

AMENDMENT NO. 2 DATED SEPTEMBER 30, 2024
to Prospectus Supplement dated August 27, 2021, as amended on March 27, 2024
(To Prospectus dated August 27, 2021)



NuCana plc

Up to \$5,407,000

American Depositary Shares representing Ordinary Shares

This Amendment No. 2 to Prospectus Supplement (this “Amendment”) amends our prospectus supplement dated August 27, 2021, as amended on March 27, 2024 (the “Prospectus Supplement”). This Amendment should be read in conjunction with the Prospectus Supplement and the accompanying prospectus dated August 27, 2021 (File No. 333-258941) (the “Prospectus”), and is qualified by reference thereto, except to the extent that the information herein amends or supersedes the information contained in the Prospectus Supplement or the Prospectus. This Amendment is not complete without, and may only be delivered or utilized in connection with, the Prospectus Supplement and the Prospectus, and any future amendments or supplements thereto.

We entered into an Open Market Sale AgreementSM with Jefferies LLC (“Jefferies”), dated August 19, 2021 (the “Sales Agreement”), relating to our American Depositary Shares (the “ADSs”), each representing twenty-five ordinary shares, nominal value £0.04 per share in our capital (the “Ordinary Shares”), offered by the Prospectus Supplement and the Prospectus. In accordance with the terms of the Sales Agreement, we may offer and sell shares of our ADSs representing Ordinary Shares having an aggregate offering price of up to \$100,000,000 from time to time through Jefferies acting as our sales agent. As of September 30, 2024, we have offered and sold 5,921,941 ADSs representing Ordinary Shares pursuant to the Sales Agreement for aggregate gross proceeds of approximately \$8.9 million. Consequently, up to approximately \$91.1 million remains available for sale under the Sales Agreement pursuant to the Prospectus Supplement.

Our ADSs representing Ordinary Shares are listed on the Nasdaq Capital Market under the symbol “NCNA.”

We are filing this Amendment to amend the Prospectus Supplement to update the amount of our ADSs representing Ordinary Shares we are eligible to sell under General Instruction I.B.5 of Form F-3 and pursuant to the Sales Agreement. As of September 30, 2024, the aggregate market value of our outstanding Ordinary Shares held by non-affiliates (the “Public Float”) was \$36,374,630, which was calculated based on 93,749,047 shares of our outstanding Ordinary Shares held by non-affiliates as of September 30, 2024, and at a price of \$0.388 per Ordinary Share, which is derived from a price of \$9.70 per ADS, the closing price of our ADSs representing Ordinary Shares on August 19, 2024. Pursuant to General Instruction I.B.5 of Form F-3, in no event will we sell our ADSs representing Ordinary Shares pursuant to the Prospectus Supplement and the Prospectus, as amended by this Amendment, with a value of more than one-third of the aggregate market value of our Ordinary Shares held by non-affiliates in any 12-month period, so long as the aggregate market value of our Ordinary Shares held by non-affiliates is less than \$75,000,000. As of the date of this Amendment, we have offered and sold 1,773,606 ADSs representing Ordinary Shares pursuant to the Sales Agreement for aggregate gross proceeds of approximately \$6,717,399 million pursuant to General Instruction I.B.5 to Form F-3 during the prior 12 calendar month period that ends on and includes the date hereof.

As a result of these limitations and the current Public Float of our Ordinary Shares, and in accordance with the terms of the Sales Agreement, we may offer and sell shares of our ADSs representing Ordinary Shares having an aggregate offering price of up to \$5,407,000 from time to time through Jefferies. If our Public Float increases such that we may sell additional amounts under the Sales Agreement, the Prospectus Supplement and the Prospectus, we will file another amendment to the Prospectus Supplement prior to making additional sales.

Investing in our ADSs representing Ordinary Shares involves a high degree of risk. Before making an investment decision, please read the information under the heading “Risk Factors” in the Prospectus Supplement, the Prospectus and the documents incorporated by reference therein.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this Amendment, the Prospectus Supplement or the Prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Jefferies

The date of this Amendment No. 2 to Prospectus Supplement is September 30, 2024.