Edinburgh, U.K. 12th September 2022

NuCana Presents Favorable Data on NUC-3373 at the European Society of Medical Oncology (ESMO) Annual Meeting 2022

NUC-3373 Demonstrates Promising Anti-Tumor Activity and Safety in Combination with Oxaliplatin (NUFOX) and Irinotecan (NUFIRI) in Heavily Pre-Treated Colorectal Cancer Patients

Randomized Study of NUFIRI vs. FOLFIRI in Second-Line Colorectal Cancer Patients Initiated

Paris, France, September 12, 2022 (GLOBE NEWSWIRE) - NuCana plc (NASDAQ: NCNA) announced data from the ongoing NuTide:302 study of NUC-3373 in combination with other agents at the European Society for Medical Oncology (ESMO) Annual Meeting being held from September 9 to 13, 2022.

Poster 345P: NUC-3373, a ProTide transformation of 5-FU, in combination with oxaliplatin (NUFOX) or irinotecan (NUFIRI) in patients with advanced colorectal cancer (NuTide:302)

NUC-3373, a phosphoramidate transformation of 5-FU, that was designed to overcome the key limitations and challenges associated with 5-FU has previously demonstrated promising anti-tumor activity and a favorable safety and pharmacokinetic profile as a single agent and in combination with leucovorin in heavily pre-treated patients with advanced colorectal cancer (CRC). Data presented at ESMO describe NUC-3373 plus leucovorin in combination with either oxaliplatin (NUFOX) or irinotecan (NUFIRI) in the dose-finding part of the study.

Both NUFOX and NUFIRI demonstrated encouraging anti-tumor activity in heavily pre-treated CRC patients with progressive disease who had all previously received regimens containing 5-FU, oxaliplatin and irinotecan. Of the 46 patients who received either NUFOX or NUFIRI, twelve (six from each cohort) achieved progression-free survival (PFS) of greater than three months, including three patients who achieved PFS of six months or longer. The disease control rates for the NUFOX and NUFIRI regimens were 80% and 55%, respectively. Data presented also indicate that NUFOX and NUFIRI have favorable safety profiles when compared to historical data for the 5-FU-containing regimens FOLFOX and FOLFIRI, with lower rates of toxicities such as neutropenia and gastrointestinal disturbances that limit their clinical utility. With these data, NuCana has established the recommended Phase 2 dose for NUC-3373 as part of NUFOX and NUFIRI regimens.

Andrew Coveler, Associate Professor, Medical Oncology at the University of Washington School of Medicine, Associate Professor, Clinical Research Division at the Fred Hutchinson Cancer Center, and lead author of the ESMO presentation said: "I am excited by the results of the NuTide:302 study in light of the heavily pre-treated nature of these patients. It is noteworthy to observe a high disease control rate and extended periods of progression-free survival in patients who had previously been treated with multiple lines of therapy that included oxaliplatin and irinotecan with 5-FU. There is a significant unmet need for new medicines to treat patients with colorectal cancer and I look forward to continuing the investigation of NUFIRI and NUFOX in combination with bevacizumab in earlier-line CRC patients."

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"These data are highly supportive of our strategy to develop NUC-3373 as a replacement for 5-FU, one of the most widely used medicines for the treatment of patients with cancer," said Hugh S. Griffith, NuCana's Founder and Chief Executive Officer. "Based on the data from NuTide:302, we have initiated a randomized study in second-line CRC patients called NuTide:323 comparing NUFIRI plus bevacizumab to FOLFIRI plus bevacizumab, the global standard of care. Due to NUC-3373's compelling biological rationale and strong clinical potential, we have also initiated the NuTide:303 study, investigating NUC-3373 in combination with either pembrolizumab in patients with various solid tumors or in combination with docetaxel in patients with non-small cell lung cancer."

About NUC-3373

NUC-3373 is a phosphoramidate transformation of 5-fluorouracil, or 5-FU, which is designed to overcome the key limitations and pharmacologic challenges that hinder the clinical utility of 5-FU, with the aim of improving 5-FU's efficacy, safety and administration challenges.

5-FU (and its other forms including capecitabine) is an inactive prodrug and its anti-cancer activity is dependent on its conversion to the active anti-cancer metabolite (FUDR-MP), which binds to and inhibits thymidylate synthase (TS), a critical enzyme in de novo nucleotide synthesis and cell survival. TS is required to convert uridine (specifically dUMP) to thymidine (specifically dTMP), one of the four nucleotides that comprise DNA. The inhibition of TS results in an imbalance in the ratio of dUMP and dTMP, thereby disrupting DNA synthesis and repair, ultimately leading to cancer cell death. However, due to multiple limitations, 5-FU is not efficiently converted to FUDR-MP.

NUC-3373 generates much higher concentrations of FUDR-MP in patients' cells. It also has a more convenient administration schedule and does not produce toxic levels of metabolites such as FBAL or FUTP (which are associated with hand-foot syndrome, neutropenia, mucositis and diarrhea) resulting in an improved safety profile.

In addition to preventing the synthesis of thymidine via TS inhibition, NUC-3373 treatment also results in the release of Damage Associate Molecular Patterns (DAMPs) and pro-inflammatory cytokines by cancer cells. These act as molecular signals to the immune system, encouraging them to kill cancer cells. Furthermore, NUC-3373 has been shown to induce the expression of PD-L1 on treated cells. In vitro experiments using NUC-3373 treated CRC cells co-cultured with immune cells have shown that NUC-3373 is able to potentiate the effects of PD-1 inhibitors, thus providing a strong scientific rationale for combining NUC-3373 and PD-1/PD-L1 inhibitors in patients.

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.

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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 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.

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