UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER PURSUANT TO RULE 13a-16 OR 15d-16 OF THE SECURITIES EXCHANGE ACT OF 1934

For the month of November 2024

(Commission File No. 001-38215)

NUCANA PLC

(Translation of registrant's name into English)

3 Lochside Way Edinburgh EH12 9DT United Kingdom (Address of registrant's principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover Form 20-F or Form 40-F.

Form 20-F	⊠ Forr	n 40-F 🗆

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101 (b) (1):

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101 (b) (7): 🗆

Other Events

On November 11, 2024, NuCana plc (the "Company") issued a press release announcing the publication of initial data from the ongoing Phase 1b/2 study of NUC-3373 in combination with pembrolizumab or docetaxel in MedRxiv, the preprint server for Health Sciences. The press release is attached as Exhibit 99.1 hereto and is incorporated by reference herein.

The information in the attached Exhibit 99.1 is being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, nor shall it be deemed incorporated by reference in any filing made by the Company under the Securities Act of 1933, as amended, or the Exchange Act, except as otherwise set forth herein or as shall be expressly set forth by specific reference in such a filing.

Exhibits

99.1 Press Release, dated November 11, 2024

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

NuCana plc

By: /s/ Donald Munoz

Name: Donald Munoz Title: Chief Financial Officer

Date: November 12, 2024

NuCana Announces Encouraging Initial Data from Phase 1b/2 Modular Study of NUC-3373 in Combination with Pembrolizumab or Docetaxel

Patients with Advanced Solid Tumors who had Exhausted All Other Treatment Options and were PD-(L)1 Experienced Achieved Significant Tumor Volume Reductions and Prolonged Progression Free Survival Following Treatment with NUC-3373 plus Pembrolizumab

One Patient Achieved a 100% Reduction in their Target Lesion

Patients with Lung Cancer who had Exhausted All Other Treatment Options Achieved Prolonged Progression Free Survival Following Treatment with NUC-3373 plus Docetaxel

Edinburgh, United Kingdom, November 11, 2024 (GLOBE NEWSWIRE) - NuCana plc (NASDAQ: NCNA) announced that initial data from the ongoing Phase 1b/2 modular study (NuTide:303) investigating NUC-3373 in combination with the PD-1 inhibitor pembrolizumab for patients with advanced solid tumors (Module 1) and in combination with docetaxel for patients with lung cancer (Module 2) have been published in MedRxiv, the preprint server for Health Sciences.

Module 1 included 12 patients with a variety of solid tumors who had exhausted all other treatment options. The majority of patients (n=9) had received prior PD-(L)1 based therapy. Encouraging signals of anti-cancer activity were observed with confirmed Partial Responses in 2 patients and Stable Disease in a further four patients, resulting in an objective response rate of 22% and a disease control rate of 67% in the efficacy evaluable population. The combination of NUC-3373 plus pembrolizumab was generally well tolerated.

Module 1 Selected Case Studies: NUC-3373 plus pembrolizumab in patients with advanced solid tumors

• 72-year-old patient with urothelial bladder cancer (Lynch syndrome) who had previously received gemcitabine plus cisplatin followed by the PD-L1 inhibitor atezolizumab (achieved a Partial Response and remained on therapy for 23 months). Following treatment with NUC-3373 plus pembrolizumab, the patient achieved 100% reduction in the target lesion (considered a confirmed Partial Response due to the presence of non-target lesions) and remains on treatment for over 10 months.

75-year-old patient with BRAF mutant metastatic cutaneous melanoma who had previously received pembrolizumab (best response of Progressive Disease within 5 months) followed by dabrafenib plus trametinib (discontinued trametinib after 1 month due to toxicity and achieved Stable Disease before progressing after seven years on dabrafenib). Following treatment with NUC-3373 plus pembrolizumab, this patient achieved a confirmed Partial Response with an 81% reduction in the target lesion and remains on treatment for over 12 months.

Module 2 included 4 patients with non-small cell lung cancer (NSCLC) or pleural mesothelioma who had disease progression on, or were unable to tolerate, prior chemotherapy-containing regimens. Docetaxel is the current standard of care for NSCLC patients without targetable alterations who progress on PD-(L)1 inhibitor-based therapy, however, it is associated with modest clinical benefit (median PFS of 3-4 months) and substantial toxicity. Following treatment of the first 4 patients in this module, enrollment was put on hold due to toxicity challenges with docetaxel. Despite this, 2 patients achieved prolonged Stable Disease. Protocol modifications to include the use of a different taxane in this combination are currently being considered.

Module 2 Selected Case Studies: NUC-3373 plus docetaxel in patients with lung cancer

- 60-year-old patient with pleural mesothelioma who had previously received carboplatin plus pemetrexed (progressed within 4 months), the PD-1 inhibitor nivolumab (progressed within 4 months), and carboplatin plus pemetrexed (progressed within 1 month). Following treatment with NUC-3373 plus docetaxel, the patient achieved Stable Disease for more than 13 months (ongoing).
- 77-year-old patient with squamous NSCLC who had previously received carboplatin plus paclitaxel plus pembrolizumab (Stable Disease for 2 months) followed by maintenance pembrolizumab (progressed within 21 months). Following treatment with NUC-3373 plus docetaxel, the patient achieved Stable Disease for 7 months.

Full details can be found in the publication: Link

Professor David Harrison, NuCana's Head of Translational Medicine stated: "We previously presented data on NUC-3373's ability to elicit the release of Damage Associated Molecular Patterns (DAMPs), promote an anti-tumor immune response, and potentiate the activity of PD-1 inhibitors in human cancer cell lines. These data led us to investigate the combination of NUC-3373 plus pembrolizumab so we are very excited to observe these encouraging clinical findings in PD-(L)1 inhibitor experienced patients."

Professor Harrison continued: "We have also demonstrated that NUC-3373 is a very potent thymidylate synthase inhibitor and causes DNA damage, leading us to hypothesize that NUC-3373 may be an attractive alternative to pemetrexed in patients with NSCLC and mesothelioma. Observing that NUC-3373 in combination with docetaxel is stabilizing disease in these hard-to-treat patient populations provides further evidence supporting this hypothesis."

Hugh S. Griffith, NuCana's Founder and Chief Executive Officer said: "We are very excited that these NUC-3373 combinations have been observed to provide a meaningful clinical benefit to patients who had exhausted all other treatment options. We recently presented encouraging efficacy and safety data at ESMO on NUC-7738 plus pembrolizumab in patients with metastatic melanoma who were refractory or resistant to PD-1 inhibitors. We are pleased to have two Phase 2 product candidates in our portfolio, each with a distinct mechanism of action, that can potentiate PD-1 inhibitors in PD-(L)1 resistant patients. We look forward to sharing additional data from the NuTide:303 study and our clinical development plans for both NUC-3373 and NUC-7738 in the near future."

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 is currently 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. 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 which is evaluating NUC-7738 as a monotherapy in patients with advanced solid tumors and in combination with melanoma.

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 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, 2023 filed with the Securities and Exchange Commission ("SEC") on March 20, 2024, 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:

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