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September 12, 2017

VIA EDGAR & HAND DELIVERY

Securities and Exchange Commission
Division of Corporation Finance
100 F Street, N.E. Washington, D.C. 20549
Attention: Division of Corporation Finance, Office of Healthcare and Insurance

Re: NuCana plc (formerly NuCana BioMed Limited)
Registration Statement on Form F-1 (File No. 333-220321)
Filed September 1, 2017
CIK No. 0001709626

Ladies and Gentlemen:

We are submitting this letter on behalf of NuCana plc (formerly NuCana BioMed Limited) (the "**Company**") in response to comments from the staff of the Division of Corporation Finance, Office of Healthcare and Insurance (the "**Staff**") of the Securities and Exchange Commission (the "**Commission**") conveyed in a telephone conversation with the undersigned on September 12, 2017, relating to the above-referenced Registration Statement.

Per the Staff's request conveyed in the telephone conversation referenced above, and in further response to Comment 1 in the letter from the Staff dated August 16, 2017 as previously responded to by the Company in its response letter to the Staff dated September 1, 2017, the Company is supplementally submitting to the Staff the Company's proposed revisions to "Summary—Overview" on page 1 of the Registration Statement and to "Risk Factors—Risks Related to Development of Our Product Candidates—Initial success in the completed and ongoing early-stage clinical trials may not be indicative of results obtained when these trials are completed or in later stage trials" on page 18 of the Registration Statement. Those proposed revisions are attached hereto as Exhibit A, marked against the existing disclosure in the Registration Statement as filed on September 1, 2017. We are providing by hand delivery to your attention five courtesy copies of this letter, including Exhibit A.

We hope that the proposed revisions reflected in Exhibit A will be acceptable to the Staff. Please do not hesitate to call me, William C. Hicks, William T. Whelan or Adam Davey of this firm at (617) 542-6000 with any comments or questions regarding the Registration Statement and this letter. We thank you for your time and attention.

Sincerely,

/s/ John T. Rudy
John T. Rudy

cc: *Securities and Exchange Commission*
Keira Nakada
Kenneth Vaughn
Jeffrey Gabor
Mary Beth Breslin

NuCana plc
Hugh S. Griffith
Donald Munoz

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
William C. Hicks
William T. Whelan
Adam Davey

Cooley LLP
Divakar Gupta
Brent B. Siler
Courtney T. Thorne

EXHIBIT A

NuCana plc Registration Statement on Form F-1 (File No. 333-220321), filed September 1, 2017

Summary – Overview (pages 1-2)

We are 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 four clinical trials across several solid tumor indications, including ovarian cancer, biliary cancer and pancreatic cancer. NUC-3373 is currently in a Phase 1 trial for the potential treatment of a wide range of advanced solid tumor cancers. We have retained worldwide rights to these lead product candidates as well as our preclinical product candidates, all of which we refer to as ProTides.

Acelarin, our most advanced product candidate, is a potential first-in-class ProTide that has been evaluated in over 130 patients. Acelarin is a ProTide transformation of gemcitabine that we believe could replace gemcitabine in certain cancer indications and have utility across a range of other cancers. In a Phase 1 dose-ranging trial in 49 evaluable patients with advanced metastatic solid tumors, Acelarin was well tolerated, achieved a ~~high~~78% disease control rate and was associated with intracellular levels of active anti-cancer metabolite over 200 times higher than those reported for gemcitabine. A subset of 14 evaluable patients with relapsed/refractory gynecological cancers achieved a ~~high~~93% disease control rate. In a Phase 1b dose-ranging trial in 23 evaluable patients with recurrent ovarian cancer, Acelarin was combined with carboplatin and achieved a ~~high~~96% disease control rate. ~~As these results were obtained in first-in-human dose-ranging trials, they are not suitable for marketing approval. However, based on the encouraging~~Based on these disease control rates and ~~the~~its tolerability profile, we have begun a Phase 2 trial of Acelarin in patients with platinum-resistant ovarian cancer, for which we expect to report interim data in 2018. Acelarin is also being evaluated in another Phase 1b trial in patients with biliary cancer to determine its optimal dose in combination with cisplatin. We expect to report data from this trial in 2018, after which we plan to commence a multi-national Phase 3 trial. In addition, the National Cancer Research Institute in the United Kingdom is facilitating a Phase 3 trial of Acelarin for the treatment of patients with pancreatic cancer. The disease control rates referred to above include complete responses, partial responses and stable disease, measured by radiographic assessment to determine changes in tumor size, and evaluated using the standard scoring system known as Response Evaluation Criteria in Solid Tumors, or RECIST. The disease control rates are based on investigator assessment of tumor response in a limited number of patients and may not be predictive of or consistent with the results of later trials.

