Boston, Massachusetts. 13th October 2023

NuCana Presents Encouraging Data on NUC-3373 in Colorectal Cancer at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics 2023

NUC-3373 Demonstrates Promising Anti-Tumor Activity and a Favorable Safety Profile as part of NUFIRI-bevacizumab and NUFOX-bevacizumab in Second-line Colorectal Cancer Patients

Several Second-line Colorectal Cancer Patients in the NuTide:302 Study Achieved a Longer Progression-Free Survival as Compared to Their First-line Treatment with 5-FU-based Therapy

NuTide:323 Randomized Study of NUFIRI-bevacizumab vs. FOLFIRI-bevacizumab in Second-Line Colorectal Cancer Patients Recruiting Well with No New Safety Signals

Boston, Massachusetts, October 13, 2023 (GLOBE NEWSWIRE) - NuCana plc (NASDAQ: NCNA) announced presentations from two ongoing clinical studies with NUC-3373 in colorectal cancer (CRC) at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics 2023 taking place October 11-15, 2023 in Boston, Massachusetts.

For the first time, data has been presented from second-line patients with CRC. Previously, NuCana announced data on NUC-3373 both as a monotherapy (NuTide:301 study) and as part of combination therapy (NuTide:302 study Parts 1 & 2) in heavily pre-treated patients who had exhausted all available standard treatments. In these studies, NUC-3373 demonstrated a favorable safety profile and encouraging signs of efficacy, including tumor volume reductions in patients who were refractory to prior fluoropyrimidine treatment.

The NuTide:302 study is now in Part 3, where second-line patients with CRC are receiving either NUC-3373 in combination with leucovorin, irinotecan and bevacizumab (NUFIRI-bev) or NUC-3373 in combination with leucovorin, oxaliplatin and bevacizumab (NUFOX-bev). Data presented today showed that both regimens had favorable tolerability profiles. Furthermore, both NUFIRI-bev and NUFOX-bev demonstrated promising anti-tumor activity, including numerous patients with tumor volume reductions. Additionally, several patients achieved a longer progression-free survival (PFS) on NUC-3373-based regimens as compared to the PFS achieved in their first-line treatment with 5-FU-based therapy.

The ongoing Phase 2 randomized NuTide:323 study is investigating NUFIRI-bev versus the global standard of care, 5-FU in combination with leucovorin, irinotecan and bevacizumab (FOLFIRI-bev), in 171 second-line patients with CRC. The study is recruiting well and aggregated safety data from the first 40 patients enrolled showed no new safety signals.

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Hugh S. Griffith, NuCana's Founder and Chief Executive Officer said: "We are delighted to have been able to showcase these data. For the first time, we have presented data from our lead program of NUC-3373 in second-line colorectal cancer from the NuTide:302 study, which has shown encouraging signs of efficacy and continues to demonstrate a favorable safety profile. Four out of seven patients who received fluoropyrimidine plus oxaliplatin-based therapy as a first-line treatment achieved a longer PFS on NUFIRI-bev in the second-line setting where PFS is typically five months shorter. This result gives us further confidence in our ongoing randomized Phase 2 NuTide:323 study."

Mr. Griffith continued: "We also shared an update from NuTide:323 which is recruiting well with no new safety signals observed. We remain on track to fully enroll the study in the coming months and we look forward to sharing further updates from this study."

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 three 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; a randomized Phase 2 study (NuTide:323) in combination with leucovorin, irinotecan, and bevacizumab for the second-line treatment of patients with advanced 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 transformation of 3'-deoxyadenosine, a novel anti-cancer nucleoside analog. NUC-7738 is in the Phase 2 part of a Phase 1/2 study in patients with advanced solid tumors which is evaluating NUC-7738 as a monotherapy and in combination with pembrolizumab.

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,

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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, 2022 filed with the Securities and Exchange Commission ("SEC") on April 4, 2023, 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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