Edinburgh, U.K. 22nd October 2018

NuCana Presents Data from Phase I Study of NUC-3373 at ESMO 2018

Single-Agent Anti-Cancer Activity Observed in Patients with Advanced Solid Tumors

NUC-3373 Demonstrates Potential Advantages Compared to 5-FU

NuCana has Initiated a Phase Ib Study of NUC-3373 in Patients with Advanced Colorectal Cancer in Combination with Other Agents Typically Administered with 5-FU

Edinburgh, United Kingdom, October 22, 2018 (GLOBE NEWSWIRE) – NuCana plc (NASDAQ: NCNA), a clinical-stage biopharmaceutical company focused on significantly improving treatment outcomes for patients with cancer, announced today the presentation of additional data from a Phase I clinical study of NUC-3373, its ProTide transformation of the active anti-cancer metabolite of 5-fluorouracil (5-FU), in patients with advanced solid tumors, at the European Society for Medical Oncology (ESMO) 2018 Congress in Munich, Germany.

To date, 36 patients, all with metastatic cancer, have been enrolled in the study, with 29 patients receiving NUC-3373 on a weekly schedule on days one, eight, 15 and 22 of a 28-day cycle at doses ranging from 125 mg/m^2 to 1,500 mg/m^2 and seven patients receiving NUC-3373 on an alternate-week, or fortnightly, schedule on days one and 15 of a 28-day cycle at doses ranging from 1,500 mg/m^2 to 1,875 mg/m^2.

Notably, three patients achieved Stable Disease after treatment, with responses lasting more than nine months at the time of data cutoff on September 25, 2018:

- A 70-year-old male with colorectal cancer who had received six previous lines of therapy, but relapsed within one to eight months following each of his four previous therapies: 5-FU-based chemoradiotherapy; 5-FU plus irinotecan (FOLFIRI); capecitabine plus oxaliplatin; FOLFIRI; trifluridine/tipiracil (LONSURF®); and single-agent irinotecan. This patient received 10 28-day cycles of NUC-3373 and achieved Stable Disease with Progression-Free Survival (PFS) of over nine months;
- A 60-year-old female with cholangiocarcinoma who relapsed within six months of receiving prior gemcitabine plus cisplatin, received 12 cycles of NUC-3373 and achieved Stable Disease with PFS of over 11 months; and
- A 55-year-old male with basal cell carcinoma who previously received two lines of therapy: vismodegib; and paclitaxel plus carboplatin. This patient received 10 cycles of NUC-3373 and achieved Stable Disease with PFS of over 10 months.

"To observe durable single-agent anti-cancer activity in these patients who have exhausted all current standards of care is noteworthy," said Dr. Sarah Blagden, Associate Professor of Experimental Cancer Medicine at the University of Oxford and Chief Investigator of the study. Professor Blagden added: "NUC-3373 was observed to be well-tolerated and to have administration advantages over 5-FU, which remains one of the most important and widely used anti-cancer drugs in the world. I believe these early results from patients in NUC-3373's Phase I trial support its continued development."

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Hugh Griffith, NuCana's Chief Executive Officer, said: "NUC-3373 is our second product candidate that uses our proprietary ProTide technology with the goal of improving the efficacy and safety of important anti-cancer agents. We are excited to have observed disease control and promising Progression-Free Survival data in patients with advanced, metastatic cancers. The PK/PD profile of this agent also appears promising and we believe NUC-3373 has the potential to replace 5-FU as the standard of care in the treatment of a wide range of cancers."

Both dosing regimens were observed to be well tolerated with no unexpected adverse events (AEs) or accumulative toxicity. Importantly, no patients developed hand-foot syndrome, which is a debilitating side effect associated with fluoropyrimidine therapy. In addition, NUC-3373 has a plasma half-life of 9.7 hours compared to the 8 to 14-minute plasma half-life of 5-FU. As a result, NUC-3373 can be infused over a much shorter time frame of 30 minutes to four hours compared to the 46-hour continuous infusion required with 5-FU.

The results of this study suggest that NUC-3373 has the potential to overcome the key cancer resistance mechanisms associated with 5-FU and capecitabine and may be capable of achieving anti-cancer activity even in patients who have progressed on prior treatment with a fluoropyrimidine.

Mr. Griffith remarked: "These data support that NUC-3373 may have a key role to play in the treatment of patients with cancer and we look forward to continuing its development. To that end, we have just initiated NuTide:302, a Phase Ib study in patients with advanced colorectal cancer in which NUC-3373 will be combined with many of the agents typically combined with 5-FU, including leucovorin, irinotecan, oxaliplatin and monoclonal antibodies."

About NuCana plc

NuCana® is a clinical-stage biopharmaceutical company focused on significantly improving treatment outcomes for cancer patients 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 tumors, their efficacy is limited by cancer cell resistance mechanisms and they are often poorly tolerated. Utilizing our proprietary technology, we are developing new medicines, ProTides, designed to overcome key cancer resistance mechanisms and generate much higher concentrations of anti-cancer metabolites in cancer cells.

Our most advanced ProTide candidates, Acelarin® and NUC-3373, are new chemical entities derived from the nucleoside analogs gemcitabine and 5-fluorouracil, respectively, two widely used chemotherapy agents. Acelarin is currently being evaluated in three clinical studies, including a Phase Ib study for patients with biliary tract cancer, a Phase II study for patients with ovarian cancer and a Phase III study for patients with pancreatic cancer. NUC-3373 is currently in a Phase I study for the potential treatment of a wide range of advanced solid tumors.

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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 potential advantages of NUC-3373, the Company's plans to conduct a Phase Ib study of NUC-3373 in patients with advanced colorectal cancer, the Company's other planned and ongoing clinical studies for the Company's product candidates, including Acelarin, NUC-3373 and NUC-7738; the initiation, enrollment, timing, progress, release of data from and results of those planned and ongoing clinical studies; and the utility of prior preclinical 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, 2017 filed with the Securities and Exchange Commission ("SEC") on March 22, 2018, 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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