NUC-3373, our second product candidate, is a ProTide transformation of the active anti-cancer metabolite of 5-fluorouracil, or 5-FU, which we believe has the potential to replace 5-FU as the standard of care in the treatment of a wide range of cancers. In preclinical studies, we observed that NUC-3373 overcame the key resistance mechanisms associated with 5-FU and generated intracellular levels of active anti-cancer metabolite over 300 times higher than that of 5-FU. NUC-3373 is currently being evaluated in a Phase 1 clinical trial of patients with advanced solid tumors and we expect to report interim data from this trial in the second half of 2017. Contingent on regulatory guidance and other factors, we plan to initiate a number of clinical trials in 2018: a Phase 1b trial of NUC-3373 in patients with colorectal cancer together with other agents routinely used in 5-FU combination regimens; a Phase 3 trial in patients with advanced colorectal cancer; and a Phase 2 trial in patients with advanced breast cancer.

NUC-7738, our third product candidate, is a ProTide transformation of cordycepin, a novel nucleoside analog that has shown potent anti-cancer activity in preclinical studies. We are evaluating NUC-7738 in preclinical studies and we expect to initiate a Phase 1 clinical trial in 2018.

Despite the widespread use of nucleoside analogs, their efficacy is severely limited by cancer cell resistance mechanisms and they are often poorly tolerated. Harnessing the power of phosphoramidate chemistry, we convert nucleoside analogs into activated nucleotide analogs with the addition of a phosphate group, which is protected by specific combinations of aryl, ester and amino acid groupings. By adding and protecting this phosphate group, we design our ProTides to avoid or overcome key cancer resistance mechanisms in the uptake, activation and breakdown of nucleoside analogs. As a result, we believe our ProTides have the potential to generate hundreds of times higher concentrations of the active anti-cancer metabolites inside tumor cells, potentially making our ProTides more effective than the current standards of care. Because our ProTides resist breakdown, and are thus more stable, we believe they are also able to reduce or eliminate the generation of toxic byproducts that can result from the breakdown of nucleoside analogs like gemcitabine and 5-FU.

Our proprietary ProTide technology was invented in the Cardiff University laboratory of our late Chief Scientific Officer, Professor Christopher McGuigan, who conceived of, and filed the original composition of matter patents for our initial ProTides. The unique feature of his discovery was the specific combination of aryl, ester and amino acid groupings that protect the activated, or phosphorylated, nucleoside analog. This phosphoramidate chemistry approach is the key to the ProTide technology. Every ProTide grouping is distinct, and Professor McGuigan and his team synthesized and tested thousands of compounds in order to identify the optimal ProTide grouping for each underlying nucleoside analog.

We have licensed what we believe to be the foundational patent estate for the application of phosphoramidate chemistry in oncology. We have granted patents in key markets, including the United States, Europe and Japan, protecting the composition of matter of Acelarin, NUC-3373 and other of our product candidates. Professor McGuigan's work preceded and helped lead to the development of several FDA-approved anti-viral drugs containing nucleotide analogs, including: sofosbuvir, or Sovaldi®, which is also a key component of Harvoni®; and tenofovir alafenamide fumarate, or TAF, which is a key component of Genvoya®, Descovy® and Odefsey®.

We are led by Hugh S. Griffith, our founder and Chief Executive Officer, who brings over 25 years of experience in the biopharmaceutical industry, including at Abbott Laboratories (now AbbVie Inc.) and Parke-Davis Warner Lambert (now Pfizer Inc.). Before founding NuCana, he led the operations of Bioenvision, Inc. from start-up through its acquisition by Genzyme Corporation. While at Bioenvision, he was instrumental in developing and commercializing clofarabine, a nucleoside analog for the treatment of pediatric leukemia. We are backed by leading life sciences investors, including Sofinnova Partners, Sofinnova Ventures, Morningside Group and Scottish Enterprise.

Risk Factors – Risks Related to Development of Our Product Candidates (p. 18)

Initial success in the completed and ongoing early-stage clinical trials may not be indicative of results obtained when these trials are completed or in later stage trials.

Acelarin is currently being evaluated in four clinical trials across numerous solid tumor indications: one Phase 1b trial in combination with cisplatin in patients with biliary cancer, one Phase 1b trial in patients with platinum-sensitive ovarian cancer, one Phase 2 trial in patients with recurrent ovarian cancer, and one multi-year investigator-sponsored Phase 3 trial in patients with pancreatic cancer. While Acelarin has shown high disease control rates and a favorable tolerability profile in early-stage trials, including in two first-in-human dose-ranging Phase 1 trials, we may not see such favorable data in future clinical trials involving Acelarin. Similarly, favorable results obtained from preclinical studies of NUC-3373 and in the ongoing Phase 1 trial in patients with advanced solid tumors may not be replicated in any future clinical trials. ~~Data~~In addition, data generated in these early stage Phase 1 trials are not ~~suitable for~~the basis on which marketing approval by the FDA or a comparable foreign regulatory authority would be sought. Furthermore, the results of our clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for marketing approval. Statistical significance means that an effect is unlikely to have occurred by chance. Clinical trial results are considered statistically significant when the probability of the results occurring by chance, rather than from the efficacy of the product candidate, is sufficiently low. There can be no assurance that any of our clinical trials will ultimately be successful or support further clinical development of any of our product candidates. There is a high failure rate for drugs proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies.