

Orlando, Florida 14th April 2023

NuCana Presents Data at the AACR 2023 Annual Meeting Highlighting Novel NUC-7738 Mechanisms of Action

NUC-7738 Reduces Secreted Forms of PD-L1 Indicating Potential Synergy with Checkpoint Inhibitors

NUC-7738 Decreases Glutaminase *in vitro* and in Cancer Tissue Demonstrating Potential for Anti-Cancer Activity in Highly Metabolic Tumors

Orlando, Florida April 14, 2023 (GLOBE NEWSWIRE)- NuCana plc (NASDAQ: NCNA) announced two posters to be presented at the American Association of Cancer Research (AACR) Annual Meeting being held from April 14-19, 2023.

Title: NUC-7738 causes reduction of soluble and exosome-associated PD-L1 in melanoma cell lines and patients

Presentation date and time: April 19th from 9.00am - 12.30pm

Abstract number: 5962

This study investigates the dynamic between NUC-7738 and the secreted forms of PD-L1 (soluble PD-L1 and exosomal PD-L1) both in a melanoma cell line and in patients treated with NUC-7738. Data from this study demonstrate that NUC-7738 reduced mRNA and protein levels of soluble PD-L1 in a melanoma cell line and that patients treated with NUC-7738 had reduced levels of exosomal PD-L1 compared to pre-treatment levels. These data indicate that NUC-7738 has the potential to act as an immune sensitizer and as an effective combination partner for PD-L1 pathway inhibitors. NUC-7738 is currently being studied in combination with pembrolizumab for patients with advanced solid tumors in the Phase 2 part of the NuTide:701 study.

Title: NUC-7738 promotes alternative polyadenylation site usage and reduces glutaminase GAC isoform

Presentation date and time: April 16th from 1.30pm - 5.00pm

Abstract number: 277

This study investigates the effect of NUC-7738 on isoforms of glutaminase 1. Glutaminase is often upregulated in cancer cells. Additionally, the GAC isoform drives more metabolically active cancers and has been associated with poorer patient outcomes. NUC-7738 reduced the expression of GAC in renal and pancreatic cancer cell lines in both hypoxic and normoxic conditions. Furthermore, tissue from patients with kidney cancer that was treated with NUC-7738 *ex vivo* demonstrated reduced levels of GAC. These data highlight a potentially meaningful anti-cancer strategy for NUC-7738 in metabolically active tumors that are able to sustain high rates of growth and proliferation in unfavorable conditions, including hypoxia.

Hugh S. Griffith, NuCana's Founder and Chief Executive Officer said: "We are excited with these data as we believe they demonstrate NUC-7738's multi-faceted mechanisms of action and are highly supportive of our clinical development strategy. We are currently investigating NUC-7738 in combination with pembrolizumab in the Phase 2 part of the NuTide:701 study and look forward to sharing data from this study in 2023."

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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, in combination with other agents, is in a Phase 1b/2 study in patients with metastatic colorectal cancer. NuCana has also initiated a randomized Phase 2 study of NUC-3373, in combination with other agents, for the second-line treatment of patients with advanced colorectal cancer. In addition, NuCana has initiated a Phase 1b/2 modular study of NUC-3373 in combination with other agents, including the PD-1 inhibitor pembrolizumab, in patients with advanced solid tumors to identify additional indications for development. 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, 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; the utility of prior non-clinical and clinical data in determining future clinical results; and the sufficiency of the Company's current cash, cash equivalents and marketable securities to fund its planned operations into 2025. 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.

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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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