Berlin, Germany. 18th Oct 2025

NuCana Presents Encouraging Data on NUC-7738 in Combination with PD-1 Inhibitors using Primary Patient-Derived Organoids and Autologous Tumor-Infiltrating Lymphocytes at the ESMO Congress 2025

NUC-7738 Synergizes with PD-1 Inhibitors to Promote Cancer Cell Death

Data Reinforces Mechanism of Action along with Efficacy and Safety Profile of NUC-7738

BERLIN, October 18, 2025 (GLOBE NEWSWIRE) – NuCana plc (NASDAQ: NCNA) ("NuCana" or the "Company") presented data at the European Society for Medical Oncology Congress 2025 ("ESMO") on a new model system investigating the synergistic effects of NUC-7738 and PD-1 inhibition in primary organoids derived from patients with renal cell carcinoma ("RCC").

Using patient-derived organoids ("PDOs") from ten patients with RCC and autologous tumor-infiltrating lymphocytes ("TILs"), co-culture experiments reveal that NUC-7738 enhances the effectiveness of PD-1 inhibitors, resulting in increased tumor cell killing. This combinatorial approach may offer a new option for cancers that no longer respond to anti-PD-1 therapy by targeting multiple aspects of the tumor microenvironment through the disruption of RNA polyadenylation and subsequent changes in cancer cell gene expression.

The data presented at ESMO reinforces the mechanism of action for NUC-7738 as observed in the ongoing Phase 1/2 NuTide:701 clinical study. Data to date from NuTide:701 have demonstrated a favorable safety profile, meaningful tumor volume reduction, and prolonged progression-free survival in patients with PD-1 inhibitor refractory and resistant metastatic melanoma.

Andrew Kay, NuCana's Executive Chairman said: "We are excited to share these new data on NUC-7738 in combination with PD-1 inhibitors in a real-time organoid model system. In addition to demonstrating clear benefits of combining PD-1 inhibitors with NUC-7738, similar to those seen in patients on the ongoing NuTide:701 study, this may lead to robust, patient-specific testing for a selection of immune checkpoint therapies."

Mr. Kay continued: "The translational data that has been generated in this study increases our confidence that the effects we are seeing are a result of NUC-7738 targeting multiple aspects of the tumor microenvironment and increasing PD-1 inhibition. Our data on mechanism of action of NUC-7738 indicate that the phenomena are not restricted to a single tumor type, and that NUC-7738 may have the ability to sensitize many cancers to PD-1 inhibitor therapy."

Based on the exciting initial data from the Phase 1/2 NuTide:701 clinical study, regulators have approved the expansion of the study to recruit an additional 28 patients with PD-1 inhibitor-resistant melanoma. NuCana is currently recruiting patients to this expansion study and plans to meet with the U.S. Food and Drug Administration to discuss the data from this study to determine the optimal registration strategy to support marketing approval.

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The details of NuCana's presentation at ESMO are as follows:

Abstract Title: Patient Derived Organoids Reveal Synergy Between NUC-7738 and PD-1 Inhibition in Renal Cell Cancer
Poster Number: 1530P
Session: Investigational Immunotherapy
Date: Sunday, October 19, 2025
Presenting Author: H. Abdullah

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-7738 and NUC-3373. 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. NUC-3373 is a new chemical entity derived from the nucleoside analog 5-fluorouracil, a widely used chemotherapy agent. NUC-3373 is being evaluated in 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.

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 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-7738 and NUC-3373; 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

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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, our ability to raise additional capital sufficient to fund our planned operations and 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, 2024 filed with the Securities and Exchange Commission ("SEC") on March 20, 2025, 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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