Barcelona, U.K. 20th November 2026

NuCana Presents Preclinical Data Showing NUC-7738 Enhances Carfilzomib Activity in Multiple Myeloma Cell Lines at the 38th EORTC-NCI-AACR Symposium

NUC-7738 Increased Proteasome Inhibition When Combined with Carfilzomib

Data Presented Identify an Additional Potential Mode of Action for NUC-7738 and Support Evaluation of Additional Indications and Combination Strategies

BARCELONA, Spain, November 20, 2026 (GLOBE NEWSWIRE) – NuCana plc (NASDAQ: NCNA) ("NuCana" or the "Company") today announced new preclinical data showing that NUC-7738 enhanced the anti-cancer activity of carfilzomib, an approved proteasome inhibitor used to treat patients with multiple myeloma. The findings were presented at the 38th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, taking place in Barcelona, Spain, from November 18-20, 2026.

Carfilzomib works by inhibiting the proteasome, a cellular system that breaks down unwanted proteins. Multiple myeloma cells depend heavily on this system to manage their high protein load. NuCana believes that increasing the effectiveness of proteasome inhibition could make these cancer cells more vulnerable to treatment.

In three multiple myeloma cell lines, NUC-7738 demonstrated single-agent activity and increased the anti-cancer activity of carfilzomib. At concentrations where the individual agents left approximately half of the cells viable, the combination reduced cell viability to 3% in two models and 26% in the third after 96 hours. In two of the three models, the combination's activity exceeded that expected if the two agents acted independently; in the third, the effect was additive. These findings provide a scientific rationale for NuCana to further investigate the combination in multiple myeloma.

Further studies showed that NUC-7738 altered proteasome function and increased the inhibition achieved with carfilzomib. In one model, proteasome activity after 24 hours was 25% of the untreated control with the combination, compared with 52% with carfilzomib alone. NuCana believes this demonstrates a measurable effect on the cellular system targeted by carfilzomib and may help explain the combination's greater anti-cancer activity.

NuCana believes the findings also suggest an additional potential mode of action for NUC-7738. Although NUC-7738 initially increased proteasome activity when used on its own, it also reduced the processed form of NFE2L1, a protein involved in the cellular response to proteasome inhibition. Our research proposes that NUC-7738's active metabolite may influence the opening of the proteasome's gate, potentially increasing access for carfilzomib. These observations offer a basis for investigating how NUC-7738 may increase cancer cells' sensitivity to proteasome inhibitors. Further studies are needed to test this proposed mode of action and assess its relevance to treatment in patients.

NuCana believes these results also support further investigation beyond multiple myeloma. In a separate laboratory screen evaluating NUC-7738 with 70 partner drugs across 35 cancer cell lines, carfilzomib ranked first on a measure of greater-than-expected combination activity. Such activity was observed in 28 of 33 solid-tumor models spanning 14 tumor types, at a single concentration of NUC-7738. These findings highlight the broad anti-cancer potential of NUC-7738 and supports further evaluation to identify the cancer indications in which the combination may offer the greatest potential.

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"These findings add an important dimension to our understanding of NUC-7738's mode of action," said Hugh S. Griffith, NuCana's Founder and Chief Executive Officer. "What is particularly encouraging is that the changes in proteasome function were accompanied by greater-than-expected anti-cancer activity in these preclinical models. We believe these data strengthen the rationale for further evaluation of NUC-7738 in combination with proteasome inhibitors and across additional tumor types."

Mr. Griffith continued: "Our priority is to define the optimal clinical development path for NUC-7738 in melanoma, informed by the forthcoming Phase 2 results and the latest translational data. We are also continuing our dialogue with the FDA regarding a potential registrational strategy. In parallel, we believe these new preclinical findings strengthen the scientific rationale for broadening the development of NUC-7738 beyond PD-1 inhibitor-resistant melanoma, through additional indications and combination strategies. With cash resources anticipated to fund our planned operations into 2029, we are focused on advancing these priorities and selecting the most promising opportunities for further development."

As previously announced, NuCana plans to present final results from the Phase 2 expansion cohort of the NuTide:701 study, evaluating NUC-7738 in combination with pembrolizumab in patients with PD-1 inhibitor-resistant metastatic melanoma, together with the latest translational data, at the ESMO Immuno-Oncology & Advanced Therapies Congress in London from December 14–16, 2026.

Details of NuCana's presentation at the 38th EORTC-NCI-AACR Symposium are as follows:

Abstract Title:	NUC-7738 Alters Functional Proteasome Activity and Enhances Carfilzomib Sensitivity in Multiple Myeloma
Poster Number:	PB-084
Topic:	Combination Therapies
Date:	Friday, November 20, 2026
Presenting Author:	Dr. Mustafa Elshani

More information regarding the 38th EORTC-NCI-AACR Symposium can be found at:
https://event.eortc.org/ena2026/

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 that 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 targeted thymidylate synthase ("TS") inhibitor designed to overcome key pharmacological limitations

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associated with other TS inhibitors. NUC-3373 has recently been 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, and NuCana is currently evaluating further characterization of mode of action and target indications for further clinical studies of NUC-3373.

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 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, 2025 filed with the Securities and Exchange Commission ("SEC") on March 19, 2026, 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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