

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion Dated January 23, 2019.

Prospectus Supplement to Prospectus dated October 22, 2018

\$75,000,000

American Depositary Shares



NuCana plc

Representing Ordinary Shares

NuCana plc is offering \$75,000,000 of American Depositary Shares, or ADSs, in this offering. Each ADS will represent one ordinary share, nominal value £0.04 per share.

Our ADSs are listed on The Nasdaq Global Select Market under the symbol "NCNA". On January 22, 2019, the last reported sale price of our ADSs was \$14.63 per ADS.

Investing in our ADSs involves a high degree of risk. See "[Risk Factors](#)" beginning on page S-12.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement. Any representation to the contrary is a criminal offense.

	Per ADS	Total
Public Offering Price	\$	\$
Underwriting Discounts and Commissions(1)	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) We refer you to "Underwriting" beginning on page S-32 for additional information regarding underwriting compensation.

The underwriters have the option to purchase up to an additional \$11,250,000 of ADSs from us at the public offering price less the underwriting discount.

Delivery of the ADSs will be made against payment in New York, New York on or about _____, 2019.

Goldman Sachs & Co. LLC

Jefferies

Cowen

SunTrust Robinson Humphrey

Prospectus Supplement dated _____, 2019

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a “shelf” registration statement on Form F-3 (File No. 333-227624) that we filed with the Securities and Exchange Commission, or SEC, on October 1, 2018, and that was declared effective by the SEC on October 22, 2018. This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of ADSs representing our ordinary shares and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, including the documents incorporated by reference therein, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

You should rely only on the information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein. We have not authorized, and the underwriters have not authorized, anyone to provide you with information that is different. The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of the securities offered hereby. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled “Where You can Find More Information” and “Incorporation of Documents by Reference” in this prospectus supplement and in the sections entitled “Where You can Find More Information” and “Incorporation of Documents by Reference” in the accompanying prospectus, respectively.

We are offering to sell, and seeking offers to buy, ADSs representing our ordinary shares only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the ADSs in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the ADSs and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless otherwise indicated or the context otherwise requires, in this prospectus supplement, “NuCana,” “NuCana plc,” the “Group,” the “company,” “we,” “us” and “our” refer to NuCana plc and its consolidated subsidiaries.

PRESENTATION OF FINANCIAL INFORMATION

We report under International Financial Reporting Standards, or IFRS, as issued by the International Accounting Standards Board, or the IASB. None of the financial statements presented or incorporated by reference in this prospectus supplement were prepared in accordance with generally accepted accounting principles in the United States. We present our financial statements in pounds sterling and in accordance with IFRS as issued by the IASB. All references in this prospectus to "\$" are to U.S. dollars and all references to "£" are to pounds sterling. Unless otherwise indicated, certain U.S. dollar amounts contained in this prospectus supplement have been translated into pounds sterling at the rate on September 28, 2018 of £1.00 to \$1.3041. These translations should not be considered representations that any such amounts have been, could have been or could be converted into pounds sterling at that or any other exchange rate as of that or any other date.

We have made rounding adjustments to some of the figures included in this prospectus supplement. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them.

PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus supplement. We urge you to read this entire prospectus, including the more detailed consolidated financial statements, notes to the consolidated financial statements and other information incorporated by reference from our other filings with the SEC. Investing in our securities involves risks. Therefore, carefully consider the risk factors set forth in our most recent filings with the SEC including our Annual Reports on Form 20-F and reports on Form 6-K, as well as other information in this prospectus supplement and the documents incorporated by reference herein or therein, before purchasing our securities. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

Overview

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 three clinical trials across several solid tumor indications, including biliary tract cancer, ovarian 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 and, in October 2018, we initiated a Phase 1b trial of NUC-3373 in patients with advanced colorectal cancer. 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 230 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 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 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 96% disease control rate. Based on these disease control rates and the tolerability profile, we are conducting a Phase 1b trial of Acelarin in patients with locally advanced or metastatic biliary tract cancers to determine its optimal dose in combination with cisplatin. In October 2018, at the European Society for Medical Oncology (ESMO) 2018 Congress, we announced combined results from cohorts 1 and 2 of this trial, also known as the ABC-08 trial, in which Acelarin in combination with cisplatin was observed to continue to achieve approximately a doubling of the response rate expected with the standard of care, gemcitane plus cisplatin. In addition, these results showed the combination was well-tolerated and several patients achieved significant reductions in their tumor volume as well as further tumor shrinkage over time. Based on these and other previously announced interim data, and contingent on

regulatory guidance and other factors, we are planning to open a Phase 3 trial of Acelarin plus cisplatin in patients with biliary tract cancer in 2019. Acelarin is also being evaluated in a Phase 2 trial in patients with platinum-resistant ovarian cancer, for which we expect to report interim data in 2019. 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. In October 2018, we announced that this trial had enrolled 152 out of an expected 328 patients. 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 the 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 for which we reported interim data in September 2017. In this trial, NUC-3373 generated high levels of the active anti-cancer metabolite inside the patients' white blood cells, resulting in complete inhibition of the target enzyme associated with cancer cell growth. The pharmacokinetic profile of NUC-3373 appeared favorable, which supports our belief that NUC-3373 may enhance efficacy, improve safety and provide a more convenient dosing regimen. In October 2018, we reported data from this trial at ESMO 2018 showing that three patients had achieved stable disease after treatment, with progression-free survival, or PFS, lasting more than nine months at September 25, 2018, the time of data cut-off for the poster presentation at ESMO 2018, as well as a continued promising pharmacokinetic and pharmacodynamic, tolerability and dosage-administration profile. Importantly, no patients developed hand-foot syndrome, as of data cut-off which is a debilitating side effect associated with fluoropyrimidine therapy. The results of this trial 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. In October 2018, we also commenced NuTide:302, a Phase 1b trial 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. Contingent on regulatory guidance and other factors, we also plan to initiate in 2019 a Phase 2/3 trial in patients with advanced colorectal 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 expect to open a Phase 1 clinical trial with NUC-7738 in patients with advanced solid tumors in 2019.

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.

Recent Developments

In October 2018, we announced combined results from cohorts 1 and 2 from the ABC-08 trial of Acelarin plus cisplatin in patients with advanced biliary tract cancer. Fourteen patients with advanced biliary tract cancer received Acelarin (625mg/m² or 725mg/m²) and cisplatin (25mg/m²) on days one and eight of a three-week cycle. In the intent-to-treat group of patients, a complete radiological response was achieved in one patient and a partial response in six patients, resulting in an objective response rate of 50%. In the eleven efficacy evaluable patients (defined as those patients who received at least one cycle of therapy), an objective response rate of 64% was achieved. The results showed that the combination of Acelarin and cisplatin was well-tolerated over multiple cycles with no unexpected adverse events, no dose-limiting toxicities, no discontinuations due to Acelarin-associated toxicity and no Grade 4 adverse events. We previously announced, in January 2018, interim data on the first eight patients recruited. In addition to the data showing the combination being well-tolerated, a response rate of 50% was achieved in those patients, including one complete response and three partial responses.

Previously the same investigators had conducted the ABC-02 clinical trial in a similar patient population comparing single agent gemcitabine (1000mg/m²) to the combination of gemcitabine (1000mg/m²) plus cisplatin (25mg/m²) and established that the combination achieved a higher response rate and improved overall survival duration. A comparison of the response rate interim data from the ABC-08 trial described above and the response rate data from the earlier ABC-02 trial is as follows: complete response of 7% (1/14) in ABC-08 trial v. 0.6% (1/161) in ABC-02 trial; partial

response of 43% (6/14) in ABC-08 trial v. 25% (41/161) in ABC-02 trial; and objective response rate of 50% (7/14) in ABC-08 trial v. 26% (42/161) in ABC-02 trial. While the ABC-08 trial was conducted by the same investigators that conducted the earlier ABC-02 trial in a similar patient population, the ABC-08 trial has many fewer patients than did the ABC-02 trial, which enrolled 410 patients.

Based on these interim data, and contingent on regulatory guidance and other factors, we are planning to open a Phase 3 trial of Acelarin plus cisplatin in patients with biliary tract cancer in 2019. We are currently in discussions with the FDA regarding the optimal design of this Phase 3 trial.

In addition, in October at ESMO 2018, we announced additional data from a Phase 1 clinical trial of NUC-3373 in patients with advanced solid tumors. As of data cut-off, 36 patients, all with metastatic cancer, have been enrolled in the trial, 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 125mg/m² to 1,500mg/m² 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 1,500mg/m² to 1,875mg/m². Evidence of durable anti-cancer activity has been noted, with three patients achieving stable disease after treatment, with PFS lasting more than nine months at September 25, 2018, the time of data cut-off for the poster presentation at ESMO 2018. Both dosing regimens were observed to be well tolerated with no unexpected adverse events or accumulative toxicity. Importantly, no patients developed hand-foot syndrome as of data cut-off. In addition, NUC-3373 had 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 trial 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.

The data from both the ABC-08 trial and the Phase 1 clinical trial of NUC-3373 are interim and both trials are still ongoing. Interim data are not necessarily predictive of final results and may change as the data are further examined, more patient data become available and the final clinical study report is prepared and issued. As a result, interim data should be viewed with caution until the final data are available. Initial success with either interim or final data in early-stage clinical trials may not be indicative of results obtained in later-stage trials, and 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. We plan to design our later stage trials to establish the statistical significance of the efficacy of our ProTides.

Financial Update

As of December 31, 2018, we had cash and cash equivalents of approximately £77.0 million. The estimated cash and cash equivalents as of December 31, 2018 are preliminary and may change, were prepared by management and are based on the most current information available to management as of the date of this prospectus supplement, and are subject to completion by management of the financial statements as of and for the year ended December 31, 2018, including completion of the review procedures, final adjustments and other developments that may arise between now and the time the financial results for this period are finalized. As a result, there can be no assurance that our cash and cash equivalents as of December 31, 2018 will not differ from these estimates and any such changes could be material. The preliminary cash and cash equivalents data included in this prospectus

supplement has been prepared by, and is the responsibility of, our management. Ernst & Young LLP has not audited, reviewed, compiled, or applied agreed-upon procedures with respect to the preliminary financial data. Accordingly, Ernst & Young LLP does not express an opinion or any other form of assurance with respect thereto. Complete annual results will be included in our Annual Report on Form 20-F for the year ended December 31, 2018, which is not expected to be filed until after this offering is completed.

Our Strategy

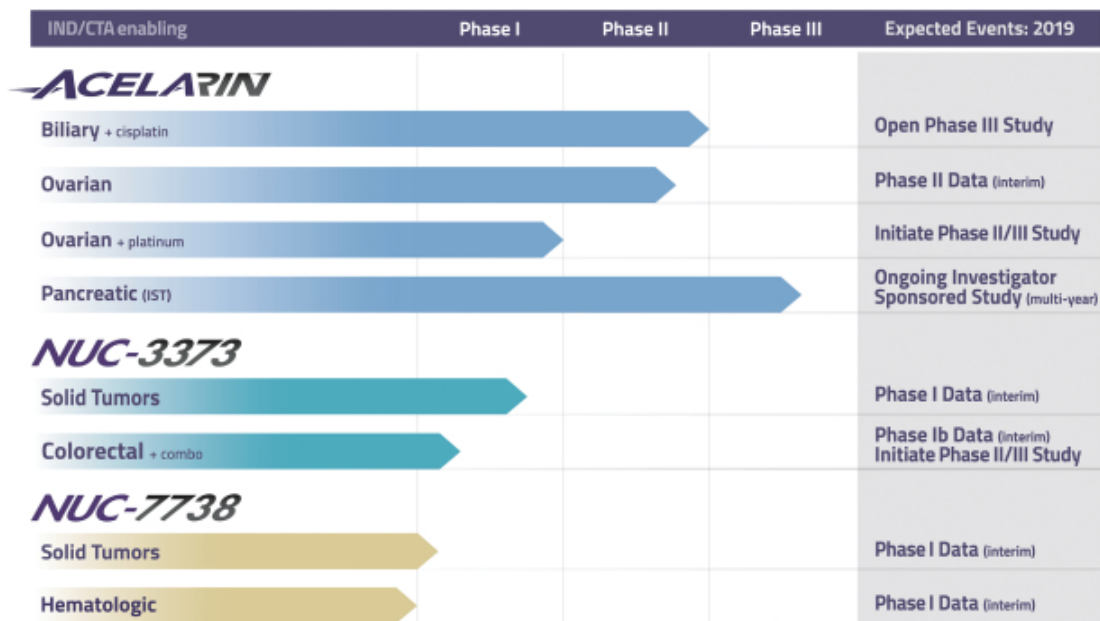
Our goal is to transform standards of care and improve survival for patients across a wide range of cancer indications. Our strategy includes the following key components:

- **Rapidly develop Acelarin as a first-in-class nucleotide analog for the treatment of patients with cancer.** We believe that Acelarin has the potential to replace the core chemotherapy component of treatment regimens for patients with various cancers, including:
 - *Biliary tract cancer.* We reported interim data from a Phase 1b trial of Acelarin in combination with cisplatin in January 2018 and in October 2018. Contingent on regulatory guidance and other factors, we plan to open a Phase 3 trial of Acelarin in combination with cisplatin as a first-line treatment of patients with advanced biliary tract cancer in 2019.
 - *Ovarian cancer.* We expect to report interim data from our ongoing PRO-105 Phase 2 trial of Acelarin in patients with platinum-resistant ovarian cancer in 2019. Contingent on regulatory guidance and other factors, we are evaluating the initiation of a Phase 2/3 trial of Acelarin in combination with a platinum agent in 2019.
 - *Pancreatic cancer.* The National Cancer Research Institute in the United Kingdom is conducting a Phase 3 trial of Acelarin as a first-line treatment compared to gemcitabine. In October 2018, we reported that 152 patients had been enrolled in this trial.
- **Rapidly develop NUC-3373 to replace 5-FU as the standard of care for the treatment of patients with various cancers.**
 - *Advanced solid tumors.* In October 2018, we reported data from a Phase 1 trial of NUC-3373 in patients with advanced solid tumors. We expect this trial to continue, with the goal of establishing the optimal dose and dosing schedule of NUC-3373 in patients with advanced solid tumors in 2019.
 - *Colorectal cancer.* In October 2018, we commenced NuTide:302, a Phase 1b trial 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. We expect to report interim data from this trial in 2019. Contingent on regulatory guidance and other factors, we intend to initiate a Phase 2/3 trial of NUC-3373 in combination with other agents in 2019.
- **Rapidly advance NUC-7738 into clinical trials.** We expect to open a Phase 1 trial with NUC-7738, a ProTide based on a novel nucleoside analog, for patients with advanced solid tumors in 2019.
- **Leverage our proprietary ProTide technology platform to develop additional product candidates.** We are pursuing both the transformation of well-established and widely used nucleoside analogs as well as novel nucleoside analogs, which we believe have the potential to address additional areas of unmet medical need in oncology.

- Continue to strengthen our intellectual property position.** We own or have exclusive rights to the core technologies underlying our ProTide technology platform. 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. We intend to further expand and enhance our intellectual property position. We also have been granted or allowed patent protection in key markets for the proposed commercial formulation of Acelarin and for uses of Acelarin in targeting cancer. Our patent portfolio has grown substantially in the past year and we are actively evaluating new intellectual property opportunities as they arise, with the intention of further expanding our intellectual property position.
- Build a focused commercial organization.** We have worldwide rights to all product candidates that we are developing. We believe that many of the cancers we are initially targeting with our ProTides can be addressed by a focused sales and marketing team. We plan to commercialize any product candidates for which we receive regulatory marketing approval using a specialized sales force in the United States and Europe.

Our Pipeline

We take a scientifically driven approach to designing our ProTides, which we believe have the potential to result in highly efficacious cancer therapies with improved tolerability. Our pipeline of product candidates is summarized below.



Intellectual Property

We actively seek to protect the intellectual property and proprietary technology that we believe is important to our business, including seeking, maintaining, enforcing and defending patent rights for our therapeutics and processes, whether developed internally or licensed from third parties. Our success

will depend on our ability to obtain and maintain patent and other protection including data/market exclusivity for our product candidates and platform technology, preserve the confidentiality of our know-how and operate without infringing the valid and enforceable patents and proprietary rights of third parties. For a discussion of certain risks, uncertainties and other factors we face, any of which could cause our actual results to differ materially, see "Item 3.D. - Risk Factors — Risks Related to Our Intellectual Property" in our Annual Report on Form 20-F for the year ended December 31, 2017, filed with the Securities and Exchange Commission, or the SEC, on March 22, 2018, as well as any subsequent filings we may make with the SEC.

Our policy is to seek to protect our proprietary position, generally by filing an initial priority filing at the U.K. Intellectual Property Office. This is followed by the filing of a patent application under the Patent Co-operation Treaty claiming priority from the initial application(s) and then filing applications for patent grant in territories including, for example, the United States, Europe and Japan. In each case, we determine the strategy and territories required after discussion with our patent attorneys so that we obtain relevant coverage in territories that are commercially important to us and our product candidates. We additionally rely on data exclusivity, market exclusivity and patent term extensions when available. We also rely on trade secrets and know-how relating to our underlying platform technology and product candidates. Prior to making any decision on filing any patent application, we consider with our patent attorneys whether patent protection is the most sensible strategy for protecting the invention concerned or whether the invention should be maintained as confidential.

As of January 18, 2019, we owned 349 granted patents (of which nine are U.S.-issued patents) and 325 pending patent applications (of which 17 are U.S. pending patent applications). Commercially or strategically important non-U.S. jurisdictions in which we hold issued or pending patent applications include: Australia, Canada, China, Eurasia (in the form of a regional patent), Europe (in the form of a regional patent), Hong Kong, India, Israel, Japan, South Korea, Malaysia, Mexico, Philippines, Singapore and South Africa. Not included in the patent count is one U.S. patent that is currently in reissue proceedings which were initiated by us for purposes of narrowing the claims covered by such patent.

Acelarin

We own 90 granted patents covering the composition of matter of our Acelarin product candidate. The patent claims are directed to the Acelarin product candidate and to a genus around that candidate. Acelarin was originally formed as a mixture of two diastereoisomers, both of which are biologically active, and each of these composition of matter patents cover Acelarin both as a single diastereoisomer and as a mixture of diastereoisomers. The patents have been granted in major territories, including Europe and Japan. These granted patents are expected to expire in 2024, excluding any patent term adjustments and any patent term extensions. As disclosed above, there is also one patent in the United States for Acelarin that is currently under reissue.

Additionally, we own 45 granted patents, as well as 33 pending patent applications, directed towards Acelarin in single diastereoisomer form. The more soluble single diastereoisomer is being used for clinical development and is the form which we expect to use in our planned upcoming clinical trials. A patent claiming the more soluble single diastereoisomer of Acelarin has been granted in Europe and the United States, and corresponding patent applications are pending in other major territories, including Japan. These granted patents and patents arising from the pending applications, if issued, are expected to expire in 2033 and 2035, excluding any patent term adjustments and any patent term extensions.

We own granted patents and patent applications covering formulations of Acelarin (including those used in the clinical trials), methods of making Acelarin (including as a single diastereoisomer), and specific uses of Acelarin, including the use of Acelarin in combination with carboplatin and Acelarin in combination with cisplatin. Patents claiming the clinical formulation of Acelarin have been granted in Europe and the United States. Patents arising from these pending applications have been filed in all major territories, including the United States, Europe and Japan and are expected to expire in 2035, 2036 and 2038 excluding any patent term adjustments and any patent term extensions.

NUC-3373

We own 57 granted patents and seven pending applications covering the composition of matter of NUC-3373, a genus around NUC-3373 and specific uses of NUC-3373. Those patents were granted in major territories, including the United States, Europe and Japan. These granted patents and patents arising from the pending applications, if issued, are expected to expire in 2032, excluding any patent term adjustments and any patent term extensions.

We own patent applications covering formulations of NUC-3373 (including those used in the clinical trials), methods of making NUC-3373, and specific uses of NUC-3373. These patents and patents arising from these pending applications are expected to expire in 2036, 2037 and 2038 excluding any patent term adjustments and any patent term extensions.

NUC-7738

We own 21 pending applications covering the composition of matter of NUC-7738, a genus around NUC-7738 and specific uses of NUC-7738. The patent applications are pending in major territories, including the United States, Europe and Japan. Patents arising from these pending applications, if issued, are expected to expire in 2035 excluding any patent term adjustments and any patent term extensions.

We own patent applications covering formulations of NUC-7738 and methods of making NUC-7738. Patents arising from these pending applications are expected to expire in 2036 and 2038 excluding any patent term adjustments and any patent term extensions.

Laws and Regulations Regarding Patent Terms

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent term may be shortened if a patent is terminally disclaimed over another patent or as a result of delays in patent prosecution by the patentee. A patent's term may be lengthened by a patent term adjustment, which compensates a patentee for administrative delays by the USPTO in granting a patent. The patent term of a European patent is 20 years from its effective filing date, which, unlike in the United States, is not subject to patent term adjustments in the same way as U.S. patents.

The term of a patent that covers an FDA-approved drug or biologic may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug or biologic is under regulatory review. Patent extension cannot extend the remaining term of a patent

beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other jurisdictions to extend the term of a patent that covers an approved drug, for example Supplementary Protection Certificates. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We anticipate that some of our issued patents may be eligible for patent term extensions but such extensions may not be available and therefore our commercial monopoly may be restricted.

