

Edinburgh, U.K. 29th August 2024

NuCana Announces Update for Phase 2 Randomized Colorectal Cancer Study

NuTide:323 Study to be Discontinued Following Pre-Planned Initial Analysis
and Recommendation from the Steering Committee

NuTide:701 and NuTide:303 Studies Continue Unchanged
with Encouraging Data on NUC-7738 plus Pembrolizumab
to be Presented at the ESMO Annual Conference in September

Edinburgh, United Kingdom, August 29, 2024 (GLOBE NEWSWIRE) – NuCana plc (NASDAQ: NCNA) announced that the NuTide:323 study is being discontinued following a pre-planned initial analysis and recommendation from the NuTide:323 Study Steering Committee. While there were prognostic imbalances favoring the control arm, the Steering Committee believed that the combination of NUC-3373 with leucovorin, irinotecan and bevacizumab (NUFIRI+bev) was unlikely to achieve the study's primary objective of superior Progression Free Survival (PFS) compared to the control arm of 5-FU, leucovorin, irinotecan and bevacizumab (FOLFIRI+bev) in the final analysis. In all three arms, the treatment regimens were observed to have a favorable safety profile and to be generally well tolerated, with only 12 of the 175 patients (four patients in each arm) discontinuing treatment due to adverse events.

"While we are disappointed with this unexpected outcome, especially for people living with colorectal cancer, we gained valuable knowledge from the NuTide:323 study which will inform our ongoing development programs. We are extremely grateful to the study participants, their families, the investigators and study teams for their participation and efforts," said Hugh S. Griffith, NuCana's Founder and Chief Executive Officer. "These results highlight the challenges associated with developing new medicines for patients with complex and heterogenous cancers such as metastatic colorectal cancer. We will leverage insights from these data to identify future potential development options for NUC-3373 in colorectal cancer."

Professor Josep Taberero, MD, PhD, Head of the Medical Oncology Department at the Vall d'Hebron University Hospital, Barcelona and Chair of the NuTide:323 Study Steering Committee stated: "In the NuTide:323 study, we were aiming to develop NUC-3373 as a replacement for 5-FU, in combination with leucovorin, irinotecan and bevacizumab in patients with second-line colorectal cancer. The premise of this ambitious goal was based on robust non-clinical and clinical data and the NuTide:323 study team are very disappointed with this outcome."

Mr. Griffith continued: "NuCana remains committed to improving survival outcomes for patients with cancer. The results of the NuTide:323 study do not impact the ongoing NuTide:303 study, in which NUC-3373 is being combined with either pembrolizumab in solid tumors or docetaxel in patients with lung cancer. Furthermore, we are excited about the potential of NUC-7738, a novel agent that profoundly impacts gene expression in cancer cells and targets multiple aspects of the tumor microenvironment. We look forward to sharing the latest data from the Phase 2 part of the NuTide:701 study of NUC-7738 in combination with pembrolizumab in patients with melanoma at the ESMO annual conference in September 2024."

Edinburgh, U.K. 29th August 2024

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, they have significant shortcomings that limit their efficacy and they are often poorly tolerated. Utilizing our proprietary technology, we are developing new medicines, ProTides, designed to overcome the key limitations of nucleoside analogs and generate much higher concentrations of anti-cancer metabolites in cancer cells. NuCana's pipeline includes NUC-3373 and NUC-7738. NUC-3373 is a new chemical entity derived from the nucleoside analog 5-fluorouracil, a widely used chemotherapy agent. NUC-3373 is currently being evaluated in two ongoing clinical studies: a Phase 1b/2 study (NuTide:302) in combination with leucovorin, irinotecan or oxaliplatin, and bevacizumab in patients with metastatic colorectal cancer and a Phase 1b/2 modular study (NuTide:303) of NUC-3373 in combination with the PD-1 inhibitor pembrolizumab for patients with advanced solid tumors and in combination with docetaxel for patients with lung cancer. NUC-7738 is a novel anti-cancer agent that disrupts RNA polyadenylation, profoundly impacts gene expression in cancer cells and targets multiple aspects of the tumor microenvironment. NUC-7738 is in the Phase 2 part of a Phase 1/2 study (NuTide:701) which is evaluating NUC-7738 as a monotherapy in patients with advanced solid tumors and in combination with pembrolizumab in patients with melanoma.

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 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 year ended December 31, 2023 filed with the Securities and Exchange Commission ("SEC") on March 20, 2024, and subsequent reports that the Company files with the SEC. Forward-looking statements

Cont'd

Edinburgh, U.K. 29th August 2024

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.

For more information, please contact:

NuCana plc
Hugh S. Griffith
Chief Executive Officer
T: +44 131-357-1111
E: info@nucana.com

ICR Westwicke,
Chris Brinzey
T: +1 339-970-2843
E: chris.brinzey@westwicke.com