Edinburgh, U.K. 14th Oct 2025

NuCana Announces Encouraging Data for NUC-3373 in Combination with Anti–PD-1 Therapy

NUC-3373 Plus Pembrolizumab Continues to Show Favorable Efficacy and Safety Profile in Heavily Pre-treated Patients

Latest Data Cut-Off Shows Patient with Melanoma Remains Progression-Free at 23 Months with a Durable Partial Response

Preclinical Data Corroborate Immunogenic Effects of NUC-3373 Observed in Patients

EDINBURGH, United Kingdom, October 14, 2025 (GLOBE NEWSWIRE) – NuCana plc (NASDAQ: NCNA) ("NuCana" or the "Company") announced the publication of new data on NUC-3373. The update includes results from the NuTide:303 clinical study, published on medRxiv, the preprint server for health sciences, together with complementary preclinical findings published in the peer-reviewed journal Public Library of Science ONE (PLOS ONE).

NUC-3373, a potent thymidylate synthase inhibitor that induces DNA damage in cancer cells, has previously shown encouraging activity in combination with the PD-1 inhibitor pembrolizumab in the Phase 1/2b modular study, NuTide:303. In Module 1 of this study, 12 patients with advanced solid tumors who had exhausted all standard treatment options and had previously received PD-1 inhibitors were treated with NUC-3373 plus pembrolizumab.

Encouraging signals of durable activity were observed, including:

- A 100% reduction in tumor lesion size (classified as a partial response due to the presence of non-target lesions) in a patient with urothelial carcinoma of the bladder who remained on treatment for over 15 months; and
- An 81% reduction in target lesions in a patient with metastatic melanoma resistant to prior pembrolizumab therapy, who continues to remain progression-free at 23 months.

These promising clinical findings are further supported by preclinical data. The published results demonstrate that NUC-3373 in a model *in vitro* system:

- Promotes the release of immunogenic damage-associated molecular patterns (DAMPs);
- Enhances activation of first-line defense immune cells, including natural killer (NK) cells; and
- In combination with a PD-1 inhibitor, enhances tumor cell death by activating lymphocytes, regardless of the tumor's genomic stability status.

"It is becoming increasingly clear that the majority of future standards of care for advanced cancers will rely on combination regimens incorporating novel immuno-oncology backbones," said Professor David Harrison, Head of Translational Medicine at NuCana. "The combination of NUC-3373 with pembrolizumab has demonstrated both a favorable safety profile and evidence of efficacy and durable disease control in this patient cohort."

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Andrew Kay, NuCana's Executive Chairman, added: "The complementary mechanisms of action of NUC-3373 and PD-1 inhibition provide a strong rationale for synergy. We are currently evaluating optimal combinations and indications for further clinical studies of NUC-3373, while continuing to maintain our anticipated cash runway into 2029. We are committed to advancing these assets and working toward our vision of delivering significantly improved treatment outcomes for patients with cancer."

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; the utility of prior non-clinical and clinical data in determining future clinical results; and the sufficiency of the Company's current cash and cash equivalents to fund its planned operations into 2029. 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

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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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