Additional Information

For additional information related to our business and operations, please refer to the reports incorporated herein by reference, including the Annual Report on Form 20-F of NuCana plc for the year ended December 31, 2017 and the Reports on Form 6-K furnished on October 1, 2018, October 22, 2018 and November 28, 2018, as described under the caption "Incorporation of Documents by Reference" on page S-39 of this prospectus supplement.

Our Corporate Information

NuCana was incorporated under the laws of England and Wales in 1997 under the name Biomed (UK) Limited, and commenced operations in 2008. On April 28, 2008, we changed our name to NuCana BioMed Limited. On August 29, 2017, we re-registered as a public limited company and changed our name to NuCana plc. ADSs representing our ordinary shares were admitted to trading on The Nasdaq Global Select Market on September 28, 2017. Our ADSs are traded under the symbol "NCNA."

Our principal executive offices are located at 3 Lochside Way, Edinburgh, EH12 9DT, United Kingdom. Our telephone number at this address is +44 (0)131 357 1111.

We maintain a website at www.nucana.com to which we regularly post copies of our press releases as well as additional information about us. The information contained on, or that can be accessed through, our website is not a part of this prospectus supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

We use our registered trademarks, NuCana® and Acelarin®, and our trademark, ProTides™, in this prospectus supplement. This prospectus supplement also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus supplement appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

THE OFFERING

Issuer	NuCana plc
ADSs offered by us	ADSs having an aggregate offering price of up to \$75.0 million.
Option to Purchase Additional ADSs	We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to an additional \$11.25 million of ADSs from us.
Ordinary shares to be outstanding immediately after this offering	37,352,910 ordinary shares (or 38,121,878 ordinary shares if the underwriters exercise in full their option to purchase additional ADSs) based on an assumed offering price of \$14.63 per ADS, the last reported sale price of our ADSs on January 22, 2019 on The Nasdaq Global Select Market.
The ADSs	<p>Each ADS represents one ordinary share, nominal value £0.04 per share. The offered ADSs may be evidenced by American Depositary Receipts, or ADRs.</p> <p>The depositary or its custodian, or a nominee of either, will hold the ordinary shares underlying your ADSs. As an ADS holder you will not be treated as one of our shareholders and you will not have shareholder rights. You will have rights as provided in the deposit agreement. You may cancel your ADSs and withdraw the underlying ordinary shares as provided in the deposit agreement. Under certain limited circumstances, we may amend or terminate the deposit agreement without your consent. If you continue to hold your ADSs following an amendment, you agree to be bound by the terms of the deposit agreement then in effect.</p> <p>To better understand the terms of the ADSs, you should carefully read the section in the accompanying prospectus titled "Description of American Depositary Shares". You should also read the deposit agreement, which is an exhibit to the registration statement that includes this prospectus.</p>
Depository	Citibank, N.A.
Custodian	Citibank, N.A. (London)

Use of proceeds

We currently intend to use the net proceeds of this offering to fund (i) the development of Acelarin for biliary tract, ovarian and pancreatic cancer, (ii) the development of NUC-3373 for colorectal cancer and other solid tumors, (iii) the development of NUC-7738 for solid tumors and hematological malignancies, and (iv) for other research and development activities, working capital and general corporate purposes. See the section titled "Use of Proceeds" on page S-19 of this prospectus supplement.

Risk factors

See "Risk Factors" beginning on page S-12 of this prospectus supplement and the other information included in, or incorporated by reference into, this prospectus supplement for a discussion of certain factors you should carefully consider before deciding to invest in our ADSs.

Nasdaq Global Select Market Symbol

"NCNA"

The number of our ordinary shares to be outstanding immediately after this offering is 37,352,910, which is based on 32,226,458 ordinary shares outstanding as of December 31, 2018. The number of shares outstanding excludes:

- 4,406,252 ordinary shares issuable upon exercise of outstanding options under our equity plans as of December 31, 2018 at a weighted average exercise price of £1.90 per share; and
- 3,442,847 ordinary shares authorized for issuance pursuant to future awards under our equity incentive plans.

To the extent that outstanding options are exercised, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities may result in further dilution to our shareholders.

RISK FACTORS

An investment in our ADSs involves a high degree of risk. Before deciding whether to invest in our ADSs, you should consider carefully the risks described below and discussed under the sections captioned "Risk Factors" contained in our most recent Annual Report on Form 20-F, which is incorporated by reference herein in their entirety, together with other information in this prospectus supplement, the information and documents incorporated by reference in this prospectus supplement, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our ADSs to decline, resulting in a loss of all or part of your investment.

Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our securities could decline due to any of these risks, and you may lose part or all of your investment. This prospectus supplement and the incorporated documents also contain forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks mentioned below. Forward-looking statements included in this prospectus supplement are based on information available to us on the date hereof, and all forward-looking statements in documents incorporated by reference are based on information available to us as of the date of such documents. We disclaim any intent to update any forward-looking statements.

Risks Related to This Offering

Our management will have broad discretion over the use of the net proceeds from this offering, and you may not agree with how we use the proceeds and the proceeds may not be invested successfully.

Our management will have broad discretion as to the use of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of this offering. Accordingly, you are relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds will be used appropriately. It is possible that the proceeds will be invested in a way that does not yield a favorable, or any, return for us.

Purchasers will experience immediate dilution in the book value per share of the ADSs purchased in the offering.

We expect that the offering price of our ADSs will be substantially higher than the net tangible book value per ADS, and per each underlying ordinary share, prior to this offering. After giving effect to the sale of ADSs in the aggregate amount of \$75.0 million at an assumed offering price of \$14.63 per ADS, the last reported sale price of our ADSs on January 22, 2019 on The Nasdaq Global Select Market, and after deducting estimated underwriting discounts and commissions and estimated offering expenses, our as adjusted net tangible book value as of September 30, 2018 would have been £136.0 million, or £3.65 per ordinary share, equivalent to \$4.76 per ordinary share and \$4.76 per ADS. This represents an immediate increase in net tangible book value of \$1.43 per ordinary share and ADS to our existing shareholders and an immediate dilution in as adjusted net tangible book value of \$9.87 per ordinary share and ADS to purchasers of ADSs in this offering.

In addition to this offering, subject to market conditions and other factors, we may pursue additional equity financings in the future, including future public offerings or future private placements of equity securities or securities convertible into or exchangeable for equity securities. Further, the

exercise of outstanding options could result in further dilution to investors and any additional ordinary shares or ADSs issued in connection with acquisitions, should we choose to pursue any, will result in dilution to investors. In addition, the market price of our ADS could fall as a result of resales of any of these ADSs due to an increased number of ADSs available for sale in the market.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional of our ADSs or other securities convertible into or exchangeable for our ADSs. We cannot assure you that we will be able to sell ADSs or other securities in any other offering at a price ADS or per share that is equal to or greater than the price per ADS paid by investors in this offering, and investors purchasing ADSs or other securities in the future could have rights superior to existing shareholders. The price per ADS at which we sell additional ADSs or other securities convertible into or exchangeable for our ADSs in future transactions may be higher or lower than the price per ADS in this offering.

We may be unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments or benefit from favorable United Kingdom tax legislation.

As a United Kingdom resident company, we are subject to U.K. corporate taxation. We have generated losses since inception. As of December 31, 2017, we had cumulative carry forward tax losses of £12.4 million. Subject to any relevant restrictions (including changes introduced in the Finance (no. 2) Act 2017 that, broadly, restrict the amount of carried forward losses that can be utilized to 50% of group profits arising in a particular tax year above £5.0 million), we expect these to be available to carry forward and offset against future operating profits. As a company that carries out extensive research and development activities, we benefit from the United Kingdom research and development tax credit regime for small and medium-sized companies, whereby we are able to surrender the trading losses that arise from our qualifying research and development activities for a payable tax credit of up to 33.35% of eligible research and development expenditures. Qualifying expenditures largely comprise employment costs for research staff, consumables and subcontract costs incurred as part of research projects. Certain subcontracted qualifying research expenditures are eligible for a cash rebate of up to 21.68%. The majority of our pipeline research, clinical trials management and manufacturing development activities are eligible for inclusion within these tax credit cash rebate claims. On October 29, 2018 the U.K. Government proposed that from April 1, 2020 the amount of payable credit that a qualifying loss-making SME business can receive through R&D relief in any one year will be capped at three times the company's total PAYE and NICs liability for that year. We may not be able to continue to claim payable research and development tax credits in the future because we may no longer qualify as a small or medium-sized company.

We may benefit in the future from the United Kingdom's "patent box" regime, which allows certain profits attributable to revenues from patented products to be taxed at an effective rate of 10%. As we have many different patents covering our products, future upfront fees, milestone fees, product revenues and royalties could be taxed at this favorably low tax rate. When taken in combination with the enhanced relief available on our research and development expenditures, we expect a long-term lower rate of corporation tax to apply to us. If, however, there are unexpected adverse changes to the United Kingdom research and development tax credit regime or the "patent box" regime, or for any reason we are unable to qualify for such advantageous tax legislation, or we are unable to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments then our business, results of operations and financial condition may be adversely affected.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, or may apply existing rules in an arbitrary or unforeseen manner, resulting in unanticipated costs, taxes or non-realization of expected benefits.

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, Her Majesty's Revenue & Customs, or HMRC, the U.S. Internal Revenue Service or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including methodologies for valuing developed technology and amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions.

A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, for example where there has been a technical violation of contradictory laws and regulations that are relatively new and have not been subject to extensive review or interpretation, in which case we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

Changes and uncertainties in the tax system in the countries in which we have operations, could materially adversely affect our financial condition and results of operations, and reduce net returns to our shareholders.

We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices in jurisdictions in which we operate, could increase the estimated tax liability that we have expensed to date and paid or accrued on our balance sheets, and otherwise affect our financial position, future results of operations, cash flows in a particular period and overall or effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders and increase the complexity, burden and cost of tax compliance.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the documents incorporated by reference in this prospectus supplement include forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Words such as, but not limited to, “believe,” “expect,” “anticipate,” “estimate,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “targets,” “likely,” “will,” “would,” “could,” “should,” “continue,” and similar expressions or phrases, or the negative of those expressions or phrases, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus supplement and incorporated by reference in this prospectus supplement, we caution you that these statements are based on our projections of the future that are subject to known and unknown risks and uncertainties and other factors that may cause our actual results, level of activity, performance or achievements expressed or implied by these forward-looking statements, to differ. The sections in our periodic reports, including our Annual Report on Form 20-F for the fiscal year ended December 31, 2017, titled “Business,” “Risk Factors,” and “Operating and Financial Review and Prospects,” as well as other sections in this prospectus supplement and the documents or reports incorporated by reference in this prospectus supplement, discuss some of the factors that could contribute to these differences. These forward-looking statements include, among other things, statements about:

- the development of Acelarin, NUC-3373 and NUC-7738, including statements regarding the expected initiation, timing, progress and availability of data from our clinical trials;
- the potential attributes and benefit of our ProTides and their competitive positions;
- our ability to successfully commercialize our ProTides, if approved;
- our estimates regarding expenses, capital requirements and our need for additional financing;
- our ability to acquire or in-license new product candidates;
- potential collaborations; and
- the duration of our patent portfolio.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important cautionary statements in this prospectus supplement or in the documents incorporated by reference in this prospectus supplement, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. For a summary of such factors, please refer to the section titled “Risk Factors” in this prospectus supplement, as updated and supplemented by the discussion of risks and uncertainties under “Risk Factors” contained in any supplements to this prospectus supplement and in our most recent Annual Report on Form 20-F, as revised or supplemented by our subsequent periodic reports filed under the Exchange Act, as well as any amendments thereto, as filed with the SEC and which are incorporated herein by reference. The information contained in this document is believed to be current as of the date of this document. We do not intend to update any of the forward-looking statements after the date of this document to conform these statements to actual results or to changes in our expectations, except as required by law.

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In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this prospectus supplement or in any document incorporated herein by reference might not occur. Investors are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this prospectus supplement or the date of the document incorporated by reference in this prospectus supplement. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to us or to any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

CAPITALIZATION

The following table presents our cash and cash equivalents and total capitalization as of September 30, 2018 derived from our unaudited condensed consolidated financial statements incorporated by reference into this prospectus supplement on:

- an actual basis; and
- an as adjusted basis to give effect to the sale by us of \$75.0 million of ADSs in this offering at an assumed public offering price of \$14.63 per ADS (the last reported sale price this offering at our ADSs on Nasdaq on January 22, 2019), after deduction of the estimated underwriting discounts and commissions and estimated offering expenses payable by us in connection with this offering and assuming no exercise of the option to purchase additional ADSs by the underwriters.

You should read the financial data in the following table in conjunction with our unaudited condensed consolidated financial statements, audited consolidated financial statements and related notes incorporated by reference into this prospectus supplement.

	As of September 30, 2018	
	Actual (unaudited)	As Adjusted(1)
	(in thousands)	
Cash and cash equivalents	£ 78,351	£ 132,231
Total equity attributable to equity holders:		
Ordinary shares, nominal value £0.04 per share, 32,185,208 shares issued and outstanding, actual; and 37,311,660 shares issued and outstanding, as adjusted	£ 1,287	£ 1,492
Share premium	79,403	133,078
Other reserves	59,431	59,431
Accumulated deficit	(55,247)	(55,247)
Total equity attributable to equity holders	84,874	138,754
Total capitalization	£ 84,874	£ 138,754

- (1) Each \$1.00 increase or decrease in the assumed public offering price of \$14.63 per ADS, which is based on the last reported sale price of our ADSs on the Nasdaq Global Select Market on January 22, 2019, would increase or decrease the as adjusted amount of each of cash and cash equivalents, total equity and total capitalization by £3.7 million, assuming the number of ADSs offered by us, as set forth on the cover page of this prospectus supplement, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase or decrease of \$10.0 million in the amount of ADSs offered by us, as set forth on the cover page of this prospectus supplement, would increase or decrease the as adjusted amount of each of cash and cash equivalents, total equity and total capitalization by £7.2 million, assuming no change in the assumed public offering price per ADS and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The number of our ordinary shares to be outstanding immediately after this offering is based on 32,185,208 ordinary shares outstanding as of September 30, 2018 and excludes:

- 4,503,752 ordinary shares issuable upon exercise of outstanding options under our equity incentive plans as of September 30, 2018 at a weighted average exercise price of £2.03 per share;

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- 41,250 ordinary shares issued upon exercise of options under our equity incentive plans subsequent to September 30, 2018 at a weighted average exercise price of £0.61 per share; and
- 3,386,597 ordinary shares authorized for issuance pursuant to future awards under our equity incentive plans.

USE OF PROCEEDS

We estimate that we will receive total estimated net proceeds from this offering of approximately \$70.3 million, based on the assumed offering public offering price of \$14.63 per ADS (the last reported sale price of our ADSs on Nasdaq on January 22, 2019), or approximately \$80.8 million if the underwriters exercise their option to purchase additional ADSs in full, in each case after deducting estimated underwriting discounts and commissions and estimated expenses of the offering payable by us. We intend to use any net proceeds from the sale of securities under this prospectus supplement to fund (i) the development of Acelarin for biliary tract, ovarian and pancreatic cancer, (ii) the development of NUC-3373 for colorectal cancer and other solid tumors, (iii) the development of NUC-7738 for solid tumors and hematological malignancies, and (iv) for other research and development activities, working capital and general corporate purposes. The amounts and timing of our actual expenditures will depend on numerous factors, including the progress of our clinical trials and other development efforts and other factors described under "Risk Factors" in this prospectus supplement and the documents incorporated by reference herein, as well as the amount of cash used in our operations. As a result, our management will have broad discretion to allocate the net proceeds, if any, we receive in connection with securities offered pursuant to this prospectus supplement for any purpose.

DILUTION

If you invest in our ADSs, your interest will be diluted to the extent of the difference between the assumed public offering price per ADS and the net tangible book value per ADS immediately after this offering. As of September 30, 2018, our net tangible book value was £82.2 million, or £2.55 per ordinary share, equivalent to \$3.33 per ordinary share and \$3.33 per ADS. Net tangible book value per ordinary share is equal to our total assets minus intangible assets and total liabilities, divided by 32,185,208, the total number of ordinary shares outstanding as of September 30, 2018.

After giving effect to the sale of our ADSs in the aggregate amount of \$75.0 million at an assumed offering price of \$14.63 per ADS, the last reported sale price of our ADSs on The Nasdaq Global Select Market on January 22, 2019, and after deducting estimated commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2018 would have been £136.0 million, or £3.65 per ordinary share, equivalent to \$4.76 per ordinary share and \$4.76 per ADS. This represents an immediate increase in net tangible book value of \$1.43 per ordinary share and ADS to our existing shareholders and an immediate dilution in net tangible book value of \$9.87 per ordinary share and ADS to new investors in this offering. The following table presents this dilution to new investors purchasing ADSs in the offering:

Assumed public offering price per ADS		\$14.63
Net tangible book value per ADS as of September 30, 2018	\$3.33	
Increase in net tangible book value per ADS attributable to the offering	<u>1.43</u>	
As adjusted net tangible book value per ADS after giving effect to the offering		4.76
Dilution per ADS to new investors participating in the offering		<u>\$ 9.87</u>

If the underwriters exercise their option to purchase 768,968 additional ADSs in full, the as adjusted net tangible book value per ADS after the offering would be \$4.94, the increase in net tangible book value per ordinary share and ADS to existing shareholders would be \$1.61 and the immediate dilution in net tangible book value per ordinary share and ADS to new investors in this offering would be \$9.69.

Each \$1.00 increase or decrease in the assumed public offering price of \$14.63 per ADS, the last reported sale price of the ADSs on the Nasdaq Global Select Market on January 22, 2019, would increase or decrease the as adjusted net tangible book value after this offering by \$0.13 per ordinary share and ADS and the dilution to new investors in this offering by \$0.87 per ADS, assuming the number of ADSs offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase of \$10.0 million in the amount of ADSs offered by us, as set forth on the cover page of this prospectus, would increase the as adjusted net tangible book value after this offering by \$0.16 per ordinary share and ADS and decrease the dilution to new investors in this offering by \$0.16 per ADS, assuming no change in the assumed public offering price per ADS and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. A decrease of \$10.0 million in the amount of ADSs offered by us, as set forth on the cover page of this prospectus, would decrease the as adjusted net tangible book value after this offering by \$0.17 per ordinary share and ADS and increase the dilution to new investors in this offering by \$0.17 per ADS, assuming no change in the assumed public offering price per ADS and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The share information excludes:

- 4,503,752 ordinary shares issuable upon exercise of outstanding options under our equity incentive plans as of September 30, 2018 at a weighted average exercise price of £2.03 per share;

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- 41,250 ordinary shares issued upon exercise of options under our equity incentive plans subsequent to September 30, 2018 at a weighted average exercise price of £0.61 per share; and
- 3,386,597 ordinary shares authorized for issuance pursuant to future awards under our equity incentive plans.

To the extent that outstanding options are exercised, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities may result in further dilution to our shareholders.

TAXATION

Material U.S. Federal Income Tax Considerations

The following discussion describes the material U.S. federal income tax consequences to U.S. Holders (as defined below) under present law of the purchase, ownership and disposition of the ADSs. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended or the Code for purposes of this discussion, in effect as of the date of this Annual Report and on U.S. Treasury regulations in effect or, in some cases, proposed, as of the date of this Annual Report, as well as judicial and administrative interpretations thereof available on or before such date. All of the foregoing authorities are subject to change, which change could apply retroactively and could affect the tax consequences described below.

This discussion applies only to U.S. Holders that hold the ADSs as capital assets for U.S. federal income tax purposes. It does not purport to be a comprehensive description of all tax considerations that may be relevant to a decision to purchase the ADSs by any particular investor. In particular, this discussion does not address tax considerations applicable to a U.S. Holder that may be subject to special tax rules, including, without limitation, a dealer in securities or currencies, a trader in securities that elects to use a mark-to-market method of accounting for securities holdings, banks, thrifts, or other financial institutions, an insurance company, a tax-exempt organization, a person that holds the ADSs as part of a hedge, straddle or conversion transaction for tax purposes, a person whose functional currency for tax purposes is not the U.S. dollar, certain former citizens or residents of the United States or a person that owns directly, indirectly or constructively 10% or more of the company's voting shares or value. Moreover, this description does not address the U.S. federal estate, gift, or alternative minimum tax consequences, or any state, local or non-U.S. tax consequences, of the acquisition, ownership and disposition of the ADSs. In addition, the discussion does not address tax consequences to an entity or arrangement treated as a partnership for U.S. federal income tax purposes that holds the ADSs, or a partner in such partnership. The U.S. federal income tax treatment of each partner of such partnership generally will depend upon the status of the partner and the activities of the partnership. Prospective purchasers that are partners in a partnership holding the ADSs are urged to consult their own tax advisers.

