3'-dATP, which had a prolonged intracellular half-life and was still detectable after 50 hours.

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Three case studies were described detailing two patients with metastatic melanoma and one patient with metastatic lung adenocarcinoma who achieved reductions in the size of target lesions coupled with prolonged stable disease. Following treatment with NUC-7738, one patient with metastatic melanoma became eligible for surgery and their tumor was completely resected.

Recruitment to the NuTide:701 study is ongoing and once the recommended Phase 2 dose has been established, NUC-7738 is expected to advance into the Phase 2 part of the study.

Acelarin

Poster Title: Phase III study of NUC-1031 + cisplatin vs gemcitabine + cisplatin for first-line treatment of patients with advanced biliary tract cancer (NuTide:121)

This trial-in-progress poster highlights the Company's global multi-center, randomized Phase 3 study comparing Acelarin, a ProTide transformation of gemcitabine, in combination with cisplatin, to gemcitabine in combination with cisplatin in up to 828 patients with advanced biliary tract cancer who have not previously received treatment for advanced disease. Enrollment of 418 evaluable patients has been achieved and the first of three interim analyses is expected to occur in the first half of 2022. NuCana believes that a statistically significant improvement in the Objective Response Rate (ORR) at the first interim analysis, accompanied by positive trends in other endpoints, has the potential to allow for accelerated approval of a new drug application (NDA) for Acelarin in the United States.

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

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 3 study for patients with advanced biliary tract cancer. NUC-3373 is in a Phase 1b/2 study in patients with metastatic colorectal cancer. Our third ProTide, NUC-7738, is a transformation of a novel anti-cancer nucleoside analog (3'-deoxyadenosine) and is in a Phase 1 study for patients with advanced solid tumors.

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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 ability to submit an NDA for Acelarin under the FDA's accelerated approval program or at all; 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, 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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