Edinburgh, U.K. 12th September 2022

NuCana Presents Promising Data on NUC-7738 at the European Society of Medical Oncology (ESMO) Annual Meeting 2022

NUC-7738 Demonstrates Encouraging Anti-Tumor Activity and a Favorable Safety Profile Across a Variety of Solid Tumors

NUC-7738 Monotherapy and Combination with Pembrolizumab to be Investigated in Phase 2

Paris, France, September 12, 2022 (GLOBE NEWSWIRE) - NuCana plc (NASDAQ: NCNA) announced data today from the ongoing NuTide:701 study of NUC-7738 in an oral presentation at the European Society for Medical Oncology (ESMO) Annual Meeting.

Oral 455MO: NUC-7738 in Patients with Advanced Solid Tumors- Phase 1 results from the NuTide:701 Phase 1 / 2 Study

Data on NUC-7738 from the Phase 1 part of NuTide:701 showed encouraging signals of anti-tumor activity across a range of tumor types, particularly melanoma. Promising data were observed in a variety of solid tumors with numerous patients staying on treatment for extended periods, including one patient with metastatic melanoma who became eligible for complete surgical resection following eleven months of treatment with NUC-7738. NUC-7738 also had a favorable safety profile with low rates of treatment-related AEs (TRAEs), very few Grade 3 TRAEs and no patients experiencing Grade 4 or 5 TRAEs.

Dr. Stefan Symeonides, Senior Lecturer in Experimental Cancer Medicine at the Edinburgh Cancer Research Centre and lead author of the ESMO presentation, said: "NUC-7738 has shown an excellent safety profile and encouraging signals of anti-tumor activity in this study which is enrolling patients who have exhausted all standard therapies. We are excited to further investigate the activity of NUC-7738 in melanoma and other tumor types."

"We remain very encouraged by what we have observed with NUC-7738," said Hugh S. Griffith. "NUC-7738's precise mode of action of disrupting RNA polyadenylation in cancer cells thereby altering the expression of genes associated with key cellular processes is very exciting. The positive signals observed in Part 1 of the NuTide:701 study, combined with NUC-7738's differentiated mode of action, provide a strong scientific rationale to expedite its development and enrich the Phase 2 part of the study for patients with melanoma. This part of the study will also include a cohort combining NUC-7738 with pembrolizumab, which is a standard of care for melanoma patients. We have begun enrolling patients into the Phase 2 part of the study and look forward to sharing these data."

About NUC-7738

NUC-7738 is a phosphoramidate transformation of 3'-deoxyadenosine (3'-dA), also known as cordycepin. 3'-dA has demonstrated potent anti-cancer activity in non-clinical studies, but has not been successfully developed as an anti-cancer agent due to its rapid breakdown by adenosine deaminase (ADA). NUC-7738 is

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designed to generate the active anti-cancer metabolite of 3'-dA directly inside cancer cells, thus overcoming 3'-dA's key limitations of breakdown, transportation and activation. The cytotoxic effect of NUC-7738 is largely attributed to the generation of the main active anti-cancer metabolite, 3'-dATP which interferes with RNA polyadenylation, causing changes in the expression of genes involved in various cellular processes, leading to cancer cell death.

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 a PD-1 inhibitor, 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 a PD-1 inhibitor.

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

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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, 2021 filed with the Securities and Exchange Commission ("SEC") on April 27, 2022, 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..

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

RooneyPartners
Marion Janic
T: +1 212-223-4017
E: mjanic@rooneyco.com