The discussion below of the U.S. federal income tax consequences to "U.S. Holders" will apply to an investor that is a beneficial owner of ADSs and that is, for U.S. federal income tax purposes,

- an individual who is a citizen or resident of the United States;
- a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) organized under the laws of the United States, any state therein or the District of Columbia;
- an estate whose income is subject to U.S. federal income taxation regardless of its source; or
- a trust that (i) is subject to the primary supervision of a court within the United States and subject to the control of one or more U.S. persons for all substantial decisions or (ii) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

For U.S. federal income tax purposes, a beneficial owner of ADSs generally will be treated as the owner of the underlying ordinary shares represented by such ADSs. Accordingly, deposits or withdrawals of the underlying ordinary shares for ADSs generally will not be subject to U.S. federal income tax. The discussion below assumes that the representations contained in the deposit agreement are true and that the obligations in the deposit agreement and any related agreement will be complied with in accordance with their terms. U.S. Treasury has expressed concerns that parties to whom ADSs are released before shares are delivered to the depository or intermediaries in the chain of ownership between the U.S. Holder of an ADS and the issuer of the security underlying the ADS

may be taking actions that are inconsistent with the claiming of foreign tax credits by U.S. Holders of ADSs. These actions would also be inconsistent with the claiming of the reduced rate of tax, described below, applicable to dividends received by certain noncorporate U.S. Holders. As a result, the creditability of non-U.S. withholding taxes (if any), and the availability of the reduced tax rate for dividends received by certain non-corporate U.S. Holders, each described below, could be affected by actions taken by such parties or intermediaries. Accordingly, U.S. persons considering an investment in ADSs should consult their own tax advisors as to the particular tax consequences applicable to them relating to the purchase, ownership and disposition of ADSs, including the applicability of U.S. federal, state and local tax laws and non U.S. tax laws.

You are urged to consult your tax advisors about the application of the U.S. federal income tax rules to your particular circumstances as well as the state, local, non-U.S. and other tax consequences of the purchase, ownership and disposition of the ADSs.

Passive Foreign Investment Company Considerations

In general, a corporation organized outside the United States will be classified as a passive foreign investment company, or PFIC, in a particular taxable year if either (i) 75% or more of the corporation's gross income for the taxable year is passive income or (ii) on average at least 50% of the value of the corporation's assets produce passive income or are held for the production of passive income. Passive income for this purpose generally includes, among other things, certain dividends, interest, royalties, rents and gains from commodities and securities transactions and from the sale or exchange of property that gives rise to passive income.

In making this determination, we will be treated as earning our proportionate share of any income and owning our proportionate share of any assets of any corporation in which we hold a 25% or greater interest (by value). Because PFIC status must be determined annually based on tests which are factual in nature, our PFIC status will depend on our income, assets and activities each year, including whether certain research and development tax credits received from the government of the United Kingdom will constitute gross income, and, if they do, whether they will constitute passive income for purposes of the PFIC income test. If we are classified as a PFIC for any taxable year, a U.S. Holder may be able to mitigate some of the resulting adverse U.S. federal income tax consequences described below with respect to owning the ADSs, provided that such U.S. Holder is eligible to make, and validly makes a "mark-to-market" election, described below. In certain circumstances a U.S. Holder can make a "qualified electing fund" election to mitigate some of the adverse tax consequences described with respect to an ownership interest in a PFIC by including in income its share of the PFIC's income on a current basis. However, we do not currently intend to prepare or provide the information that would enable a U.S. Holder to make a qualified electing fund election.

In the event that we are classified as a PFIC in any year in which a U.S. Holder holds the ADSs, and the "mark-to-market" election described below is not made by a taxable U.S. Holder, a special tax regime will apply with respect to such U.S. Holder to both (a) any gain realized on the sale or other disposition of the ADSs and (b) any "excess distribution" by us to such U.S. Holder (generally, such U.S. Holder's ratable portion of distributions received by such U.S. Holder in any year which are greater than 125% of the average annual distribution received by such U.S. Holder in the shorter of the three preceding years or such U.S. Holder's holding period for the ADSs). Any gain recognized by such U.S. Holder on a sale or other disposition (including a pledge) of the ADSs and any excess distribution would be allocated ratably over such U.S. Holder's holding period for the ADSs. The amounts allocated to the taxable year of the sale or other disposition and to any year before we became a PFIC would be taxed as ordinary income. The amount allocated to each other taxable year would be subject to tax at the highest rate in effect for individuals or corporations, as appropriate, for that taxable year, and the interest charge generally applicable to underpayments of tax would be imposed on taxes deemed to

have been payable in for the relevant taxable PFIC years. Classification as a PFIC may also have other adverse tax consequences, including, in the case of U.S. Holders that are individuals, the denial of a step-up in the basis of such U.S. Holder's ADSs at death.

Based on our estimated gross income, the average value of our assets, including goodwill and the nature of our active business, we do not expect to be treated as a PFIC for U.S. income tax purposes for the current taxable year ending December 31, 2019. The determination of PFIC status is based on an annual determination that cannot be made until the close of the taxable year and involves extensive factual and legal investigation. Accordingly, we cannot assure that we will not be treated as a PFIC for our current taxable year or any future taxable year.

Mark-to-Market Election

If we are a PFIC for any taxable year during which a U.S. Holder holds the ADSs, then in lieu of being subject to the special tax regime and interest charge rules discussed above, a U.S. Holder may make an election to include gain on the ADSs as ordinary income under a mark-to-market method, provided that the ADSs are treated as "regularly traded" on a "qualified exchange." In general, the ADSs will be treated as "regularly traded" for a given calendar year if more than a *de minimis* quantity of the ADSs are traded on a qualified exchange on at least 15 days during each calendar quarter of such calendar year. Although the U.S. Internal Revenue Service, or the IRS, has not published any authority identifying specific exchanges that may constitute "qualified exchanges," Treasury Regulations provide that a qualified exchange is (a) a U.S. securities exchange that is registered with the Securities and Exchange Commission, or the SEC, (b) the U.S. market system established pursuant to section 11A of the Securities and Exchange Act of 1934, or (c) a non-U.S. securities exchange that is regulated or supervised by a governmental authority of the country in which the market is located, provided that (i) such non-U.S. exchange has trading volume, listing, financial disclosure, surveillance and other requirements designed to prevent fraudulent and manipulative acts and practices, to remove impediments to and perfect the mechanism of a free and open, fair and orderly, market, and to protect investors; and the laws of the country in which such non-U.S. exchange is located and the rules of such non-U.S. exchange ensure that such requirements are actually enforced and (ii) the rules of such non-U.S. exchange effectively promote active trading of listed shares. We have received approval to list our ADSs on the Nasdaq Global Select Market, which is a U.S. securities exchange that is registered with the SEC. However, no assurance can be given that the ADSs will meet the requirements to be treated as "regularly traded" for purposes of the mark-to-market election. In addition, because a mark-to-market election cannot be made for any lower-tier PFICs that we may own, a U.S. Holder may continue to be subject to the special tax regime with respect to such holder's indirect interest in any investments held by us that are treated as an equity interest in a PFIC for U.S. federal income tax purposes, including shares in any future subsidiary of ours that is treated as a PFIC.

If a U.S. Holder makes this mark-to-market election, such U.S. Holder will be required in any year in which we are a PFIC to include as ordinary income the excess of the fair market value of such U.S. Holder's ADSs at year-end over its basis in those ADSs. In addition, the excess, if any, of such U.S. Holder's basis in the ADSs over the fair market value of such U.S. Holder's ADSs at year-end is deductible as an ordinary loss in an amount equal to the lesser of (i) the amount of the excess or (ii) the amount of the net mark-to-market gains that have been included in income in prior years by such U.S. Holder. Any gain recognized by such U.S. Holder upon the sale of such U.S. Holder's ADSs will be taxed as ordinary income in the year of sale. Amounts treated as ordinary income will not be eligible for the preferential tax rate applicable to qualified dividend income or long-term capital gains. A U.S. Holder's adjusted tax basis in the ADSs will be increased by the amount of any income inclusion and decreased by the amount of any deductions under the mark-to-market rules. If a U.S. Holder makes a mark-to market election, it will be effective for the taxable year for which the election is made

and all subsequent taxable years unless the ADSs are no longer regularly traded on a qualified exchange or the IRS consents to the revocation of the election.

Controlled Foreign Corporation

The Tax Cuts and Jobs Act (the “Tax Act”) eliminated the prohibition on “downward attribution” from non-U.S. persons to U.S. persons under Section 958(b)(4) of the Code for purposes of determining constructive stock ownership under the controlled foreign corporation (“CFC”) rules. As a result, our U.S. subsidiary will be deemed to own all of the stock of our non-U.S. subsidiaries held by the Company for CFC purposes. To the extent a non-U.S. subsidiary is treated as a CFC for any taxable year, each U.S. person treated as a “10% U.S. Shareholder” with respect to such CFC that held our common shares directly or indirectly through non-U.S. entities (including the Company) as of the last day in such taxable year that the subsidiary was a CFC would generally be required to include in gross income as ordinary income its pro rata share of certain investment income of the CFC, regardless of whether that income was actually distributed to such U.S. person (with certain adjustments). For tax years beginning on or after January 1, 2018, a “10% U.S. Shareholder” of a non-U.S. corporation includes any U.S. person that owns (or is treated as owning) stock of the non-U.S. corporation possessing 10% or more of the total voting power or total value of such non-U.S. corporation’s stock. The legislative history under the Tax Act indicates that this change was not intended to cause our non-U.S. subsidiaries to be treated as CFCs with respect to a 10% U.S. Shareholder that is not related to our U.S. subsidiary. However, it is not clear whether the IRS or a court would interpret the change made by the Tax Act in a manner consistent with such indicated intent.

You are strongly urged to consult your own tax advisors to determine whether your ownership of the ADSs will cause you to become a 10% U.S. Shareholder and the impact of such a classification.

Information Reporting Requirements

If we are a PFIC for any taxable year during which a U.S. Holder holds the ADSs, each such U.S. Holder generally will be required to file an annual information return on IRS Form 8621 containing such information as the U.S. Treasury Department may require. The failure to file IRS Form 8621 could result in the imposition of penalties and the extension of the statute of limitations with respect to U.S. federal income tax.

The U.S. federal income tax rules relating to PFICs are complex. U.S. Holders are urged to consult their tax advisors with respect to the purchase, ownership and disposition of the ADSs, the availability of the mark-to-market election and whether making the election would be advisable in their particular circumstances, and the IRS information reporting obligations with respect to the purchase, ownership and disposition of the ADSs.

Taxation of Dividends and Other Distributions on the ADSs

Subject to the discussion above under the heading “—Passive Foreign Investment Company Considerations,” generally, the gross amount of distributions made by us, if any, to a U.S. Holder with respect to the ADSs, before reduction for any non-U.S. taxes withheld therefrom, will be includable in gross income as a dividend to the extent that such distribution is paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). To the extent, if any, that the amount of any cash distribution exceeds our current and accumulated earnings and profits, it will be treated first as a tax-free return of such U.S. Holder’s tax basis in its ADSs, and to the extent the amount of the distribution exceeds such U.S. Holder’s tax basis, the excess will be taxed as capital

gain. We do not intend to calculate our earnings and profits under U.S. federal income tax principles. Therefore, a U.S. Holder should expect that a distribution will generally be treated as a dividend even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above. A dividend in respect of the ADSs will not be eligible for the dividends-received deduction allowed to corporations in respect of dividends received from other U.S. corporations. Non-corporate U.S. Holders may qualify for the lower rates of taxation with respect to dividends on ADSs applicable to long term capital gains (i.e., gains from the sale of capital assets held for more than one year), provided that certain conditions are met, including certain holding period requirements and the absence of certain risk reduction transactions. However, such reduced rate shall not apply if we are a PFIC for the taxable year in which we pay a dividend, or were a PFIC in the preceding taxable year. As indicated in the section titled "Dividends and Dividend Policy" herein, we intend to retain any earnings for use in our business and do not currently intend to pay dividends on our ordinary shares.

Subject to the paragraph below, dividends generally will constitute income from sources outside the United States, which may be relevant in calculating a U.S. Holder's foreign tax credit limitation. Subject to certain conditions and limitations, non-U.S. tax withheld on dividends may be deducted from such U.S. Holder's taxable income or credited against such U.S. Holder's U.S. federal income tax liability. The limitation on foreign taxes eligible for credit is calculated separately with respect to specific classes of income. For this purpose, dividends that we distribute generally should constitute "passive category income," or, in the case of certain U.S. Holders, "general category income." A foreign tax credit for foreign taxes imposed on distributions may be denied if a U.S. Holder does not satisfy certain minimum holding period requirements.

Notwithstanding the paragraph above, if 50% or more of the ADSs are treated as held by U.S. persons, we will be treated as a "U.S.-owned foreign corporation." In that case, dividends may be treated for U.S. foreign tax credit purposes as income from sources outside the United States to the extent paid out of our non-U.S. source earnings and profits, and as income from sources within the United States to the extent paid out of our U.S. source earnings and profits. There can be no assurance that we will not be treated as a U.S.-owned foreign corporation. If the dividends are taxed at the lower tax rates generally applicable to long-term capital gains (as discussed above), the amount of the dividend taken into account for purposes of calculating the U.S. foreign tax credit limitation will generally be limited to the gross amount of the dividend, multiplied by the preferential rate divided by the highest rate of tax normally applicable to dividends. The rules relating to the determination of the foreign tax credit are complex, and U.S. Holders are urged to consult their tax advisors to determine whether and to what extent such U.S. Holder will be entitled to a foreign tax credit.

Taxation of Dispositions of ADSs

Subject to the discussion above under "—Passive Foreign Investment Company Considerations," a U.S. Holder will recognize taxable gain or loss on any sale, exchange or other taxable disposition of an ADS equal to the difference between the amount realized (the amount of cash (in U.S. dollars) plus the fair market value of any property received) for the ADS and such U.S. Holder's tax basis (in U.S. dollars) in the ADS. The gain or loss will generally be capital gain or loss. Such capital gain or loss generally will be long-term capital gain taxable at a reduced rate for non-corporate U.S. Holders or long-term capital loss if, on the date of sale, exchange or other disposition, the ADSs were held by the U.S. Holder for more than one year. The deductibility of capital losses is subject to limitations. Any such gain or loss generally will be treated as U.S. source income or loss for U.S. foreign tax credit purposes.

Disposition of Foreign Currency

U.S. Holders are urged to consult their tax advisors regarding the tax consequences of receiving, converting or disposing of any non-U.S. currency received as dividends on our ADSs or on the sale or retirement of an ADS.

Tax on Net Investment Income

Additional 3.8% Medicare tax on some or all of such U.S. Holder's "net investment income." Net investment income generally includes income from the ADSs unless such income is derived in the ordinary course of the conduct of a trade or business (other than a trade or business that consists of certain passive or trading activities). You should consult your tax advisors regarding the effect this Medicare tax may have, if any, on your acquisition, ownership or disposition of the ADSs.

Information Reporting and Backup Withholding

Distributions with respect to ADSs and proceeds from the sale, exchange or disposition of ADSs may be subject to information reporting to the IRS, and possible U.S. backup withholding. Backup withholding will not apply, however, to a U.S. Holder who furnishes a correct taxpayer identification number and makes any other required certification or who is otherwise exempt from backup withholding. U.S. Holders who are required to establish their exempt status generally must provide such certification on U.S. Internal Revenue Service Form W-9. U.S. Holders are urged to consult their tax advisors regarding the application of the U.S. information reporting and backup withholding rules.

Backup withholding is not an additional tax. Amounts withheld as backup withholding may be credited against a U.S. Holder's U.S. federal income tax liability, and a U.S. Holder may obtain a refund of any excess amounts withheld under the backup withholding rules by filing the appropriate claim for refund with the IRS and furnishing any required information.

Foreign Financial Asset Information Reporting

U.S. Holders who are either individuals or certain domestic entities may be required to submit certain information to the IRS with respect to such holder's beneficial ownership of the ADSs, if such ADSs are not held on such holder's behalf by a financial institution, as our ordinary shares are considered "specified foreign financial assets." This law also imposes penalties and potential other adverse tax consequences if a U.S. Holder is required to submit such information to the IRS and fails to do so. U.S. Holders are urged to consult their tax advisors regarding the potential information reporting obligations that may be imposed with respect to the ownership and disposition of the ADSs.

The above description is not intended to constitute a complete analysis of all tax consequences relating to acquisition, ownership and disposition of the ADSs. Prospective purchasers are urged to consult their tax advisors concerning the tax consequences related to their particular circumstances.

United Kingdom Tax Considerations

The following is a general summary of certain United Kingdom tax considerations relating to the ownership and disposal of the ADSs and does not address all possible tax consequences relating to an investment in the ADSs. It is based on current U.K. tax law and published HM Revenue & Customs, or HMRC, practice as of the date of this prospectus supplement, both of which are subject to change, possibly with retrospective effect.

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This United Kingdom taxation section is written on the basis that the company is and remains resident for tax purposes in the United Kingdom only and will therefore be subject to the U.K. tax regime and not the U.S. tax regime (save as discussed in the section titled "Material U.S. Federal Income Tax Considerations" above). On this basis, dividends paid by the company will be regarded as U.K. dividends, not U.S. dividends.

Except as provided otherwise, this summary applies only to persons who are resident (and, in the case of individuals, domiciled or deemed domiciled) in the United Kingdom for tax purposes and who are not resident for tax purposes in any other jurisdiction, and do not have a permanent establishment or fixed base in any other jurisdiction with which the holding of the ADSs is connected. Such persons are referred to herein as U.K. Holders. Persons (a) who are not resident (or, if resident, are not domiciled or deemed domiciled) in the United Kingdom for tax purposes, including those individuals and companies who trade in the United Kingdom through a branch, agency or permanent establishment in the United Kingdom to which the ADSs are attributable, or (b) who are resident or otherwise subject to tax in a jurisdiction outside the United Kingdom, are recommended to seek the advice of professional advisers in relation to their taxation obligations.

This summary is for general information only and is not intended to be, nor should it be considered to be, legal or tax advice to any particular investor. It does not address all of the tax considerations that may be relevant to specific investors in light of their particular circumstances or to investors subject to special treatment under U.K. tax law. In particular:

- this summary only applies to the absolute beneficial owners of the ADSs (and where the ADSs are not held through an Individual Savings Account or a Self-Invested Personal Pension); and
- this summary: (a) only addresses the principal U.K. tax consequences for investors who hold the ADSs as capital assets, (b) does not address the tax consequences that may be relevant to certain special classes of investor such as dealers, brokers or traders in shares or securities and other persons who hold the ADSs otherwise than as an investment, (c) does not address the tax consequences for holders that are financial institutions, insurance companies, collective investment schemes, pension schemes, charities or tax-exempt organizations, (d) assumes that the holder is not an officer or employee of the company (or of any related company) and has not (and is not deemed to have) acquired the ADSs or related ordinary shares by virtue of an office or employment, and (e) assumes that the holder does not control or hold (and is not deemed to control or hold), either alone or together with one or more associated or connected persons, directly or indirectly (including through the holding of the related ordinary shares or ADSs), an interest of 10% or more in the issued share capital (or in any class thereof or ADSs), voting power, rights to profits or capital of the company, and is not otherwise connected with the company.

This summary further assumes, on the basis of HMRC guidance, that a holder of ADSs will be regarded by HMRC as the beneficial owner of the underlying ordinary shares and of any dividends paid in respect of the related ordinary shares (where the dividends are regarded for U.K. tax purposes as that person's own income (and not the income of some other person)) for U.K. tax purposes.

Potential investors in ADSs should satisfy themselves prior to investing as to the overall tax consequences, including, specifically, the consequences under U.K. tax law and HMRC practice of the acquisition, ownership and disposal of ADSs in their own particular circumstances by consulting their own tax advisers. In particular, non-U.K. resident or domiciled persons are advised to consider the potential impact of any relevant double taxation agreements.

Taxation of dividends

Withholding Tax. Dividend payments in respect of ADSs or ordinary shares may be made without withholding or deduction for or on account of U.K. tax.

United Kingdom Income Tax. An individual U.K. Holder (being an individual who is resident for tax purposes in the United Kingdom) who receives a dividend from the company will generally be subject to income tax on the dividend. For the tax year 2018/2019, an individual U.K. Holder will generally pay income tax at a rate of 0% on the first £2,000 of dividends received by such U.K. Holder. Dividend income taxed at 0% will be taken into account in determining the rate at which income in excess of this tax-free allowance will (subject to the availability of any income tax personal allowance) be taxed.

An individual U.K. Holder who is subject to income tax at the basic rate will be liable to tax on the dividend at the marginal rate of 7.5%. An individual U.K. Holder who is subject to income tax at the higher rate (but not the additional rate) will be liable to income tax on the dividend at the rate of 32.5% to the extent that such sum, when treated as the top slice of that holder's income, exceeds the threshold for higher rate income tax.

An individual U.K. Holder liable to income tax at the additional rate will be subject to income tax on the dividend at the rate of 38.1% to the extent that the holder's income (including the dividend) exceeds the threshold for the additional rate.

An individual who is not a U.K. Holder (other than one carrying on a trade, profession or vocation in the United Kingdom through a branch or agency to which the ADSs are attributable) who is resident for tax purposes outside the United Kingdom will not have any U.K. tax to pay on dividends received from the company.

United Kingdom Corporation Tax. A U.K. Holder within the charge to U.K. corporation tax may be entitled to exemption from U.K. corporation tax in respect of dividend payments. If the conditions for the exemption are not satisfied, or such U.K. Holder elects for an otherwise exempt dividend to be taxable, United Kingdom corporation tax will be chargeable on the amount of any dividends. The main rate of United Kingdom corporation tax for the 2018/2019 tax year is 19%. If potential investors are in any doubt as to their position, they should consult their own professional advisers.

A corporate holder of ADSs that is not a U.K. Holder will not be subject to U.K. corporation tax on dividends received from the company, unless it carries on a trade in the United Kingdom through a permanent establishment to which the ADSs are attributable. In these circumstances, such holder may, depending on its individual circumstances and if the exemption from U.K. corporation tax discussed above does not apply, be chargeable to U.K. corporation tax on dividends received from the company.

Taxation of Disposals

U.K. Holders. A disposal or deemed disposal of ADSs by an individual U.K. Holder may, depending on his or her individual circumstances, give rise to a chargeable gain or to an allowable loss for the purpose of U.K. capital gains tax. The principal factors that will determine the capital gains tax position on a disposal of ADSs are the extent to which the U.K. Holder realizes any other capital gains in the tax year in which the disposal is made, the extent to which the holder has incurred capital losses in that or any earlier tax year and the level of the annual allowance of tax-free gains in that tax year (the "annual exemption"). The annual exemption for the 2018/2019 tax year is £11,700. If, after all allowable deductions, an individual U.K. Holder who is subject to U.K. income tax at either the higher

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or the additional rate becomes liable to U.K. capital gains tax on the disposal of ADSs, the current applicable rate would be 20%. For an individual U.K. Holder who is subject to U.K. income tax at the basic rate and, after all allowable deductions, liable to U.K. capital gains tax on such disposal, the current applicable rate would be 10%, save to the extent that any capital gains exceed the unused basic rate tax band. In that case, the current rate applicable to the excess would be 20%.

An individual U.K. Holder who ceases to be resident in the United Kingdom (or who fails to be regarded as resident in a territory outside the United Kingdom for the purposes of double taxation relief) for a period of less than five years and who disposes of his or her ADSs during that period of temporary non-residence may be liable to U.K. capital gains tax on a chargeable gain accruing on such disposal on his or her return to the United Kingdom (or upon ceasing to be regarded as resident outside the United Kingdom for the purposes of double taxation relief) (subject to available exemptions or reliefs).

A disposal or deemed disposal of ADSs by a corporate U.K. Holder may give rise to a chargeable gain or an allowable loss for the purpose of U.K. corporation tax. Indexation allowance (which historically would have applied to reduce the amount of chargeable gain that is subject to corporation tax) will not operate to reduce any gains on disposals of ADSs acquired on or after January 1, 2018 that arise to corporate U.K. Holders. Indexation allowance may be available in relation to disposals of assets acquired prior to January 1, 2018, but will be calculated applying the Retail Price Index for December 2017 regardless of the actual date of disposal.

Non-United Kingdom Holders. The paragraphs below relating to the liability of non U.K. Holders to U.K. tax on chargeable gains assume that:

(a) the draft U.K. legislation published on January 9, 2019 relating to the taxation of gains made by non-residents on U.K. land are enacted into U.K. law as envisaged in the draft legislation; and

(b) the company does not (and will not) derive 75% or more of its gross asset value from U.K. land.

An individual holder who is not a U.K. Holder will not be liable to U.K. capital gains tax on capital gains realized on the disposal of his or her ADSs unless such holder carries on (whether solely or in partnership) a trade, profession or vocation in the United Kingdom through a permanent establishment in the United Kingdom to which the ADSs are attributable. In these circumstances, such holder may, depending on his or her individual circumstances, be chargeable to U.K. capital gains tax on chargeable gains arising from a disposal of his or her ADSs.

A corporate holder of ADSs that is not a U.K. Holder will not be liable for U.K. corporation tax on chargeable gains realized on the disposal of its ADSs unless it carries on a trade in the United Kingdom through a permanent establishment to which the ADSs are attributable. In these circumstances, a disposal of ADSs by such holder may give rise to a chargeable gain or an allowable loss for the purposes of U.K. corporation tax.

Stamp Duty and Stamp Duty Reserve Tax

The statements below in relation to U.K. stamp duty and stamp duty reserve tax, or SDRT, apply irrespective of whether the relevant holder of ADSs is resident or domiciled in the United Kingdom.

Issue and Transfer of Ordinary Shares

Issue (including to a depositary or clearance service). No U.K. stamp duty is payable on the issue of the ordinary shares.

Based on current published HMRC practice and recent case law, there should be no SDRT payable on the issue of ordinary shares to a depositary receipt system or a clearance service. We understand that HMRC recognizes DTC as a clearance service for United Kingdom stamp duty and SDRT purposes.

Transfer to a depositary or clearance service. Transfers of, and unconditional agreements to transfer, ordinary shares to, or to a nominee or agent for, a person whose business is or includes issuing depositary receipts or the provision of clearance services, will generally be regarded by HMRC as subject to SDRT (and, where the transfer is effected by a written instrument, stamp duty) at a rate of 1.5% of the amount or value of the consideration or, in certain circumstances, the value of the ordinary shares transferred unless, in the case of a clearance service, it has made an election under section 97A(1) Finance Act 1986, or such transfer can be regarded as an integral part of an issue of share capital. In a recent Court of Justice of the European Union judgment (*Air Berlin plc v HMRC* [2017]) the Court considered the application of this test but, as yet, the UK domestic law and HMRC's published practice remain unchanged. Accordingly, we anticipate that the charge will continue to be collected and anticipate that this liability for stamp duty or SDRT would be borne by the person depositing the relevant shares in the depositary receipt system or clearance service. Transfers of ordinary shares between depositary receipt systems and clearance services will generally be exempt from stamp duty and SDRT unless, in the case of a clearance service, it has made an election under section 97A(1) Finance Act 1986. Our understanding is that DTC has not made such an election.

Transfer on sale. The transfer on sale of ordinary shares by a written instrument of transfer will generally be liable to U.K. stamp duty at the rate of 0.5% of the amount or value of the consideration for the transfer. The purchaser normally pays the stamp duty.

The transfer of ordinary shares within a depositary receipt system or clearance service should not be subject to stamp duty or SDRT, except where a clearance service has made an election under section 97A(1) Finance Act 1986. Our understanding is that DTC has not made such an election.

An agreement to transfer ordinary shares outside a depositary receipt system or a clearance service will generally give rise to a liability on the purchaser to SDRT at the rate of 0.5% of the amount or value of the consideration. Such SDRT is payable on the seventh day of the month following the month in which the charge arises, but where an instrument of transfer is executed and duly stamped before the expiry of a period of six years beginning with the date of that agreement, (i) any SDRT that has not been paid ceases to be payable, and (ii) any SDRT that has been paid may be recovered from HMRC, generally with interest.

Issue or Transfer of ADSs

Based on current HMRC published practice, no U.K. stamp duty or SDRT should be payable on the issue or transfer of (including an unconditional agreement to transfer) an ADS, on the basis that an ADS is not regarded as "stock" or a "marketable security" for UK stamp duty purposes and is not considered a "chargeable security" for the purposes of SDRT.

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the ADSs being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of ADSs indicated in the following table. Goldman Sachs & Co. LLC, 200 West Street, 29th Floor, New York, New York 10282, Jefferies LLC, 520 Madison Avenue, New York, New York 10022, and Cowen and Company, LLC, 599 Lexington Avenue, 27th Floor, New York, New York 10022, are the representatives of the underwriters.

<u>Underwriters</u>	<u>Number of ADSs</u>
Goldman, Sachs & Co. LLC	
Jefferies LLC	
Cowen and Company, LLC	
SunTrust Robinson Humphrey, Inc.	
Total	

The underwriters are committed to take and pay for all of the ADSs being offered, if any are taken, other than the ADSs covered by the option described below unless and until this option is exercised.

The underwriters have an option to buy up to an additional ADSs from us. They may exercise that option for 30 days. If any ADSs are purchased pursuant to this option, the underwriters will severally purchase ADSs in approximately the same proportion as set forth in the table above.

The following table shows the per ADS and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional ADSs.

<u>Paid by Us</u>	<u>No Exercise</u>	<u>Full Exercise</u>
Per ADS	\$	\$
Total	\$	\$

ADSs sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus. Any ADSs sold by the underwriters to securities dealers may be sold at a discount of up to \$ per ADS from the public offering price. If all the ADSs are not sold at the public offering price, the representatives may change the offering price and the other selling terms. The offering of the ADSs by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

Subject to certain limited exceptions, we and our executive officers and directors have agreed that, for a period of 90 days from the date of this prospectus supplement, and certain holders of our ordinary shares or ADSs have agreed that, for a period of 60 days from the date of this prospectus supplement, we and they will not, without the prior written consent of Goldman Sachs & Co. LLC, Jefferies LLC and Cowen and Company, LLC, offer, sell, contract, sell, pledge or otherwise dispose of, including the filing of a registration statement in respect of, or hedge any of our ordinary shares, ADSs, or any securities convertible into, or exercisable or exchangeable for our ordinary shares.

Our ADSs are listed on the Nasdaq Global Select Market under the symbol "NCNA."

In connection with the offering, the underwriters may purchase and sell ADSs in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of ADSs

than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short position that is not greater than the amount of additional ADSs for which the underwriters' option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional ADSs or purchasing ADSs in the open market. In determining the source of ADSs to cover the covered short position, the underwriters will consider, among other things, the price of ADSs available for purchase in the open market as compared to the price at which they may purchase additional ADSs pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional ADSs for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing ADSs in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the ADSs in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of ADSs made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased ADSs sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the company's ADSs, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the ADSs. As a result, the price of the ADSs may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on The Nasdaq Global Select Market, in the over-the-counter market or otherwise.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act.

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately \$235,000. We have agreed to reimburse the underwriters for all expenses related to the clearance of the offering with the Financial Industry Regulatory Authority and the qualification of our ADSs under state securities laws (in a combined amount not to exceed \$15,000).

Other Relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such

investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Selling Restrictions

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State") an offer to the public of our ADSs may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of our ADSs may be made at any time under the following exemptions under the Prospectus Directive:

- to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the representatives for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive;

provided that no such offer of our ADSs shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to public" in relation to our ADSs in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our ADSs to be offered so as to enable an investor to decide to purchase our ADSs, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (as amended), including by Directive 2010/73/EU and includes any relevant implementing measure in the Relevant Member State.

This European Economic Area selling restriction is in addition to any other selling restrictions set out below.

United Kingdom

In the United Kingdom, this prospectus is only addressed to and directed as qualified investors who are (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order); or (ii) high net worth entities and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (e) of the Order (all such persons together being referred to as "relevant persons"). Any investment or investment activity to which this prospectus relates is available only to relevant persons and will only be engaged with relevant persons. Any person who is not a relevant person should not act or relay on this prospectus or any of its contents.

Canada

The securities may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106

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Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions, and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption form, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this offering memorandum (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

The ADSs may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) ("Companies (Winding Up and Miscellaneous Provisions) Ordinance") or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) ("Securities and Futures Ordinance"), or (ii) to "professional investors" as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the ADSs may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to ADSs which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the ADSs may not be circulated or distributed, nor may the ADSs be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA")) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the ADSs are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1)

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of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the ADSs under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation's securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore ("Regulation 32")

Where the ADSs are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the ADSs under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S\$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended), or the FIEA. The securities may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

LEGAL MATTERS

The validity of our ordinary shares underlying the ADSs and certain matters governed by English law will be passed on for us by Bristows LLP. Certain matters of U.S. federal law will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. The underwriters are being represented in connection with this offering by Cooley LLP, New York, New York, and Cooley (UK) LLP, London, United Kingdom.

EXPERTS

The consolidated financial statements of NuCana plc appearing in NuCana's Annual Report on Form 20-F for the year ended December 31, 2017, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The registered business address of Ernst & Young LLP is 144 Morrison Street, Edinburgh, EH3 8EX, United Kingdom.

ENFORCEMENT OF JUDGMENTS

We are a public limited company incorporated under the laws of England and Wales. Certain of our directors and executive officers and experts named in this prospectus supplement reside outside of the United States, and a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may not be possible for an investor to effect service of process on us or our directors and executive officers in the United States or to compel any of them to appear in court in the United States or to enforce judgments obtained in U.S. courts against them or us, including judgments based on civil liability provisions of the federal securities laws of the United States. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in the United Kingdom. An award for monetary damages under the U.S. securities laws would be considered punitive in the United Kingdom if it does not seek to compensate the claimant for loss or damage suffered and is instead intended to punish the defendant. The enforceability of any judgment in the United Kingdom will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and the United Kingdom do not currently have a treaty providing for the mutual recognition and enforcement of judgments in civil and commercial matters (although the United States and the United Kingdom are both parties to the New York Convention on the Recognition and Enforcement of Foreign Arbitral Awards).

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the periodic reporting and other informational requirements of the Exchange Act. Under the Exchange Act, we file Annual Reports on Form 20-F and other information with the SEC. As a foreign private issuer, we are exempt from, among other things, the rules under the Exchange Act prescribing the furnishing and content of proxy statements and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act.

Information filed with the SEC by us can be inspected and copied at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of

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this information by mail from the Public Reference Room of the SEC at prescribed rates. Further information on the operation of the SEC's Public Reference Room in Washington, D.C. can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site that contains reports and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is www.sec.gov.

This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement of which this prospectus supplement forms a part. Statements in this prospectus supplement or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement at the SEC's Public Reference Room in Washington, D.C. or through the SEC's website, as provided above.

We also maintain a website at www.nucana.com through which you can access our SEC filings. The information set forth on our website is not part of this prospectus supplement.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede this information. We filed a registration statement on Form F-3 under the Securities Act of 1933, as amended, with the SEC with respect to the securities we may offer pursuant to this prospectus. This prospectus supplement omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus supplement. Statements in this prospectus supplement regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in “Where You Can Find More Information.” The documents we are incorporating by reference are:

- our Annual Report on Form 20-F for the year ended December 31, 2017, filed with the SEC on March 22, 2018;
- our Reports on Form 6-K furnished to the SEC on October 1, 2018, October 22, 2018 and November 28, 2018 (other than Exhibit 99.3) that we incorporate by reference into this prospectus supplement; and
- the description of ADSs representing our ordinary shares contained in our Registration Statement on Form 8-A filed with the SEC on September 22, 2017, including any amendments or reports filed for the purpose of updating such description.

We are also incorporating by reference all subsequent Annual Reports on Form 20-F that we file with the SEC and certain reports on Form 6-K that we furnish to the SEC after the date of this prospectus supplement (if they state that they are incorporated by reference into this prospectus supplement) prior to the termination of this offering. In all cases, you should rely on the later information over different information included in this prospectus supplement or any accompanying prospectus.

Unless expressly incorporated by reference, nothing in this prospectus supplement shall be deemed to incorporate by reference information furnished to, but not filed with, the SEC. Copies of all documents incorporated by reference in this prospectus supplement, other than exhibits to those documents unless such exhibits are specifically incorporated by reference in this prospectus supplement, will be provided at no cost to each person, including any beneficial owner, who receives a copy of this prospectus supplement on the written or oral request of that person made to:

NuCana plc
3 Lochside Way
Edinburgh, EH12 9DT
United Kingdom
Telephone: +44 (0)131 357 1111

You may also access these documents on our website, www.nucana.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

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You should rely only on information contained in, or incorporated by reference into, this prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus supplement or incorporated by reference in this prospectus supplement. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.



\$400,000,000

**American Depositary Shares representing Ordinary Shares
Debt Securities
Warrants
Rights
Units**

This prospectus will allow us to issue, from time to time at prices and on terms to be determined at or prior to the time of the offering, up to \$400,000,000 of any combination of the securities described in this prospectus, either individually or in units. We may also offer: American Depositary Shares, or ADSs, representing ordinary shares upon conversion of or exchange for the debt securities or upon the exercise of the warrants or rights.

This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide you with the specific terms of any offering in one or more supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any prospectus supplement, as well as any documents incorporated by reference into this prospectus or any prospectus supplement, carefully before you invest.

Our securities may be sold directly by us to you, through agents designated from time to time or to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section titled "Plan of Distribution" in this prospectus and in the applicable prospectus supplement. If any underwriters or agents are involved in the sale of our securities with respect to which this prospectus is being delivered, the names of such underwriters or agents and any applicable fees, commissions or discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

Our ADSs are listed on The Nasdaq Global Select Market under the symbol "NCNA." On September 28, 2018, the last reported sale price of our ADSs on The Nasdaq Global Select Market was \$24.94 per ADS. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The Nasdaq Global Select Market or any securities market or other securities exchange of the securities covered by the prospectus supplement. Prospective purchasers of our securities are urged to obtain current information as to the market prices of our securities, where applicable.

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 4 of this prospectus under the caption "[Risk Factors](#)." We may also include specific risk factors in supplements to this prospectus under the caption "Risk Factors." This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is October 22, 2018.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process. Under this shelf registration process, we may offer ADSs representing our ordinary shares, various series of debt securities or warrants, and rights to purchase any of such securities, either individually or in units, in one or more offerings, with a total value of up to \$400,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering.

This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. The prospectus supplement may also add, update or change information contained or incorporated by reference in this prospectus. However, no prospectus supplement will offer a security that is not registered and described in this prospectus at the time of its effectiveness. This prospectus, together with the applicable prospectus supplements and the documents incorporated by reference into this prospectus, includes all material information relating to the offering of securities under this prospectus. You should carefully read this prospectus, the applicable prospectus supplement, the information and documents incorporated herein by reference and the additional information under the headings “Where You Can Find More Information” and “Incorporation of Documents by Reference” before making an investment decision.

You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained or incorporated by reference in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated herein by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus may not be used to consummate sales of our securities unless it is accompanied by a prospectus supplement. To the extent there are inconsistencies between any prospectus supplement, this prospectus and any documents incorporated by reference, the document with the most recent date will control.

On August 29, 2017, we re-registered NuCana BioMed Limited as a public limited company and changed our name from NuCana BioMed Limited to NuCana plc. Unless otherwise indicated or the context otherwise requires, in this prospectus, “NuCana,” “NuCana BioMed Limited,” “NuCana plc,” the “Group,” the “company,” “we,” “us” and “our” refer to (i) NuCana BioMed Limited and its consolidated subsidiaries prior to the re-registration of NuCana BioMed Limited as a public limited company and (ii) NuCana plc and its consolidated subsidiaries after the re-registration of NuCana BioMed Limited as a public limited company. See “Description of Share Capital.”

PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus. We urge you to read this entire prospectus, including the more detailed consolidated financial statements, notes to the consolidated financial statements and other information incorporated by reference from our other filings with the SEC or included in any applicable prospectus supplement. Investing in our securities involves risks. Therefore, carefully consider the risk factors set forth in any prospectus supplements and in our most recent filings with the SEC including our Annual Reports on Form 20-F and reports on Form 6-K, as well as other information in this prospectus and any prospectus supplements and the documents incorporated by reference herein or therein, before purchasing our securities. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

About NuCana plc

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 three clinical trials, including a Phase 1b trial for patients with biliary tract cancer, a Phase 2 trial for patients with ovarian cancer and a Phase 3 trial for patients with pancreatic cancer. NUC-3373 is currently in a Phase 1 trial for the potential treatment of a wide range of advanced solid tumors. 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.

Additional Information

For additional information related to our business and operations, please refer to the reports incorporated herein by reference, including the Annual Report on Form 20-F of NuCana plc for the year ended December 31, 2017 and the Report on Form 6-K furnished on October 1, 2018, as described under the caption "Incorporation of Documents by Reference" on page 59 of this prospectus.

Our Corporate Information

NuCana was incorporated under the laws of England and Wales in 1997 under the name Biomed (UK) Limited, and commenced operations in 2008. On April 28, 2008, we changed our name to NuCana BioMed Limited. On August 29, 2017, we re-registered as a public limited company and changed our name to NuCana plc. ADSs representing our ordinary shares were admitted to trading on The Nasdaq Global Select Market on September 28, 2017. Our ADSs are traded under the symbol "NCNA."

Our principal executive offices are located at 3 Lochside Way, Edinburgh, EH12 9DT, United Kingdom. Our telephone number at this address is +44 (0)131 357 1111.

We maintain a website at www.nucana.com to which we regularly post copies of our press releases as well as additional information about us. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

We use our registered trademarks, NuCana® and Acelarin®, and our trademark, ProTides™, in this prospectus. This prospectus also includes trademarks, trade names and service marks that are the property of other organizations. Solely for convenience, trademarks and trade names referred to in this prospectus appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and trade names.

Offerings Under This Prospectus

Under this prospectus, we may offer ADSs representing our ordinary shares, various series of debt securities or warrants or rights to purchase any of such securities, either individually or in units, with a total value of up to \$400,000,000, from time to time at prices and on terms to be determined by market conditions at the time of the offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion or sinking fund terms, if any;
- voting or other rights, if any; and
- conversion or exercise prices, if any.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we offer securities through agents or underwriters, we will include in the applicable prospectus supplement:

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

This prospectus may not be used to consummate a sale of any securities unless it is accompanied by a prospectus supplement.

RISK FACTORS

Investing in our securities involves significant risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in the company. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading “Risk Factors” in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the heading “Risk Factors” included in our most recent Annual Report on Form 20-F and any subsequent Annual Reports on Form 20-F we file after the date of this prospectus, and all other information contained in or incorporated by reference into this prospectus or the registration statement of which this prospectus forms a part, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and the risk factors and other information contained in any applicable prospectus supplement before acquiring any of our securities. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

RATIO OF EARNINGS TO FIXED CHARGES

Any time debt securities are offered pursuant to this prospectus, we will provide a table setting forth our ratio of earnings to fixed charges on a historical basis in the applicable prospectus supplement, if required.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Words such as, but not limited to, “believe,” “expect,” “anticipate,” “estimate,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “targets,” “likely,” “will,” “would,” “could,” “should,” “continue,” and similar expressions or phrases, or the negative of those expressions or phrases, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus and incorporated by reference in this prospectus, we caution you that these statements are based on our projections of the future that are subject to known and unknown risks and uncertainties and other factors that may cause our actual results, level of activity, performance or achievements expressed or implied by these forward-looking statements, to differ. The sections in our periodic reports, including our Annual Report on Form 20-F for the fiscal year ended December 31, 2017, titled “Business,” “Risk Factors,” and “Operating and Financial Review and Prospects,” as well as other sections in this prospectus and the documents or reports incorporated by reference in this prospectus, discuss some of the factors that could contribute to these differences. These forward-looking statements include, among other things, statements about:

- the development of Acelarin, NUC-3373 and NUC-7738, including statements regarding the expected initiation, timing, progress and availability of data from our clinical trials;
- the potential attributes and benefit of our ProTides and their competitive positions;
- our ability to successfully commercialize our ProTides, if approved;
- our estimates regarding expenses, capital requirements and our need for additional financing;
- our ability to acquire or in-license new product candidates;
- potential collaborations; and
- the duration of our patent portfolio.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important cautionary statements in this prospectus or in the documents incorporated by reference in this prospectus, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. For a summary of such factors, please refer to the section titled “Risk Factors” in this prospectus, as updated and supplemented by the discussion of risks and uncertainties under “Risk Factors” contained in any supplements to this prospectus and in our most recent Annual Report on Form 20-F, as revised or supplemented by our subsequent periodic reports filed under the Exchange Act, as well as any amendments thereto, as filed with the SEC and which are incorporated herein by reference. The information contained in this document is believed to be current as of the date of this document. We do not intend to update any of the forward-looking statements after the date of this document to conform these statements to actual results or to changes in our expectations, except as required by law.

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In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this prospectus or in any document incorporated herein by reference might not occur. Investors are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this prospectus or the date of the document incorporated by reference in this prospectus. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to us or to any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

CAPITALIZATION

The following table presents our total capitalization and cash and cash equivalents as of June 30, 2018 derived from our unaudited condensed consolidated financial statements incorporated by reference into this prospectus.

You should read the financial data in the following table in conjunction with our unaudited condensed consolidated financial statements, audited consolidated financial statements and related notes incorporated by reference into this prospectus.

	<u>As of June 30, 2018</u> (unaudited) (in thousands)
Cash and cash equivalents	£ 81,469
Total equity attributable to equity holders:	
Ordinary shares, nominal value £0.04 per share, 31,811,146 shares issued and outstanding	£ 1,272
Share premium	79,236
Other reserves	59,072
Accumulated deficit	(52,871)
Total equity attributable to equity holders	<u>86,709</u>
Total capitalization	<u>£ 86,709</u>

The outstanding share information excludes:

- 4,802,814 ordinary shares issuable upon exercise of outstanding options under our equity incentive plans as of June 30, 2018 at a weighted average exercise price of £1.66 per share; and
- 112,500 ordinary shares issuable upon exercise of outstanding options under our equity incentive plans that were granted after June 30, 2018 at a weighted average exercise price of £18.05 per share; and
- 374,062 ordinary shares issued upon exercise of options under our equity incentive plans subsequent to June 30, 2018 at a weighted average exercise price of £0.49 per share; and
- 3,349,097 ordinary shares authorized for issuance pursuant to future awards under our equity incentive plans.

EXCHANGE RATE INFORMATION

Fluctuations in the exchange rate between the pound sterling and the U.S. dollar will affect the U.S. dollar amounts received by owners of the ADSs on conversion of dividends, if any, paid in pound sterling on the ordinary shares and affect the U.S. dollar price of the ADSs on Nasdaq. The table below shows the period end, average, high and low exchange rates of U.S. dollars per pound sterling for the periods shown. Average rates are computed by using the noon buying rate of the Federal Reserve Bank of New York for the U.S. dollar on the last business day of each month during the relevant year indicated or each business day during the relevant month indicated. The rates set forth below are provided solely for your convenience and may differ from the actual rates used in the preparation of our consolidated financial statements included in this prospectus and other financial data appearing in this prospectus.

Period	Noon Buying Rate			
	End	Average (1)	High	Low
(\$ per £ 1.00)				
Period:				
2013	1.6574	1.5668	1.6574	1.4837
2014	1.5578	1.6461	1.7165	1.5517
2015	1.4746	1.5250	1.5882	1.4648
2016	1.2337	1.3444	1.4800	1.2155
2017	1.3259	1.2957	1.3578	1.2118
2018 (through September 21, 2018)	1.3067	1.3489	1.4332	1.2685
April 2018	1.3751	1.4079	1.4332	1.3751
May 2018	1.3289	1.3470	1.3611	1.3258
June 2018	1.3197	1.3294	1.3429	1.3095
July 2018	1.3125	1.3162	1.3266	1.2987
August 2018	1.2964	1.2878	1.3120	1.2685
September 2018 (through September 21, 2018)	1.3067	1.3045	1.3237	1.2833

(1) The average of the noon buying rate for pounds sterling on the last day of each full month during the relevant year or each business day during the relevant month indicated.

On September 21, 2018, the noon buying rate of the Federal Reserve Bank of New York for the U.S. dollar was £1.00 to \$1.3067.

PRICE HISTORY OF OUR ADSs

Our ADSs shares have been listed on The Nasdaq Global Select Market under the symbol "NCNA" since September 28, 2017. Prior to that date, there was no public trading market for our ADSs or our ordinary shares. Our initial public offering was priced at \$15.00 per ADS on September 28, 2017. The following table sets forth for the periods indicated the high and low sales prices per ADS as reported on The Nasdaq Global Select Market:

	Price Per ADS	
	High	Low
Annual (Year Ended December 31):		
2017 (September 28, 2017 through December 31, 2017)	\$18.72	\$10.00
2018 (through September 30, 2018)	\$28.25	\$10.04
Quarterly:		
Third Quarter 2017 (September 28, 2017 through September 30, 2017)	\$18.37	\$16.15
Fourth Quarter 2017	\$18.72	\$10.00
First Quarter 2018	\$28.25	\$10.04
Second Quarter 2018	\$32.00	\$20.49
Third Quarter 2018	\$30.10	\$19.32
Most Recent Six Months:		
April 2018	\$30.41	\$20.49
May 2018	\$29.01	\$23.00
June 2018	\$32.00	\$21.20
July 2018	\$25.35	\$21.00
August 2018	\$30.10	\$20.59
September 2018	\$26.25	\$22.08

On September 28, 2018, the last reported sale price of our ADSs on The Nasdaq Global Select Market was \$24.94 per ADS.

USE OF PROCEEDS

Unless otherwise indicated in the applicable prospectus supplement, we intend to use any net proceeds from the sale of securities under this prospectus to fund activities relating to the advancement of our drug discovery and development programs, and for other general corporate purposes, including, but not limited to, working capital, capital expenditures, investments, acquisitions, should we choose to pursue any, and collaborations. We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds, if any, we receive in connection with securities offered pursuant to this prospectus for any purpose. Pending application of the net proceeds as described above, we may initially invest the net proceeds in short-term, investment-grade and interest-bearing securities.

PLAN OF DISTRIBUTION

We may offer securities under this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities (1) through underwriters or dealers, (2) through agents or (3) directly to one or more purchasers, or through a combination of such methods. We may distribute the securities from time to time in one or more transactions at:

- a fixed price or prices, which may be changed from time to time;
- market prices prevailing at the time of sale;
- prices related to the prevailing market prices; or
- negotiated prices.

We may directly solicit offers to purchase the securities being offered by this prospectus. We may also designate agents to solicit offers to purchase the securities from time to time, and may enter into arrangements for “at-the-market,” equity line or similar transactions. We will name in a prospectus supplement any underwriter or agent involved in the offer or sale of the securities.

If we utilize a dealer in the sale of the securities being offered by this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale, and we will provide the name of any underwriter in the prospectus supplement which the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of the securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

With respect to underwritten public offerings, negotiated transactions and block trades, we will provide in the applicable prospectus supplement information regarding any compensation we pay to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof.

If so indicated in the applicable prospectus supplement, we will authorize underwriters, dealers or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in each applicable prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in each applicable prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other

institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

One or more firms, referred to as “remarketing firms,” may also offer or sell the securities, if a prospectus supplement so indicates, in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own accounts or as our agents. These remarketing firms will offer or sell the securities in accordance with the terms of the securities. Each prospectus supplement will identify and describe any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm’s compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket. Remarketing firms may be entitled under agreements that may be entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

Certain underwriters may use this prospectus and any accompanying prospectus supplement for offers and sales related to market-making transactions in the securities. These underwriters may act as principal or agent in these transactions, and the sales will be made at prices related to prevailing market prices at the time of sale. Any underwriters involved in the sale of the securities may qualify as “underwriters” within the meaning of Section 2(a)(11) of the Securities Act. In addition, the underwriters’ commissions, discounts or concessions may qualify as underwriters’ compensation under the Securities Act and the rules of the Financial Industry Regulatory Authority, Inc., or FINRA.

ADSs representing our ordinary shares sold pursuant to the registration statement of which this prospectus is a part will be authorized for listing and trading on The Nasdaq Global Select Market. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The Nasdaq Global Select Market or any securities market or other securities exchange of the securities covered by the prospectus supplement. Underwriters may make a market in our ADSs, but will not be obligated to do so and may discontinue any market making at any time without notice. We can make no assurance as to the liquidity of or the existence, development or maintenance of trading markets for any of the securities.

In order to facilitate the offering of the securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing the applicable security in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

The underwriters, dealers and agents may engage in other transactions with us, or perform other services for us, in the ordinary course of their business.

DESCRIPTION OF SHARE CAPITAL

The following describes our issued share capital, summarizes the material provisions of our articles of association and highlights certain differences in corporate law in the United Kingdom and the United States. Please note that this summary is not intended to be exhaustive. For further information please refer to the full version of our articles of association, which is included as an exhibit to the registration statement of which this prospectus is part.

General

We were incorporated in England and Wales with the Registrar of Companies of England and Wales, United Kingdom on January 28, 1997 under the name Biomed (UK) Limited as a private company limited by shares with company number 03308778.

On April 28, 2008, our name was changed to NuCana BioMed Limited. On August 29, 2017, we re-registered as a public limited company and changed our name to NuCana plc. Such re-registration required the passing of special resolutions by our shareholders to approve the re-registration as a public limited company, the name change to NuCana plc and to effect certain amendments to our articles of association.

Our registered office is located at 77/78 Cannon Street, London, EC4N 6AF, United Kingdom. The principal legislation under which we operate and our shares are issued is the Companies Act 2006.

Issued Share Capital

Our issued share capital as of August 31, 2018 was £1,287,408.32, comprised of 32,185,208 ordinary shares of £0.04 each. A summary of increases in, and changes to, our issued share capital since our incorporation is set out below.

We issued one quarter of one ordinary share of £4.00 each to each of London Law Services Limited and London Law Secretarial Limited, respectively, upon incorporation.

On March 20, 2008, we subdivided the outstanding issued fractions of ordinary shares of £4.00 each into 50 ordinary shares of £0.04 each and we subdivided the remaining authorized yet unissued fractions of the ordinary shares of £4.00 each into 2,450 ordinary shares of £0.04 each. Further, our authorized share capital was increased from £100 to £500,000 by the creation of 12,497,500 new ordinary shares of £0.04 each. On March 20, 2008, we issued 4,499,950 ordinary shares of £0.04 each.

On July 27, 2008, we issued a further 200,000 ordinary shares of £0.04 each. On August 20, 2009, we issued 350,000 ordinary shares of £0.04 each. On December 18, 2009, we issued 1,816,976 ordinary shares of £0.04 each (500,000 of which were available for such issue, having previously been issued to, but subsequently surrendered by, a shareholder). On December 14, 2010, we issued 1,566,359 ordinary shares of £0.04 each.

On November 24, 2011, we issued 7,483,334 series A convertible participating shares of £0.04 each.

On March 28, 2012, we issued 222,222 ordinary shares of £0.04 each.

On March 31, 2014, we issued 8,462,500 series B convertible participating shares of £0.004 each.

On November 30, 2016, we issued 37,500 ordinary shares of £0.04 each, pursuant to the exercise of share options granted under the 2012 Share Option Scheme.

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On December 31, 2016, we issued 45,750 ordinary shares of £0.04 each, pursuant to the exercise of share options granted under the 2016 Share Option Scheme.

On August 17, 2017, we issued 30,000 ordinary shares of £0.04 each, pursuant to the exercise of share options granted under the 2016 Share Option Scheme.

On September 14, 2017, we completed a one-for-four reverse share split and an associated, prior, bonus allotment of three ordinary shares and five series A convertible participating shares to eliminate fractional entitlements. References to the one-for-four reverse share split in this prospectus include the associated bonus allotment. The share numbers and nominal values set out above have, for presentational purposes, been adjusted to reflect the aforementioned reverse share split (which has necessitated reference to notional fractions of shares and resulted in certain numbers of shares having been rounded up). These share numbers and nominal values are therefore not representative of, for example, the entries made at the relevant time in our statutory registers nor filings we have made at the UK Registrar of Companies.

On October 2, 2017, immediately prior to closing our initial public offering, we converted all issued series A convertible participating shares, series B convertible participating shares, founder ordinary 1 shares and founder ordinary 2 shares into ordinary shares, on a one-for-one basis. For the purpose of facilitating the conversion of each series B convertible participating share (nominal value £0.004 per share), into an ordinary share (nominal value £0.04 per share), immediately prior to this conversion, on October 2, 2017, we allotted to holders of series B convertible participating shares an additional nine series B convertible participating shares for each series B convertible participating share held.

On October 2, 2017, we issued 7,596,505 ordinary shares pursuant to our initial public offering.

Ordinary Shares

As of August 31, 2018, we had issued and outstanding 32,185,208 ordinary shares of £0.04 each, held by 18 shareholders of record. Each issued ordinary share is fully paid.

Holders of ordinary shares are entitled to one vote for each share held of record on all matters submitted to a vote of shareholders and do not have cumulative voting rights.

Any distribution made as result of winding-up, dissolution or liquidation of our company and any dividend declared will be distributed in proportion to the number of fully paid ordinary shares held.

Options

We have established equity incentive plans pursuant to which we have issued options to purchase ordinary shares to employees and directors. As of August 31, 2018, there were 3,689,708 ordinary shares issuable upon exercise of outstanding options under our equity incentive plans. The options lapse after ten years from the date of the grant.

Registration Rights

We have entered into a registration rights agreement pursuant to which we have agreed under specified circumstances to file a registration statement to register the resale of the ordinary shares held by some of our existing shareholders, as well as to cooperate in specified public offerings of such shares. These rights are described below.

Demand Registration Rights. If at any time when we are eligible to use a Form F-3 registration statement, the holders of at least 25% of the registrable securities then outstanding have the right to demand that we file a Form F-3 registration statement with respect to such registrable securities.

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These registration rights are subject to specified conditions and limitations, including the right of the underwriters, if any, to limit the number of shares included in any such registration under specified circumstances. Upon such a request, we are required to use commercially reasonable efforts to effect such registration.

Company Registration. If we propose to register any of our equity securities under the Securities Act, other than in connection with certain specified registrations, including a registration relating solely to our employee equity incentive plans or a registration relating solely to certain business combinations or mergers involving us, the holders of these registrable securities are entitled to notice of such registration and are entitled to include their ordinary shares in the registration. Under certain circumstances, the underwriters, if any, may limit the number of ordinary shares included in any such registration.

Termination of Registration Rights. The registration rights granted under the registration rights agreement shall terminate upon the earlier to occur of (i) the fifth anniversary of the closing of our initial public offering and (ii) the date on which there are no registrable securities remaining pursuant to the registration rights agreement.

Articles of Association

The following is a summary of certain provisions of our articles of association. Please note that this is only a summary and is not intended to be exhaustive. For further information please refer to the full version of our articles of association, which is included as an exhibit to our most recent Annual Report on Form 20-F.

Shares and Rights Attaching to Them

General. All ordinary shares have the same rights and rank *pari passu* in all respects. Subject to the provisions of the Companies Act 2006 and any other relevant legislation, our board of directors may, from time to time, allot and issue shares following an ordinary resolution of the shareholders granting authority to the directors to allot shares (and if applicable, and not already disappplied, a special resolution to disapply pre-emption rights).

Our shares may be issued with or have attached to them any preferred, deferred, qualified or other special rights or restrictions, whether in relation to dividends, returns of capital, voting or otherwise, as set out in our articles of association or as the shareholders may determine by ordinary resolution (or, if the shareholders have not so determined, as our board of directors may determine).

Voting rights. Subject to any other provisions of our articles of association and without prejudice to any special rights, privileges or restrictions as to voting attached to any shares forming part of our share capital, the voting rights of shareholders are as follows. Unless a poll vote is demanded, shareholders shall vote on all resolutions on a show of hands. Our articles of association provide that a poll vote may be demanded before, or on the declaration of, the result of a vote on a show of hands: (a) by the chairman of a general meeting, (b) by at least five shareholders present at a meeting and entitled to vote, or (c) by any shareholder or shareholders present representing not less than ten per cent of the total voting rights or more than ten per cent of the total sum paid up on all voting shares. For these purposes, a shareholder will be present at a meeting if attending in person, by proxy, or, in the case of a shareholder that is a corporation (as broadly defined under the Companies Act 2006), by duly authorized representative.

On a show of hands, each shareholder present in person, and each duly authorized representative present in person of a shareholder that is a corporation, has one vote. On a show of hands, each proxy present in person who has been duly appointed by one or more shareholders has one vote, but a proxy has one vote for and one vote against a resolution if the proxy is instructed to vote on a resolution by more than one shareholder and is instructed to vote in different ways on such resolution.

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On a poll, each shareholder present in person or by proxy or, with respect to a corporation, by a duly authorized representative has one vote for each share held by the shareholder. We are prohibited from exercising any rights to attend or vote at meetings in respect of any shares held by us as treasury shares.

Restrictions on voting where sums overdue on shares. None of our shareholders is entitled to vote at any general meeting or at any separate class meeting in respect of any share held by him or her unless all calls or other sums payable by him or her in respect of that share have been paid.

Calls on shares. The directors may from time to time make calls on shareholders in respect of any amounts unpaid on their shares, whether in respect of nominal value of the shares or by way of premium. Shareholders are required to pay the called amount on shares subject to receiving at least 14 clear days' notice specifying the time and place for payment. Under our articles of association, a period of "clear days" excludes the day on which a notice is given or deemed to have been given and the day for which it is given or on which it is to take effect. If a shareholder fails to pay any part of a call, the board of directors may serve further notice naming another day not being less than 14 clear days from the date of the further notice requiring payment and stating that in the event of non-payment the shares in respect of which the call was made will be liable to be forfeited. Subsequent forfeiture requires a resolution by the board of directors.

Dividends. Subject to the U.K. Companies Act 2006, the provisions of all other relevant legislation, and our articles of association, we may by ordinary resolution declare dividends out of profits available for distribution in accordance with the respective rights of shareholders, but no such dividend shall exceed the amount recommended by the board of directors. If, in the opinion of the board of directors, our profits available for distribution justify such payments, the board of directors may pay fixed dividends payable on any of our shares with preferential rights, half-yearly or otherwise, on fixed dates and from time to time pay interim dividends to the holders of any class of shares. Subject to any special rights attaching to, or terms of issue of, any shares, all dividends shall be declared and paid according to the amounts paid up on the shares on which the dividend is paid. No dividend shall be payable to us in respect of any shares held by us as treasury shares.

We may, upon the recommendation of the board of directors, by ordinary resolution, direct payment of a dividend wholly or partly by the distribution of specific assets.

All dividends unclaimed for one year after having been declared may be invested or otherwise used at the directors' discretion for our benefit until claimed (subject as provided in the articles of association), and all dividends unclaimed after a period of 12 years from the date when such dividend became due for payment shall be forfeited and shall revert to us.

The board of directors may, if so authorized by ordinary resolution passed at any general meeting, offer any holders of the ordinary shares the right to elect to receive in lieu of that dividend an allotment of ordinary shares credited as fully paid.

We may cease to send any check or warrant by mail or may stop the transfer of any sum by any bank or other funds transfer system for any dividend payable on any of our shares, which is normally paid in that manner on those shares if in respect of at least two consecutive dividends the check or warrants have been returned undelivered or remain uncashed or the transfer has failed, or in respect of one dividend the check or warrant has been returned undelivered or remains uncashed or the transfer has failed and reasonable inquiries made by us have failed to establish any new address of the holder.

We or the directors may specify a "record date" on which persons registered as the holders of shares shall be entitled to receipt of any dividend.

Distribution of assets on winding-up. Subject to any special rights attaching to, or the terms of issue of any shares, on any winding-up of the company our surplus assets remaining after satisfaction of our liabilities will be distributed among our shareholders in proportion to their respective holdings of shares and the amounts paid up on those shares.

On any winding-up of the company (whether the liquidation is voluntary, under supervision or by the Court), the liquidator may with the authority of a special resolution of the company and any other sanction required by any relevant legislation, divide among our shareholders (excluding the company itself to the extent that it is a shareholder by virtue of its holding any shares or treasury shares) in specie or in kind the whole or any part of our assets (subject to any special rights attached to any shares issued by us in the future) and may for that purpose set such value as he deems fair upon any one or more class or classes of property and may determine how that division shall be carried out as between the shareholders or different classes of shareholders. The liquidator may, with that sanction, vest the whole or any part of the assets in trustees upon such trusts for the benefit of the shareholders as he with the relevant authority determines, and the liquidation of the company may be closed and the company dissolved, but so that no shareholders shall be compelled to accept any shares or other property in respect of which there is a liability.

Variation of rights. The rights or privileges attached to any class of shares may (unless otherwise provided by the terms of the issue of the shares of that class) be varied or abrogated with the consent in writing of the holders of three-fourths in requisite nominal value of the issued shares of that class (excluding any shares of that class held as treasury shares) or with the approval of a special resolution passed at a separate general meeting of the shareholders of that class, but not otherwise.

Transfer of shares. All of our shares are in registered form and may be transferred by a transfer in any usual or common form or any form acceptable to the board of directors and permitted by the Companies Act 2006 and any other relevant legislation.

The board of directors may decline to register a transfer of a share that is:

- not fully paid or on which we have a lien;
- (except where uncertificated shares are transferred without a written instrument) not lodged duly stamped (if it is required to be stamped) at our registered office or at such other place as the board of directors may appoint;
- (except where a certificate has not been issued) not accompanied by the certificate of the share to which it relates or such other evidence reasonably required by the directors to show the right of the transferor to make the transfer;
- in respect of more than one class of share; or
- in the case of a transfer to joint holders of a share, the number of joint holders to whom the share is to be transferred exceeds four.

Capital variations. We may, by ordinary resolution, consolidate and divide all or any of our share capital into shares of a larger nominal amount than our existing shares or sub-divide our shares, or any of them, into shares of a smaller nominal amount than our existing shares. Subject to the provisions of the Companies Act 2006 and any other applicable legislation, we may by special resolution reduce our share capital, any capital redemption reserve fund or any share premium account and may redeem or purchase any of our own shares.

Pre-emption rights. There are no rights of pre-emption under our articles of association in respect of transfers of issued ordinary shares. In certain circumstances, our shareholders may have statutory pre-emption rights under the Companies Act 2006 in respect of the allotment of new shares in the

company. These statutory pre-emption rights, when applicable, would require us to offer new shares for allotment to existing shareholders on a pro rata basis before allotting them to other persons. In such circumstances, the procedure for the exercise of such statutory pre-emption rights would be set out in the documentation by which such ordinary shares would be offered to our shareholders. These statutory pre-emption rights may be disapplied by a special resolution passed by shareholders in a general meeting in accordance with the provisions of the Companies Act 2006.

Directors

Number. Unless and until we in a general meeting of our shareholders otherwise determine, the number of directors comprising our board of directors shall not be subject to any maximum but shall not be less than two.

Classified board of directors. Our board of directors is divided into three classes, "Class I," whose initial term expires at the annual general meeting of the shareholders to be held in 2020, "Class II," whose initial term expires at the annual general meeting of the shareholders to be held in 2019, and "Class III", whose term expires at the annual general meeting of the shareholders to be held in 2021, with the classes as nearly equal in number as possible. The Class I directors are Hugh Griffith and Christopher Wood, the Class II directors are Rafaèle Tordjman, James Healy and Cyrille Leperlier, and the Class III directors are Isaac Cheng, Martin Mellish and Adam George.

Borrowing powers. Our board of directors may exercise all the powers of the company to borrow money, mortgage or charge all or any part or parts of its undertaking, property and uncalled capital, and issue debentures and other securities whether outright or as collateral security for any debt, liability or obligation of the company or of any third party.

Directors' interests and restrictions.

(a) The board of directors may, in accordance with our articles of association and the requirements of the Companies Act 2006, authorize a matter proposed to us which would, if not authorized, involve a breach by a director of his or her duty under section 175 of the Companies Act 2006 to avoid a situation in which he or she has, or can have, a direct or indirect interest that conflicts, or possibly may conflict, with our interests. A director is not required, by reason of being a director, to account to the company for any remuneration or other benefit that he or she derives from a relationship involving a conflict of interest or possible conflict of interest that has been authorized by the board of directors.

(b) Subject to the provisions of any relevant legislation and provided that he or she has disclosed to the directors the nature and extent of any material interest of his or hers, a director may be a party to, or otherwise interested in, any transaction, contract or arrangement and that director shall not, by reason of his or her office, be accountable to the company for any benefit that he or she derives from any such transaction or arrangement; and no such transaction or arrangement shall be liable to be voided on the ground of any such interest or benefit.

(c) Except as provided in our articles of association, a director shall not vote at a meeting of the directors in respect of any transaction or arrangement or any other proposal whatsoever in which he or she has an interest that is to his or her knowledge material (together with any person connected with him or her within the meaning of section 252 of the Companies Act 2006), other than (i) an interest in shares or debentures or other securities of the company, (ii) where permitted by the terms of any authorization of a conflict of interest or by an ordinary resolution, or (iii) in the circumstances set out in paragraph (d) below, and shall not be counted in the quorum at a meeting in relation to any resolution on which he or she is not entitled to vote.

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(d) A director shall (in the absence of some material interest other than those indicated below) be entitled to vote (and be counted in the quorum) in respect of any resolution concerning any of the following matters:

(i) the giving of any guarantee, security or indemnity to him or her in respect of money lent to or an obligation incurred by him or her at the request of or for the benefit of us or any of our subsidiaries;

(ii) the giving to a third party of any guarantee, security or indemnity in respect of a debt or obligation of ours or any of our subsidiaries for which he himself or she herself has assumed responsibility in whole or in part under a guarantee or indemnity or by the giving of security;

(iii) any proposal or contract concerning an offer of shares or debentures or other securities of or by the company or any of its subsidiaries, if he or she takes part because he or she is or may be entitled to participate as a holder of shares, debentures or other securities, or if he or she takes part in the underwriting, sub-underwriting or guarantee of the offer;

(iv) any proposal concerning any other company in which he or she is interested, directly or indirectly and whether as an officer or shareholder or otherwise, provided that he or she (together with persons connected with him or her) does not to his or her knowledge hold an interest in shares representing one percent or more of the issued shares of any class of such company or of the voting rights available to shareholders of the relevant company;

(v) any proposal concerning arrangements pursuant to which benefits are made available to our employees and which does not award him or her any privilege or benefit not generally awarded to the employees to whom such arrangement relates;

(vi) any proposal under which he or she may benefit concerning the giving of indemnities to our directors or other officers that the directors are empowered to give under our articles of association;

(vii) any proposal under which he or she may benefit concerning the purchase or maintenance of insurance for any of our directors or other officers; and

(viii) any proposal under which he or she may benefit concerning the provision to directors of funds to meet expenditures in defending proceedings.

(e) Where proposals are under consideration to appoint two or more directors to offices or employments with us or with any company in which we are interested or to fix or vary the terms of such appointments, such proposals may be divided and considered in relation to each director separately and in such case each of the directors concerned (if not debarred from voting under paragraph (d)(iv) above) shall be entitled to vote (and be counted in the quorum) in respect of each resolution, except that concerning his or her own appointment.

(f) If any question shall arise at any meeting as to the materiality of a director's interest or as to the entitlement of any director to vote and such question is not resolved by his or her agreeing voluntarily to abstain from voting, such question shall be referred to the chairman of the meeting (or where the interest concerns the chairman himself to the deputy chairman of the meeting) and his or her ruling in relation to any director shall be final and conclusive, except in a case where the nature or extent of the interests of the director concerned have not been fairly disclosed.

Remuneration.

(a) Each of the directors (other than alternate directors) may (in addition to any amounts payable under paragraph (b) and (c) below or under any other provision of our articles of association) be paid out of the funds of the company such sum by way of directors' fees as the board of directors may from time to time determine.

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(b) Any director who is appointed to hold any employment or executive office with us or who, by our request, goes or resides abroad for any purposes of the company or who otherwise performs services that in the opinion of the board of directors are outside the scope of his or her ordinary duties may be paid such additional remuneration (whether by way of salary, commission, participation in profits or otherwise) as the board of directors (or any duly authorized committee of the board of directors) may determine and either in addition to or in lieu of any remuneration provided for by or pursuant to any other article.

(c) Each director may be paid his or her reasonable traveling expenses (including hotel and incidental expenses) of attending and returning from meetings of the directors or committees of the board of directors or general meetings or any separate meeting of the holders of any class of our shares or any other meeting that as a director he or she is entitled to attend and shall be paid all expenses properly and reasonably incurred by him or her in the conduct of the company's business or in the discharge of his or her duties as a director.

Pensions and other benefits. The board of directors may exercise all the powers of the company to provide benefits, either by the payment of gratuities or pensions or by insurance or in any other manner whether similar to the foregoing or not, for any director or former director, or any person who is or was at any time employed by, or held an executive or other office or place of profit in, the company or any body corporate that is or has been a subsidiary of the company or a predecessor of the business of the company or of any such subsidiary and for the families and persons who are or was a dependent of any such persons and for the purpose of providing any such benefits contribute to any scheme trust or fund or pay any premiums.

Appointment and retirement of directors.

(a) The board of directors shall have power to appoint any person who is willing to act to be a director, either to fill a casual vacancy or as an additional director but so that the total number of directors shall not exceed the maximum number fixed (if any) by or in accordance with our articles of association. Any director so appointed shall retire from office at our annual general meeting following such appointment, and then shall be eligible for re-election for the remaining portion of the term of office of the Class to which he or she is eligible for election.

(b) Subject as provided in our articles of association, the shareholders may by ordinary resolution elect any person who is willing to act as a director either to fill a casual vacancy or as an addition to the existing directors or to replace a director removed from office under our articles of association but so that the total number of directors shall not at any one time exceed any maximum number fixed by or in accordance with our articles of association.

(c) Subject to paragraph (a) above and the initial terms described in "Description of Share Capital—Articles of Association—Directors—Classified board of directors", each director within each class shall retire at the third annual general meeting following the annual general meeting at which he or she was elected or last re-elected. Except where there is an increase in the number of directors (in which case the newly created directorships shall be apportioned by our board amongst our existing classes) or in accordance with paragraph (a) above, directors elected or re-elected at an annual general meeting shall be appointed to the class whose term expires at such meeting.

(d) A director retiring at an annual general meeting shall be eligible for re-election. If a retiring director is not re-elected, he or she shall hold office until the meeting elects someone in his or her place or, if it does not do so, until the end of the meeting.

Company name. The board of directors may resolve to change our company name.

Indemnity of officers. Subject to the provisions of any relevant legislation, each of our directors and other officers may be indemnified by us against all costs, charges, losses, expenses and

liabilities incurred by him in the execution and discharge of his duties or in relation to those duties. The Companies Act 2006 renders void an indemnity for a director against any liability attaching to him or her in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he or she is a director as described in “— Differences in Corporate Law — Liability of Directors and Officers.”

Shareholders' Meetings

Annual general meetings. We shall in each year hold an annual general meeting of our shareholders in addition to any other meetings in that year, and shall specify the meeting as such in the notice convening it. The annual general meeting shall be held at such time and place as the board of directors may appoint.

Calling of general meetings. The board of directors may call a general meeting of shareholders. The board of directors must call a general meeting if the shareholders and the Companies Act 2006 require them to do so. The arrangements for the calling of general meetings are described in “— Differences in Corporate Law — Notice of General Meetings” below.

Quorum of meetings. No business shall be transacted at any general meeting unless a quorum is present when the meeting proceeds to business but the absence of a quorum shall not preclude the appointment of a chairman, which shall not be treated as part of the business of a meeting. One or more qualifying persons present at a meeting and between them holding (or being the proxy or corporate representative of the holders of) at least one-third in number of the issued shares (excluding any shares held as treasury shares) entitled to vote on the business to be transacted are a quorum. A qualifying person for these purposes is an individual who is a shareholder, a person authorized to act as the representative of a shareholder (being a corporation) in relation to the meeting or a person appointed as proxy of a shareholder in relation to the meeting.

Other United Kingdom law considerations

Mandatory purchases and acquisitions. Pursuant to Sections 979 to 991 of the Companies Act 2006, where a takeover offer has been made for us and the offeror has acquired or unconditionally contracted to acquire not less than 90% in value of the shares to which the offer relates and not less than 90% of the voting rights carried by those shares, the offeror may give notice to the holder of any shares to which the offer relates which the offeror has not acquired or unconditionally contracted to acquire that he wishes to acquire, and is entitled to so acquire, those shares on the same terms as the general offer. The “squeeze-out” of the minority shareholders can be completed at the end of six weeks from the date the notice has been given, subject to the minority shareholders failing to successfully lodge an application to the court to prevent such squeeze-out any time prior to the end of those six weeks, following which the offeror can execute a transfer of the outstanding shares in its favor and pay the consideration to us, to be held on trust for the outstanding minority shareholders. The consideration offered to the outstanding minority shareholders whose shares are compulsorily acquired under the Companies Act 2006 must, in general, be the same as the consideration that was available under the takeover offer.

Sell-out. The Companies Act 2006 also gives our minority shareholders a right to be bought out in certain circumstances by an offeror who has made a takeover offer for all of our shares. The holder of shares to which the offer relates, and who has not otherwise accepted the offer, may require the offeror to acquire his shares if, prior to the expiry of the acceptance period for such offer, (i) the offeror has acquired or agreed to acquire not less than 90% in value of our voting shares, and (ii) not less than 90% of the voting rights carried by those shares. The offeror may impose a time limit on the rights of minority shareholders to be bought out that is not less than three months after the end of the acceptance period. If a shareholder exercises his rights to be bought out, the offeror is required to acquire those shares on the terms of the takeover offer or on such other terms as may be agreed.

Disclosure of interest in shares. Pursuant to Part 22 of the Companies Act 2006 and our articles of association, we are empowered to require, by notice in writing, any person whom we know to be, or have reasonable cause to believe to be, interested in our shares, or at any time during the three years immediately preceding the date on which the notice is issued has been so interested, within a reasonable time to disclose to us particulars of that person's own interest and (so far as is within that person's knowledge) particulars of any other interest, agreement or arrangement relating to the exercise of any rights conferred by the holding of the shares that subsists or subsisted in those shares.

Under our articles of association, if a person defaults in supplying us with the required particulars in relation to the shares in question (referred to herein as "default shares"), the board of directors may by notice direct that:

- in respect of the default shares, the relevant shareholder shall not be entitled to vote or exercise any other right conferred by his holding shares in relation to general meetings; or
- where the default shares represent at least 0.25% of their class, (a) any dividend or other money payable in respect of the default shares shall be retained by us without liability to pay interest and, if applicable, any election to receive ordinary shares instead of money in respect of the default shares shall be ineffective; (b) no transfers of shares by the relevant shareholder other than certain approved transfers may be registered (unless the shareholder himself is not in default and the transfer does not relate to default shares) or (c) any shares held by the relevant shareholder in uncertificated form shall be converted into certificated form.

Purchase of own shares. Under English law, a limited company may only purchase its own shares out of its distributable profits or the proceeds of a fresh issue of shares made for the purpose of financing the purchase, provided it is not restricted from doing so by its articles. A limited company may not purchase its own shares if, as a result of the purchase, there would no longer be any issued shares of the company other than redeemable shares or shares held as treasury shares. Shares must be fully paid in order to be repurchased.

We may purchase our own fully paid shares otherwise than on a recognized investment exchange pursuant to a purchase contract authorized by resolution of shareholders before the purchase takes place. Any authority will not be effective if any shareholder from whom we propose to purchase shares votes on the resolution and the resolution would not have been passed if he had not done so. The resolution authorizing the purchase must specify a date, not being later than five years after the passing of the resolution, on which the authority to purchase is to expire.

Preemptive Rights. English law generally provides shareholders with preemptive rights when new shares are issued for cash; however, it is possible for a company's articles of association, or shareholders in general meeting, to exclude preemptive rights. Such an exclusion of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the exclusion is contained in the articles of association, or from the date of the shareholder resolution, if the exclusion is by shareholder resolution. In either case, this exclusion would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). On June 27, 2018, our shareholders approved the exclusion of preemptive rights in connection with the allotment of shares with an aggregate nominal value of up to £640,000, for a period ending at the conclusion of our next annual general meeting. On September 14, 2017, our shareholders also approved the exclusion of preemptive rights for the allotment of ordinary shares in connection with our share schemes, up to an aggregate nominal value of £200,331 for a period of five years from the date of approval, which exclusion will need to be renewed upon expiration (i.e., at least every five years) to remain effective, but may be sought more frequently for additional five-year terms (or any shorter period).

City code on takeovers and mergers, or the Takeover Code. As a public company incorporated in England and Wales with its place of central management and control in the United Kingdom, we are

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subject to the United Kingdom City Code on Takeovers and Mergers (referred to herein as the Takeover Code). The Takeover Code contains rules concerning the conduct of takeover offers for the company. For example, under Rule 9 of the Takeover Code, if a person:

(a) acquires an interest in our shares that, when taken together with shares in which he or persons acting in concert with him are interested, carries 30% or more of the voting rights of our shares; or

(b) who, together with persons acting in concert with him, is interested in shares that in the aggregate carry not less than 30% and not more than 50% of the voting rights in the company, acquires additional interests in shares that increase the percentage of shares carrying voting rights in which that person is interested;

the acquirer and, depending on the circumstances, its concert parties, would be required (except with the consent of the Takeover Panel) to make a cash offer for our outstanding shares at a price not less than the highest price paid for any interests in the shares by the acquirer or its concert parties during the previous 12 months. Some provisions in the Takeover Code might have anti-takeover effects that could discourage an acquisition of us by others even if an acquisition would be beneficial to our shareholders.

Distributions and dividends. Under the Companies Act 2006, before a company can lawfully make a distribution or dividend, it must ensure that it has sufficient distributable reserves (on a non-consolidated basis). The basic rule is that a company's profits available for the purpose of making a distribution are its accumulated, realized profits, so far as not previously utilized by distribution or capitalization, less its accumulated, realized losses, so far as not previously written off in a reduction or reorganization of capital duly made. The requirement to have sufficient distributable reserves before a distribution or dividend can be paid applies to us and to each of our subsidiaries that has been incorporated under English law.

It is not sufficient that we, as a public company, have made a distributable profit for the purpose of making a distribution. An additional capital maintenance requirement is imposed on us to ensure that the net worth of the company is at least equal to the amount of its capital. A public company can only make a distribution:

(a) if, at the time that the distribution is made, the amount of its net assets (that is, the total excess of assets over liabilities) is not less than the total of its called up share capital and undistributable reserves; and

(b) if, and to the extent that, the distribution itself, at the time that it is made, does not reduce the amount of the net assets to less than that total.

Exchange controls. There are no governmental laws, decrees, regulations or other legislation in the United Kingdom that may affect the import or export of capital, including the availability of cash, cash equivalents and short-term deposits for use by us, or that may affect the remittance of dividends, interest, or other payments by us to non-resident holders of our ordinary shares or ADSs, other than withholding tax requirements. There is no limitation imposed by English law or in the articles of association on the right of non-residents to hold or vote shares.

Differences in Corporate Law

The applicable provisions of the Companies Act 2006 differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of the Companies Act 2006 applicable to us and the Delaware General

Corporation Law relating to shareholders' rights and protections. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to Delaware law and English law.

	<u>England and Wales</u>	<u>Delaware</u>
Number of Directors	Under the Companies Act 2006, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.
Removal of Directors	Under the Companies Act 2006, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided 28 clear days' notice of the resolution has been given to the company and its shareholders. On receipt of notice of an intended resolution to remove a director, the company must forthwith send a copy of the notice to the director concerned. Certain other procedural requirements under the Companies Act 2006 must also be followed such as allowing the director to make representations against his or her removal either at the meeting or in writing.	Under Delaware law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (a) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, shareholders may effect such removal only for cause, or (b) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.
Vacancies on the Board of Directors	Under English law, the procedure by which directors (other than a company's initial directors) are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public limited company by a single resolution of the shareholders such resolution must not be put to shareholders unless a resolution that it should be so made has first been agreed to by the shareholders without any vote being against it.	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (a) otherwise provided in the certificate of incorporation or by-laws of the corporation or (b) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.

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	England and Wales	Delaware
Annual General Meeting	<p>Under the Companies Act 2006, a public limited company must hold an annual general meeting in each six-month period beginning with the day following the company's annual accounting reference date.</p>	<p>Under Delaware law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.</p>
General Meeting	<p>Under the Companies Act 2006, a general meeting of the shareholders of a public limited company may be called by the directors.</p> <p>Shareholders holding at least 5% of the paid-up capital of the company carrying voting rights at general meetings can require the directors to call a general meeting and, if the directors fail to do so within a prescribed period, may themselves, or any of them representing more than one half of the total voting rights of all of them, call a general meeting.</p>	<p>Under Delaware law, special meetings of the stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.</p>
Notice of General Meetings	<p>Under the Companies Act 2006, 21 clear days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, at least 14 clear days' notice is required for any other general meeting of a public limited company which fulfil certain conditions. In addition, certain matters, such as resolutions to remove directors or auditors, require special notice, which is 28 clear days' notice. The shareholders of a company may in all cases consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the shareholders having a right to attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.</p>	<p>Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than 10 nor more than 60 days before the date of the meeting and shall specify the place, date, hour, and purpose or purposes of the meeting.</p>

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	<u>England and Wales</u>	<u>Delaware</u>
Quorum	Subject to the provisions of a company's Articles, the Companies Act provides that two shareholders present at a meeting (in person, by proxy or authorized under the Companies Act) shall constitute a quorum for companies with more than one shareholder.	The certificate of incorporation or bylaws may specify the number of shares, the holders of which shall be present or represented by proxy at any meeting in order to constitute a quorum, but in no event shall a quorum consist of less than one third of the shares entitled to vote at the meeting. In the absence of such specification in the certificate of incorporation or bylaws, a majority of the shares entitled to vote, present in person or represented by proxy, shall constitute a quorum at a meeting of stockholders.
Proxy	Under the Companies Act 2006, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.	Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.
Pre-emptive Rights	Under the Companies Act 2006, "equity securities", being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution ("ordinary shares") or (ii) rights to subscribe for, or to convert securities into, ordinary shares, proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless the period during which any such offer may be accepted as expired or the company has received notice of acceptance of refusal, or an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise (in each case in accordance with the provisions of the Companies Act 2006).	Under Delaware law, shareholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.

England and Wales

Delaware

Authority to Allot

Under the Companies Act 2006, the directors of a company must not allot shares or grant rights to subscribe for or to convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise (in each case in accordance with the provisions of the Companies Act 2006).

Under Delaware law, if the corporation's charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. It may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.

Liability of Directors and Officers

Under the Companies Act 2006, any provision (whether contained in a company's articles of association or any contract or otherwise) that purports to exempt a director of a company, to any extent, from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company is void.

Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act 2006, which provides exceptions for the company to (a) purchase and maintain insurance against such liability; (b) provide a "qualifying third party indemnity" (being an indemnity against liability incurred by the director to a person other than the company or an associated company; and (c) provide a "qualifying pension scheme indemnity" (being an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan).

Under Delaware law, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for:

- any breach of the director's duty of loyalty to the corporation or its stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or
- any transaction from which the director derives an improper personal benefit.

England and Wales

Delaware

Voting Rights

Under the model articles of public companies, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or by the company's articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act 2006, a poll may be demanded by (a) not fewer than five shareholders having the right to vote on the resolution; (b) any shareholder(s) representing not less than 10% of the total voting rights of all the shareholders having the right to vote on the resolution; or (c) any shareholder(s) holding shares in the company conferring a right to vote on the resolution being shares on which an aggregate sum has been paid up equal to not less than 10% of the total sum paid up on all the shares conferring that right. A company's articles of association may provide more extensive rights for shareholders to call a poll.

Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present, in person or by proxy, who, being entitled to vote, vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present, in person or by proxy, at the meeting.

Delaware law provides that, unless otherwise provided in the certificate of incorporation, each stockholder is entitled to one vote for each share of capital stock held by such stockholder.

England and Wales

Delaware

Shareholder Vote on Certain Transactions

The Companies Act 2006 provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors that are used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. These arrangements require:

- the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number of shareholders or creditors representing 75% in value of the capital held by, or a class thereof, the class of shareholders or creditors, or class thereof present and voting, either in person or by proxy; and
- the approval of the court.

Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires:

- the approval of the board of directors; and
- approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of a corporation entitled to vote on the matter.

Standard of Conduct for Directors

Under English law, a director owes various statutory and fiduciary duties to the company, including: to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its shareholders as a whole, subject in certain specified circumstances to consider or act in the interests of the creditors of the company;

- to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or possibly conflicts, with the interests of the company;
- to act in accordance with the company's constitution and only exercise his powers for the purposes for which they are conferred;
- to exercise independent judgement;
- to exercise reasonable care, skill and diligence;

Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the stockholders.

Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to

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- not to accept benefits from a third party conferred by reason of his being a director or doing, or not doing, anything as a director; and
- a duty to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.

be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation.

In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.

Shareholder Litigation

Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the Companies Act 2006 provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from an act or omission involving a director's negligence, default, breach of duty or breach of trust and (ii) a shareholder may bring a claim for a court order where the company's affairs have been or are being conducted in a manner that is unfairly prejudicial to some or all of its shareholders.

Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must:

- state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiff's shares thereafter devolved on the plaintiff by operation of law; and
- allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the reasons for the plaintiff's failure to obtain the action; or
- State the reasons for not making the effort.

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Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.

Listing

Our ADSs are listed on The Nasdaq Global Select Market under the symbol "NCNA."

Transfer Agent and Registrar

Our share register is maintained by our registrar, Computershare Investor Services plc. The transfer agent and registrar for our ADSs is Citibank N.A.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer pursuant to this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we so indicate in a prospectus supplement, the terms of any debt securities offered under such prospectus supplement may differ from the terms we describe below, and to the extent the terms set forth in a prospectus supplement differ from the terms described below, the terms set forth in the prospectus supplement shall control.

We may sell from time to time, in one or more offerings under this prospectus, debt securities, which may be senior or subordinated. We will issue any such senior debt securities under a senior indenture that we will enter into with a trustee to be named in the senior indenture. We will issue any such subordinated debt securities under a subordinated indenture, which we will enter into with a trustee to be named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement, of which this prospectus is a part. We use the term "indentures" to refer to either the senior indenture or the subordinated indenture, as applicable. The indentures will be qualified under the Trust Indenture Act of 1939, as in effect on the date of the indenture. We use the term "debenture trustee" to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities.

General

Each indenture provides that debt securities may be issued from time to time in one or more series and may be denominated and payable in foreign currencies or units based on or relating to foreign currencies. Neither indenture limits the amount of debt securities that may be issued thereunder, and each indenture provides that the specific terms of any series of debt securities shall be set forth in, or determined pursuant to, an authorizing resolution and/or a supplemental indenture, if any, relating to such series.

We will describe in each prospectus supplement the following terms relating to a series of debt securities:

- title or designation;
- the aggregate principal amount and any limit on the amount that may be issued;
- the currency or units based on or relating to currencies in which debt securities of such series are denominated and the currency or units in which principal or interest or both will or may be payable;
- whether we will issue the series of debt securities in global form, the terms of any global securities and who the depository will be;
- the maturity date and the date or dates on which principal will be payable;
- the interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the date or dates interest will be payable and the record dates for interest payment dates or the method for determining such dates;

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- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- the terms of the subordination of any series of subordinated debt;
- the place or places where payments will be payable;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional redemption provisions;
- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities;
- whether the indenture will restrict our ability to pay dividends, or will require us to maintain any asset ratios or reserves;
- whether we will be restricted from incurring any additional indebtedness;
- a discussion of any material or special U.S. federal income tax considerations applicable to a series of debt securities;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities. We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms, if any, on which a series of debt securities may be convertible into or exchangeable for our ordinary shares or our other securities. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of ordinary shares or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale; No Protection in Event of a Change of Control or Highly Leveraged Transaction

The indentures do not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate.

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change of control or in the event of a highly leveraged transaction (whether or not such transaction results in a change of control), which could adversely affect holders of debt securities.

Events of Default Under the Indenture

The following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and our failure continues for 90 days and the time for payment has not been extended or deferred;

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- if we fail to pay the principal, or premium, if any, when due and the time for payment has not been extended or delayed;
- if we fail to observe or perform any other covenant set forth in the debt securities of such series or the applicable indentures, other than a covenant specifically relating to and for the benefit of holders of another series of debt securities, and our failure continues for 90 days after we receive written notice from the debenture trustee or holders of not less than a majority in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur as to us.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an event of default with respect to any other series of debt securities. The occurrence of an event of default may constitute an event of default under any bank credit agreements we may have in existence from time to time. In addition, the occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness outstanding from time to time.

If an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than a majority in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the debenture trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) of and premium and accrued and unpaid interest, if any, on all debt securities of that series. Before a judgment or decree for payment of the money due has been obtained with respect to debt securities of any series, the holders of a majority in principal amount of the outstanding debt securities of that series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal, premium, if any, and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the applicable indenture (including payments or deposits in respect of principal, premium or interest that had become due other than as a result of such acceleration). We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

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A holder of the debt securities of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

- These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.
- the holder previously has given written notice to the debenture trustee of a continuing event of default with respect to that series;
- the holders of at least a majority in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and
- the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series (or at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) other conflicting directions within 60 days after the notice, request and offer.

We will periodically file statements with the applicable debenture trustee regarding our compliance with specified covenants in the applicable indenture.

Modification of Indenture; Waiver

The debenture trustee and we may change the applicable indenture without the consent of any holders with respect to specific matters, including:

- to fix any ambiguity, defect or inconsistency in the indenture; and
- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series issued pursuant to such indenture.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) that is affected. However, the debenture trustee and we may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or any premium payable upon the redemption of any debt securities;
- reducing the principal amount of discount securities payable upon acceleration of maturity;
- making the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment or waiver.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such

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series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series or in respect of a covenant or provision, which cannot be modified or amended without the consent of the holder of each outstanding debt security of the series affected; *provided, however*, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for obligations to:

- the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged with respect to a series, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, the premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange, and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange or in the applicable indenture, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under the applicable indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee under such indenture must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay the principal of and any premium and interest due on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check which we will mail to the holder. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the debenture trustee in the City of New York as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any debt securities which remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Subordination of Subordinated Debt Securities

Our obligations pursuant to any subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of senior indebtedness we may incur. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

General

We may issue warrants to purchase our ordinary shares represented by ADSs and/or debt securities in one or more series together with other securities or separately, as described in the applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the warrant agreements and the prospectus supplement relating to the warrants.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the designation, amount and terms of the securities purchasable upon exercise of the warrants;
- if applicable, the exercise price for our ADSs and the number of ADSs to be received upon exercise;
- if applicable, the exercise price for our debt securities, the amount of debt securities to be received upon exercise, and a description of that series of debt securities;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences and any applicable material U.K. tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- if applicable, the date from and after which the warrants and the ADSs and/or debt securities will be separately transferable;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of the warrants, if any;
- any redemption or call provisions;
- whether the warrants may be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Transfer Agent and Registrar

The transfer agent and registrar for any warrants will be set forth in the applicable prospectus supplement.

DESCRIPTION OF RIGHTS

General

We may issue rights to our shareholders to purchase our ordinary shares represented by ADSs or the other securities described in this prospectus. We may offer rights separately or together with one or more additional rights, debt securities, ordinary shares represented by ADSs, or warrants, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. Each series of rights will be issued under a separate rights agreement to be entered into between us and a bank or trust company, as rights agent. The rights agent will act solely as our agent in connection with the certificates relating to the rights of the series of certificates and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights. The following description sets forth certain general terms and provisions of the rights to which any prospectus supplement may relate. The particular terms of the rights to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the rights so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the rights, rights agreement or rights certificates described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable rights agreement and rights certificate for additional information before you decide whether to purchase any of our rights. We will provide in a prospectus supplement the following terms of the rights being issued:

- the date of determining the shareholders entitled to the rights distribution;
- the aggregate number of ordinary shares represented by ADSs or other securities purchasable upon exercise of the rights;
- the exercise price;
- the aggregate number of rights issued;
- whether the rights are transferrable and the date, if any, on and after which the rights may be separately transferred;
- the date on which the right to exercise the rights will commence, and the date on which the right to exercise the rights will expire;
- the method by which holders of rights will be entitled to exercise;
- the conditions to the completion of the offering, if any;
- the withdrawal, termination and cancellation rights, if any;
- whether there are any backstop or standby purchaser or purchasers and the terms of their commitment, if any;
- whether shareholders are entitled to oversubscription rights, if any;
- any applicable material U.S. federal income tax considerations and any applicable material U.K. tax considerations; and
- any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights, as applicable.

Each right will entitle the holder of rights to purchase for cash the principal amount of ordinary shares represented by ADSs or other securities at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of

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the rights agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the ordinary shares represented by ADS or other securities, as applicable, purchasable upon exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than shareholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

Rights Agent

The rights agent for any rights we offer will be set forth in the applicable prospectus supplement.

DESCRIPTION OF UNITS

The following description, together with the additional information that we include in any applicable prospectus supplements summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus, as well as any related free writing prospectuses and the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each security included in the unit. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those set forth in any prospectus supplement or as described under "Description of Share Capital," "Description of American Depositary Shares," "Description of Debt Securities," "Description of Warrants," and "Description of Rights" will apply to each unit, as applicable, and to any ordinary shares represented by ADSs, debt security, warrant or right included in each unit, as applicable.

Unit Agent

The name and address of the unit agent, if any, for any units we offer will be set forth in the applicable prospectus supplement.

Issuance in Series

We may issue units in such amounts and in such numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

DESCRIPTION OF AMERICAN DEPOSITARY SHARES

American Depositary Shares

Citibank, N.A., or Citibank, has agreed to act as the depository for the ADSs. Citibank's depository offices are located at 388 Greenwich Street, New York, New York 10013. ADSs represent ownership interests in securities that are on deposit with the depository. ADSs may be represented by certificates that are commonly known as American Depositary Receipts, or ADRs. The depository typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank, N.A., London Branch.

We have appointed Citibank as depository pursuant to a deposit agreement. A copy of the deposit agreement is on file with the SEC under cover of a registration statement on Form F-6. You may obtain a copy of the deposit agreement from the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and from the SEC's website (www.sec.gov). Please refer to registration number 333-220392 when retrieving such copy.

We are providing you with a summary description of the material terms of the ADSs and of your material rights as an owner of ADSs. Please remember that summaries by their nature lack the precision of the information summarized and that the rights and obligations of an owner of ADSs will be determined by reference to the terms of the deposit agreement and not by this summary. We urge you to review the deposit agreement in its entirety.

Each ADS represents the right to receive, and to exercise the beneficial ownership interests in, one ordinary share that is on deposit with the depository or custodian. An ADS also represents the right to receive, and to exercise the beneficial interests in, any other property received by the depository or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. We and the depository may agree to change the ADS-to-share ratio by amending the deposit agreement. This amendment may give rise to, or change, the depository fees payable by ADS owners. The custodian, the depository and their respective nominees will hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depository, the custodian or their nominees. Beneficial ownership in the deposited property will under the terms of the deposit agreement be vested in the beneficial owners of the ADSs. The depository, the custodian and their respective nominees will be the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. A beneficial owner of ADSs may or may not be the holder of ADSs. Beneficial owners of ADSs will be able to receive, and to exercise beneficial ownership interests in, the deposited property only through the registered holders of the ADSs, the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depository, and the depository (on behalf of the owners of the corresponding ADSs) directly, or indirectly, through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.

If you become an owner of ADSs, you will become a party to the deposit agreement and therefore will be bound to its terms and to the terms of any ADR that represents your ADSs. The deposit agreement and the ADR specify our rights and obligations as well as your rights and obligations as owner of ADSs and those of the depository. As an ADS holder you appoint the depository to act on your behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of ordinary shares will continue to be governed by the laws of England and Wales, which may be different from the laws in the United States.

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with

such reporting requirements and obtaining such approvals. Neither the depositary, the custodian, us or any of their or our respective agents or affiliates shall be required to take any actions whatsoever on your behalf to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations. You agree to comply with information requests from us pursuant to applicable laws, stock exchange rules and our Articles of Association. We may restrict transfers of ADSs and take other actions necessary to comply with any applicable ownership restrictions.

As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depositary will hold on your behalf the shareholder rights attached to the ordinary shares underlying your ADSs. As an owner of ADSs you will be able to exercise the shareholders rights for the ordinary shares represented by your ADSs through the depositary only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.

As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depositary in your name reflecting the registration of uncertificated ADSs directly on the books of the depositary (commonly referred to as the direct registration system or DRS). The direct registration system reflects the uncertificated (book-entry) registration of ownership of ADSs by the depositary. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depositary to the holders of the ADSs. The direct registration system includes automated transfers between the depositary and The Depository Trust Company, or DTC, the central book-entry clearing and settlement system for equity securities in the United States. If you decide to hold your ADSs through your brokerage or safekeeping account, you must rely on the procedures of your broker or bank to assert your rights as ADS owner. Banks and brokers typically hold securities such as the ADSs through clearing and settlement systems such as DTC. The procedures of such clearing and settlement systems may limit your ability to exercise your rights as an owner of ADSs. Please consult with your broker or bank if you have any questions concerning these limitations and procedures. All ADSs held through DTC will be registered in the name of a nominee of DTC, which nominee will be the only "holder" of such ADSs for purposes of the deposit agreement and any applicable ADR. This summary description assumes you have opted to own the ADSs directly by means of an ADS registered in your name and, as such, we will refer to you as the "holder." When we refer to "you," we assume the reader owns ADSs and will own ADSs at the relevant time.

The registration of the ordinary shares in the name of the depositary or the custodian shall, to the maximum extent permitted by applicable law, vest in the depositary or the custodian the record ownership in the applicable ordinary shares with the beneficial ownership rights and interests in such ordinary shares being at all times vested with the beneficial owners of the ADSs representing the ordinary shares. The depositary or the custodian shall at all times be entitled to exercise the beneficial ownership rights in all deposited property, in each case only on behalf of the holders and beneficial owners of the ADSs representing the deposited property.

Dividends and Other Distributions

As a holder of ADSs, you generally have the right to receive the distributions we make on the securities deposited with the custodian. Your receipt of these distributions may be limited, however, by practical considerations and legal limitations. Holders of ADSs will receive such distributions under the terms of the deposit agreement in proportion to the number of ADSs held as of the specified record date, after deduction the applicable fees, taxes and expenses.

Distributions of Cash

Whenever we make a cash distribution for the securities on deposit with the custodian, we will deposit the funds with the custodian. Upon receipt of confirmation of the deposit of the requisite funds, the depositary will arrange for the funds to be converted into U.S. dollars and for the distribution of the U.S. dollars to the holders, subject to the laws and regulations of England and Wales. The conversion into U.S. dollars will take place only if practicable and if the U.S. dollars are transferable to the United States. The depositary will apply the same method for distributing the proceeds of the sale of any property (such as undistributed rights) held by the custodian in respect of securities on deposit.

The distribution of cash will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. The depositary will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable holders and beneficial owners of ADSs until the distribution can be effected or the funds that the depositary holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States.

Distributions of Shares

Whenever we make a free distribution of ordinary shares for the securities on deposit with the custodian, we will deposit the applicable number of ordinary shares with the custodian. Upon receipt of confirmation of such deposit, the depositary will either distribute to holders new ADSs representing the ordinary shares deposited or modify the ADS-to-ordinary shares ratio, in which case each ADS you hold will represent rights and interests in the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-ordinary shares ratio upon a distribution of ordinary shares will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depositary may sell all or a portion of the new ordinary shares so distributed.

No such distribution of new ADSs will be made if it would violate a law (e.g., the U.S. securities laws) or if it is not operationally practicable. If the depositary does not distribute new ADSs as described above, it may sell the ordinary shares received upon the terms described in the deposit agreement and will distribute the proceeds of the sale as in the case of a distribution of cash.

Distributions of Rights

Whenever we intend to distribute rights to purchase additional ordinary shares, we will give prior notice to the depositary and we will assist the depositary in determining whether it is lawful and reasonably practicable to distribute rights to purchase additional ADSs to holders.

The depositary will establish procedures to distribute rights to purchase additional ADSs to holders and to enable such holders to exercise such rights if it is lawful and reasonably practicable to make the rights available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement (such as opinions to address the lawfulness of the transaction). You may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs upon the exercise of your rights. The depositary is not obligated to establish procedures to facilitate the distribution and exercise by holders of rights to purchase new ordinary shares other than in the form of ADSs.

The depositary will not distribute the rights to you if:

- we do not timely request that the rights be distributed to you or we request that the rights not be distributed to you; or

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- we fail to deliver satisfactory documents to the depositary; or
- it is not reasonably practicable to distribute the rights.

The depositary will sell the rights that are not exercised or not distributed if such sale is lawful and reasonably practicable. The proceeds of such sale will be distributed to holders as in the case of a cash distribution. If the depositary is unable to sell the rights, it will allow the rights to lapse.

Elective Distributions

Whenever we intend to distribute a dividend payable at the election of shareholders either in cash or in additional shares, we will give prior notice thereof to the depositary and will indicate whether we wish the elective distribution to be made available to you. In such case, we will assist the depositary in determining whether such distribution is lawful and reasonably practicable.

The depositary will make the election available to you only if it is reasonably practicable and if we have provided all of the documentation contemplated in the deposit agreement. In such case, the depositary will establish procedures to enable you to elect to receive either cash or additional ADSs, in each case as described in the deposit agreement.

If the election is not made available to you, you will receive either cash or additional ADSs, depending on what a shareholder in England and Wales would receive upon failing to make an election, as more fully described in the deposit agreement.

Other Distributions

Whenever we intend to distribute property other than cash, ordinary shares or rights to purchase additional ordinary shares, we will notify the depositary in advance and will indicate whether we wish such distribution to be made to you. If so, we will assist the depositary in determining whether such distribution to holders is lawful and reasonably practicable.

If it is reasonably practicable to distribute such property to you and if we provide all of the documentation contemplated in the deposit agreement, the depositary will distribute the property to the holders in a manner it deems practicable.

The distribution will be made net of fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes and governmental charges, the depositary may sell all or a portion of the property received.

The depositary will not distribute the property to you and will sell the property if:

- we do not request that the property be distributed to you or if we ask that the property not be distributed to you; or
- we do not deliver satisfactory documents to the depositary; or
- the depositary determines that all or a portion of the distribution to you is not reasonably practicable.

The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

Redemption

Whenever we decide to redeem any of the securities on deposit with the custodian, we will notify the depositary in advance. If it is practicable and if we provide all of the documentation contemplated in the deposit agreement, the depositary will provide notice of the redemption to the holders.

The custodian will be instructed to surrender the shares being redeemed against payment of the applicable redemption price. The depository will convert the redemption funds received into U.S. dollars upon the terms of the deposit agreement and will establish procedures to enable holders to receive the net proceeds from the redemption upon surrender of their ADSs to the depository. You may have to pay fees, expenses, taxes and other governmental charges upon the redemption of your ADSs. If less than all ADSs are being redeemed, the ADSs to be retired will be selected by lot or on a pro rata basis, as the depository may determine.

Changes Affecting Ordinary Shares

The ordinary shares held on deposit for your ADSs may change from time to time. For example, there may be a change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of such ordinary shares or a recapitalization, reorganization, merger, consolidation or sale of assets of our company.

If any such change were to occur, your ADSs would, to the extent permitted by law, represent the right to receive the property received or exchanged in respect of the ordinary shares held on deposit. The depository may in such circumstances deliver new ADSs to you, amend the deposit agreement, the ADRs and the applicable registration statement(s) on Form F-6, call for the exchange of your existing ADSs for new ADSs and take any other actions that are appropriate to reflect as to the ADSs the change affecting the ordinary shares. If the depository may not lawfully distribute such property to you, the depository may sell such property and distribute the net proceeds to you as in the case of a cash distribution.

Issuance of ADSs upon Deposit of Ordinary Shares

Any ordinary shares being offered pursuant to this prospectus will be deposited by us with the custodian. Upon receipt of confirmation of such deposit, the depository will issue ADSs pursuant to our instruction.

The depository may create ADSs on your behalf if you or your broker deposit ordinary shares with the custodian. The depository will deliver these ADSs to the person you indicate only after you pay any applicable issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian and provide such documentation as may be required pursuant to the deposit agreement. Your ability to deposit ordinary shares and receive ADSs may be limited by U.S. and England and Wales legal considerations applicable at the time of deposit.

The issuance of ADSs may be delayed until the depository or the custodian receives confirmation that all required approvals have been given and that the ordinary shares have been duly transferred to the custodian. The depository will only issue ADSs in whole numbers.

When you make a deposit of ordinary shares, you will be responsible for transferring good and valid title to the depository. As such, you will be deemed to represent and warrant that:

- the ordinary shares are duly authorized, validly allotted and issued, fully paid, not subject to any call for the payment of further capital and legally obtained;
- all preemptive (and similar) rights, if any, with respect to such ordinary shares have been validly waived, disappplied or exercised;
- you are duly authorized to deposit the ordinary shares;
- the ordinary shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, and are not, and the ADSs issuable upon such deposit will not be, "restricted securities" (as defined in the deposit agreement); and
- the ordinary shares presented for deposit have not been stripped of any rights or entitlements.

If any of the representations or warranties are incorrect in any way, we and the depositary may, at your cost and expense, take any and all actions necessary to correct the consequences of the misrepresentations.

Transfer, Combination and Split Up of ADRs

As an ADR holder, you will be entitled to transfer, combine or split up your ADRs and the ADSs evidenced thereby. For transfers of ADRs, you will have to surrender the ADRs to be transferred to the depositary and also must:

- ensure that the surrendered ADR is properly endorsed or otherwise in proper form for transfer;
- provide such proof of identity and genuineness of signatures, and of such other matters contemplated in the deposit agreement, as the depositary deems appropriate;
- comply with applicable laws and regulations, including regulations imposed by us and the depositary consistent with the deposit agreement, the ADR and applicable law;
- provide any transfer stamps required by the State of New York or the United States; and
- pay all applicable fees, charges, expenses, taxes and other government charges payable by ADR holders pursuant to the terms of the deposit agreement, upon the transfer of ADRs.

To have your ADRs either combined or split up, you must surrender the ADRs in question to the depositary with your request to have them combined or split up, and you must pay all applicable fees, charges and expenses payable by ADR holders, pursuant to the terms of the deposit agreement, upon a combination or split up of ADRs.

Withdrawal of Ordinary Shares Upon Cancellation of ADSs

As a holder, you will be entitled to present your ADSs to the depositary for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. Your ability to withdraw the ordinary shares held in respect of the ADSs may be limited by U.S. and England and Wales considerations applicable at the time of withdrawal. In order to withdraw the ordinary shares represented by your ADSs, you will be required to pay to the depositary the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares. You assume the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

If you hold ADSs registered in your name, the depositary may ask you to provide proof of identity and genuineness of any signature and such other documents as the depositary may deem appropriate before it will cancel your ADSs. The withdrawal of the ordinary shares represented by your ADSs may be delayed until the depositary receives satisfactory evidence of compliance with all applicable laws and regulations. Please keep in mind that the depositary will only accept ADSs for cancellation that represent a whole number of securities on deposit.

You will have the right to withdraw the securities represented by your ADSs at any time except as a result of:

- temporary delays that may arise because (i) the transfer books for the ordinary shares or ADSs are closed, or (ii) ordinary shares are immobilized on account of a shareholders' meeting or a payment of dividends;
- obligations to pay fees, taxes and similar charges; or
- restrictions imposed because of laws or regulations applicable to ADSs or the withdrawal of securities on deposit.

The deposit agreement may not be modified to impair your right to withdraw the securities represented by your ADSs except to comply with mandatory provisions of law.

Voting Rights

As a holder, you generally have the right under the deposit agreement to instruct the depositary to exercise the voting rights for the ordinary shares represented by your ADSs. The voting rights of holders of ordinary shares are described in “Description of Share Capital—Articles of Association” in this prospectus.

At our request, the depositary will distribute to you any notice of shareholders’ meeting received from us together with information explaining how to instruct the depositary to exercise the voting rights of the securities represented by ADSs.

If the depositary timely receives voting instructions from a holder of ADSs, it will endeavor to vote the securities (in person or by proxy) represented by the holder’s ADSs as follows:

- In the event of voting by show of hands, the depositary will vote (or cause the custodian to vote) all ordinary held on deposit at that time in accordance with the voting instructions received from a majority of holders of ADSs who provide timely voting instructions.
- In the event of voting by poll, the depositary will vote (or cause the custodian to vote) the ordinary shares held on deposit in accordance with the voting instructions received from the holders of ADSs.

The depositary will not join in demanding a vote by poll.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated herein). If voting is by poll and the depositary does not receive timely voting instructions from a holder of ADSs, such holder shall be deemed to have instructed the depositary to give a discretionary proxy to a person designated by us to vote the deposited securities represented by such ADSs in any manner such person wishes, which may not be in your best interests; provided, however, that no such discretionary proxy shall be given with respect to any matter to be voted upon as to which we inform the depositary that (a) we do not wish such proxy to be given, (b) substantial opposition exists, or (c) the rights of holders of deposited securities may be adversely affected. Please note that the ability of the depositary to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities on deposit. We cannot assure you that you will receive voting materials in time to enable you to return voting instructions to the depositary in a timely manner.

Fees and Charges

As an ADS holder, you will be required to pay the following fees under the terms of the deposit agreement:

<u>Service</u>	<u>Fee</u>
Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares or upon a change in the ADS(s)-to-ordinary shares ratio), excluding ADS issuances as a result of distributions of ordinary shares	Up to \$0.05 per ADS issued
Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property or upon a change in the ADS(s)-to-ordinary shares ratio)	Up to \$0.05 per ADS cancelled
Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to \$0.05 per ADS held
Distribution of ADSs pursuant to (i) share dividends or other distributions, or (ii) exercise of rights to purchase additional ADSs	Up to \$0.05 per ADS held
Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to \$0.05 per ADS held
ADS services	Up to \$0.05 per ADS held on the applicable record date(s) established by the depository

As an ADS holder you will also be responsible to pay certain charges such as:

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depository or any nominees upon the making of deposits and withdrawals, respectively;
- certain cable, telex and facsimile transmission and delivery expenses;
- the expenses and charges incurred by the depository in the conversion of foreign currency;
- the fees and expenses incurred by the depository in connection with compliance with exchange control regulations and other regulatory requirements applicable to ordinary shares, ADSs and ADRs; and
- the fees and expenses incurred by the depository, the custodian, or any nominee in connection with the servicing or delivery of deposited property.

ADS fees and charges payable upon (i) the issuance of ADSs, and (ii) the cancellation of ADSs are charged to the person to whom the ADSs are issued (in the case of ADS issuances) and to the person whose ADSs are cancelled (in the case of ADS cancellations). In the case of ADSs issued by the depository into DTC, the ADS issuance and cancellation fees and charges may be deducted from distributions made through DTC, and may be charged to the DTC participant(s) receiving the ADSs being issued or the DTC participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the beneficial owner(s) and will be charged by the DTC participant(s) to the account of the

applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participants as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are charged to the holders as of the applicable ADS record date. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs.

In the event of refusal to pay the depositary fees or charges, the depositary may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary fees and charges from any distribution to be made to the ADS holder.

Note that the fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary. You will receive prior notice of such changes. The depositary may reimburse us for certain expenses incurred by us in respect of the ADR program, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary agree from time to time.

Amendments and Termination

We may agree with the depositary to modify the deposit agreement at any time without your consent. We undertake to give ADS holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to your substantial rights any modifications or supplements that are reasonably necessary for the ADSs to be registered under the Securities Act or to be eligible for book-entry settlement, in each case without imposing or increasing the fees and charges you are required to pay. In addition, we may not be able to provide you with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

You will be bound by the modifications to the deposit agreement if you continue to hold your ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent you from withdrawing the ordinary shares represented by your ADSs (except as permitted by law).

We have the right to direct the depositary to terminate the deposit agreement. Similarly, the depositary may in certain circumstances on its own initiative terminate the deposit agreement. In either case, the depositary must give notice to the holders at least 30 days before termination. Until termination, your rights under the deposit agreement will be unaffected.

Termination

After termination, the depositary will continue to collect distributions received (but will not distribute any such property until you request the cancellation of your ADSs) and may sell the securities held on deposit. After the sale, the depositary will hold the proceeds from such sale and any other funds then held for the holders of ADSs in a non-interest bearing account. At that point, the depositary will have no further obligations to ADS holders other than to account for the funds then held for the holders of ADSs still outstanding (after deduction of applicable fees, taxes and expenses).

In connection with the termination of the deposit agreement, the depositary may, but shall not be obligated to, independently and without the need for any action by us, make available to holders a

means to withdraw the ordinary shares and other deposited securities represented by their ADSs and to direct the deposit of such ordinary shares and other deposited securities into an unsponsored American depositary shares program established by the depositary, upon such terms and conditions as the depositary may deem reasonably appropriate, subject however, in each case, to satisfaction of the applicable registration requirements by the unsponsored American depositary shares program under the Securities Act, and to receipt by the depositary of payment of the applicable fees and charges of, and reimbursement of the applicable expenses incurred by, the depositary.

Books of Depositary

The depositary will maintain ADS holder records at its depositary office. You may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

The depositary will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up and transfer of ADSs. These facilities may be closed from time to time, to the extent not prohibited by law.

Transmission of Notices, Reports and Proxy Soliciting Material

The depositary will make available for your inspection at its office all communications that it receives from us as a holder of deposited securities that we make generally available to holders of deposited securities. Subject to the terms of the deposit agreement, the depositary will send you copies of those communications or otherwise make those communications available to you if we ask it to.

Limitations on Obligations and Liabilities

The deposit agreement limits our obligations and the depositary's obligations to you. Please note the following:

- We and the depositary are obligated only to take the actions specifically stated in the deposit agreement without negligence or bad faith.
- The depositary disclaims any liability for any failure to carry out voting instructions, for any manner in which a vote is cast or for the effect of any vote, provided it acts in good faith and in accordance with the terms of the deposit agreement.
- The depositary disclaims any liability for any failure to accurately determine the lawfulness or practicality of any action, for the content of any document forwarded to you on our behalf or for the accuracy of any translation of such a document, for the investment risks associated with investing in ordinary shares, for the validity or worth of the ordinary shares, for any tax consequences that result from the ownership of ADSs or other deposited property, for the credit-worthiness of any third party, for allowing any rights to lapse under the terms of the deposit agreement, for the timeliness of any of our notices or for our failure to give notice or for any act or omission of or information provided by DTC or any DTC participant.
- The depositary shall not be liable for acts or omissions of any successor depositary in connection with any matter arising wholly after the resignation or removal of the depositary.
- We and the depositary will not be obligated to perform any act that is inconsistent with the terms of the deposit agreement.
- We and the depositary disclaim any liability if we or the depositary are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or future of any law or regulation, including regulations of any stock exchange or by reason of present or future provisions of our Articles of Association, or any

provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our or the depositary's control.

- We and the depositary disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our Articles of Association or in any provisions of or governing the securities on deposit.
- We and the depositary further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting ordinary shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information.
- We and the depositary also disclaim liability for the inability by any ADS holder or beneficiary owner to benefit from any distribution, offering, right or other benefit that is made available to holders of ordinary shares but is not, under the terms of the deposit agreement, made available to you.
- We and the depositary may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.
- We and the depositary also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.
- We and the depositary disclaim liability arising out of losses, liabilities, taxes, charges or expenses resulting from the manner in which a holder or beneficial owner of ADSs holds ADSs, including resulting from holding ADSs through a brokerage account.
- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.

Pre-Release Transactions

Subject to the terms and conditions of the deposit agreement, the depositary may issue to broker/dealers ADSs before receiving a deposit of ordinary shares or release ordinary shares to broker/dealers before receiving ADSs for cancellation. These transactions are commonly referred to as "pre-release transactions," and are entered into between the depositary and the applicable broker/dealer. The deposit agreement limits the aggregate size of pre-release transactions (not to exceed 30% of the ordinary shares on deposit in the aggregate, such limit being subject to change or disregard in the depositary's discretion) and imposes a number of conditions on such transactions (e.g., the need to receive collateral, the type of collateral required, the representations required from brokers, etc.). The depositary may retain the compensation received from the pre-release transactions.

Taxes

You will be responsible for the taxes and other governmental charges payable on the ADSs and the securities represented by the ADSs. We, the depositary and the custodian may deduct from any distribution the taxes and governmental charges payable by ADS holders and may sell any and all property on deposit to pay the taxes and governmental charges payable by ADS holders. You will be liable for any deficiency if the sale proceeds do not cover the taxes that are due.

The depositary may refuse to issue ADSs, to deliver, transfer, split and combine ADRs or to release securities on deposit until all taxes and charges are paid by the applicable ADS holder. The depositary and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depositary and to the custodian proof of taxpayer status and residence and such other information as the depositary and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depositary and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign Currency Conversion

The depositary will arrange for the conversion of all foreign currency received into U.S. dollars if such conversion is practical, and it will distribute the U.S. dollars in accordance with the terms of the deposit agreement. You may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

If the conversion of foreign currency is not practical or lawful, or if any required approvals are denied or not obtainable at a reasonable cost or within a reasonable period, the depositary may take any of the following actions in its discretion:

- Convert the foreign currency to the extent practical and lawful and distribute the U.S. dollars to the ADS holders for whom the conversion and distribution is lawful and practical.
- Distribute the foreign currency to ADS holders for whom the distribution is lawful and practical.
- Hold the foreign currency (without liability for interest) for the applicable ADS holders.

Governing Law/Waiver of Jury Trial

The deposit agreement and the ADRs will be interpreted in accordance with the laws of the State of New York. The rights of holders of ordinary shares (including ordinary shares represented by ADSs) are governed by the laws of England and Wales.

AS A PARTY TO THE DEPOSIT AGREEMENT, YOU WAIVE YOUR RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF THE DEPOSIT AGREEMENT OR THE ADRs AGAINST US OR THE DEPOSITARY.

EXPENSES

The following is an estimate of the expenses (all of which are to be paid by us) that we may incur in connection with the securities being registered hereby, other than the SEC registration fee and the FINRA filing fee.

SEC registration fee	\$48,480
FINRA filing fee	60,500
Legal fees and expenses	(1)
Accounting fees and expenses	(1)
Printing expenses	(1)
Miscellaneous expenses	(1)
Total	<u>\$ (1)</u>

(1) These fees are calculated based on the securities offered and the number of issuances and accordingly cannot be estimated at this time.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the debt securities, warrants and units governed by U.S. law and certain other matters of U.S. law will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. Unless the applicable prospectus supplement indicates otherwise, the validity of our ordinary shares underlying the ADSs and certain matters governed by English law will be passed on for us by Bristows LLP. Additional legal matters may be passed upon for any underwriters, dealers or agents by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of NuCana plc appearing in NuCana's Annual Report on Form 20-F for the year ended December 31, 2017, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The registered business address of Ernst & Young LLP is 144 Morrison Street, Edinburgh, EH3 8EX, United Kingdom.

ENFORCEMENT OF JUDGMENTS

We are a public limited company incorporated under the laws of England and Wales. Certain of our directors and executive officers and experts named in this prospectus reside outside of the United States, and all or a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may be difficult for an investor to serve process on us or our directors and executive officers or to compel any of them to appear in Court in the United States or to enforce judgments obtained in U.S. courts against them or us, including judgments based on civil liability provisions of the securities laws of the United States. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in the United Kingdom. An award for monetary damages under the U.S. securities laws would be considered punitive in the United Kingdom if it does not seek to compensate the claimant for loss or damage suffered and is intended to punish the defendant. The enforceability of any judgment in the United Kingdom will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and the United Kingdom do not currently have a treaty providing for the mutual recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the periodic reporting and other informational requirements of the Exchange Act. Under the Exchange Act, we file Annual Reports and other information with the SEC. As a foreign private issuer, we are exempt from, among other things, the rules under the Exchange Act prescribing the furnishing and content of proxy statements and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act.

Information filed with the SEC by us can be inspected and copied at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of this information by mail from the Public Reference Room of the SEC at prescribed rates. Further

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information on the operation of the SEC's Public Reference Room in Washington, D.C. can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site that contains reports and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is www.sec.gov.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement of which this prospectus forms a part. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement at the SEC's Public Reference Room in Washington, D.C. or through the SEC's website, as provided above.

We also maintain a website at www.nucana.com through which you can access our SEC filings. The information set forth on our website is not part of this prospectus.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We filed a registration statement on Form F-3 under the Securities Act of 1933, as amended, with the SEC with respect to the securities we may offer pursuant to this prospectus. This prospectus omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in “Where You Can Find More Information.” The documents we are incorporating by reference are:

- our Annual Report on Form 20-F for the year ended December 31, 2017, filed with the SEC on March 22, 2018;
- our Report on Form 6-K furnished to the SEC on October 1, 2018 that we incorporate by reference into this prospectus; and
- the description of ADSs representing our ordinary shares contained in our Registration Statement on Form 8-A filed with the SEC on September 22, 2017, including any amendments or reports filed for the purpose of updating such description.

We are also incorporating by reference all subsequent Annual Reports on Form 20-F that we file with the SEC and certain reports on Form 6-K that we furnish to the SEC after the date of this prospectus (if they state that they are incorporated by reference into this prospectus) prior to the termination of this offering. In all cases, you should rely on the later information over different information included in this prospectus or any accompanying prospectus supplement.

Unless expressly incorporated by reference, nothing in this prospectus shall be deemed to incorporate by reference information furnished to, but not filed with, the SEC. Copies of all documents incorporated by reference in this prospectus, other than exhibits to those documents unless such exhibits are specifically incorporated by reference in this prospectus, will be provided at no cost to each person, including any beneficial owner, who receives a copy of this prospectus on the written or oral request of that person made to:

NuCana plc
3 Lochside Way
Edinburgh, EH12 9DT
United Kingdom
Telephone: +44 (0)131 357 1111

You may also access these documents on our website, www.nucana.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

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You should rely only on information contained in, or incorporated by reference into, this prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference in this prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

\$75,000,000

American Depositary Shares

NuCana plc

Representing

Ordinary Shares



PROSPECTUS SUPPLEMENT

Goldman Sachs & Co. LLC

Jefferies

Cowen

SunTrust Robinson Humphrey
