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# SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

**SCHEDULE 13D**  
(RULE 13d-101)

**INFORMATION TO BE INCLUDED IN STATEMENTS FILED PURSUANT TO RULE 13d-1(a)  
AND AMENDMENTS THERETO FILED PURSUANT TO RULE 13d-2(a)**

(Amendment No. 2)\*

**NuCana plc**  
(Name of Issuer)

American Depositary Shares representing Ordinary Shares, nominal value £0.04 per share  
(Title of Class of Securities)

67022C106  
(CUSIP Number)

Nathalie Auber  
Sofinnova Investments, Inc.  
3000 Sand Hill Road, Bldg 4, Suite 250  
Menlo Park, CA 94025  
(650) 681-8420  
(Name, Address and Telephone Number of Person  
Authorized to Receive Notices and Communications)

**COPY TO:**

Jonathan Goodwin  
c/o Gunderson Dettmer Stough Villeneuve Franklin & Hachigian, LLP  
550 Allerton Street, Redwood City, CA 94063  
(650) 321-2400

November 18, 2021  
(Date of Event Which Requires Filing of This Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of §§ 240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box

Note: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See Rule 240.13d-7 for other parties to whom copies are to be sent.

\*The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

This information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

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1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY) Sofinnova Venture Partners VIII, L.P. ("SVP VIII")	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP <span style="float: right;">(a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/></span>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS WC	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 5,777,777 Ordinary Shares (including 1,777,777 Ordinary Shares represented by 1,777,777 American Depositary Shares), except that Sofinnova Management VIII, L.L.C. ("SM VIII"), the general partner of SVP VIII, may be deemed to have sole voting power, and Dr. James I. Healy ("Healy"), the managing member of SM VIII, may be deemed to have sole power to vote these shares.
	8	SHARED VOTING POWER See response to row 7.
	9	SOLE DISPOSITIVE POWER 5,777,777 Ordinary Shares (including 1,777,777 Ordinary Shares represented by 1,777,777 American Depositary Shares), except that SM VIII, the general partner of SVP VIII, may be deemed to have sole dispositive power and Healy, the managing member of SM VIII, may be deemed to have sole power to dispose of these shares.
	10	SHARED DISPOSITIVE POWER See response to row 9.
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON	5,777,777
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW 11 EXCLUDES CERTAIN SHARES	<input type="checkbox"/>
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 11	11.1%
14	TYPE OF REPORTING PERSON	PN

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY) Sofinnova Management VIII, L.L.C. ("SM VIII")	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP <span style="float: right;">(a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/></span>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS AF	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 5,777,777 Ordinary Shares (including 1,777,777 Ordinary Shares represented by 1,777,777 American Depositary Shares), all of which are owned directly by SVP VIII. SM VIII, the general partner of SVP VIII, may be deemed to have sole voting power, and Healy, the managing member of SM VIII, may be deemed to have sole power to vote these shares.
	8	SHARED VOTING POWER See response to row 7.
	9	SOLE DISPOSITIVE POWER 5,777,777 Ordinary Shares (including 1,777,777 Ordinary Shares represented by 1,777,777 American Depositary Shares), all of which are owned directly by SVP VIII. SM VIII, the general partner of SVP VIII, may be deemed to have sole dispositive power, and Healy, the managing member of SM VIII, may be deemed to have sole dispositive power over these shares.
	10	SHARED DISPOSITIVE POWER See response to row 9.
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON	5,777,777
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW 11 EXCLUDES CERTAIN SHARES	<input type="checkbox"/>
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 11	11.1%
14	TYPE OF REPORTING PERSON	OO

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY) Dr. James I. Healy ("Healy")	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP <span style="float: right;">(a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/></span>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS AF	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION U.S. Citizen	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 5,859,039 Ordinary Shares (including 1,780,169 Ordinary Shares represented by 1,780,169 American Depositary Shares), of which 5,777,777 are owned directly by SVP VIII and 81,262 are owned directly by Healy. SM VIII, the general partner of SVP VIII, may be deemed to have sole voting power of the shares owned directly by SVP VIII. Healy, the managing member of SM VIII and a director of the Issuer, may be deemed to have sole voting power to vote these shares.
	8	SHARED VOTING POWER 2,222,222 Ordinary Shares (including 2,222,222 Ordinary Shares represented by 2,222,222 American Depositary Shares), all of which are owned directly by SVP X. SM X, the general partner of SVP X, may be deemed to have sole voting power of the shares owned directly by SVP X. Healy, a managing member of SM X and a director of the Issuer, may be deemed to have shared voting power to vote these shares.
	9	SOLE DISPOSITIVE POWER 5,859,039 Ordinary Shares (including 1,780,169 Ordinary Shares represented by 1,780,169 American Depositary Shares), of which 5,777,777 are owned directly by SVP VIII and 81,262 are owned directly by Healy. SM VIII, the general partner of SVP VIII, may be deemed to have sole dispositive power of the shares owned directly by SVP VIII. Healy, the managing member of SM VIII and a director of the Issuer, may be deemed to have sole power to dispose of these shares.
	10	SHARED DISPOSITIVE POWER 2,222,222 Ordinary Shares (including 2,222,222 Ordinary Shares represented by 2,222,222 American Depositary Shares), all of which are owned directly by SVP X. SM X, the general partner of SVP X, may be deemed to have sole dispositive power of the shares owned directly by SVP X. Healy, a managing member of SM X and a director of the Issuer, may be deemed to have shared power to dispose of these shares.
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON	8,081,261
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW 11 EXCLUDES CERTAIN SHARES	<input type="checkbox"/>
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 11	15.5%
14	TYPE OF REPORTING PERSON	IN

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY) Dr. Maha Katabi ("Katabi")	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP <span style="float: right;">(a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/></span>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS AF	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION Canadian Citizen	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER -0-
	8	SHARED VOTING POWER 2,222,222 Ordinary Shares (including 2,222,222 Ordinary Shares represented by 2,222,222 American Depositary Shares), all of which are owned directly by SVP X. SM X, the general partner of SVP X, may be deemed to have sole voting power, and Katabi, a managing member of SM X, may be deemed to have shared voting power to vote these shares.
	9	SOLE DISPOSITIVE POWER -0-
	10	SHARED DISPOSITIVE POWER 2,222,222 Ordinary Shares (including 2,222,222 Ordinary Shares represented by 2,222,222 American Depositary Shares), all of which are owned directly by SVP X. SM X, the general partner of SVP X, may be deemed to have sole dispositive power, and Katabi, a managing member of SM X, may be deemed to have shared power to dispose of these shares.
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON	2,222,222
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW 11 EXCLUDES CERTAIN SHARES	<input type="checkbox"/>
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 11	4.3%
14	TYPE OF REPORTING PERSON	IN

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY) Sofinnova Venture Partners X, L.P. ("SVP X")		
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP <span style="float: right;">(a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/></span>		
3	SEC USE ONLY		
4	SOURCE OF FUNDS WC		
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>		
6	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 2,222,222 Ordinary Shares (including 2,222,222 Ordinary Shares represented by 2,222,222 American Depositary Shares), except that Sofinnova Management X, L.L.C. ("SM X"), the general partner of SVP X, may be deemed to have sole voting power, and Healy and Dr. Maha Katabi ("Katabi"), the managing members of SM X, may be deemed to have shared power to vote these shares.	
	8	SHARED VOTING POWER See response to row 7.	
	9	SOLE DISPOSITIVE POWER 2,222,222 Ordinary Shares (including 2,222,222 Ordinary Shares represented by 2,222,222 American Depositary Shares), except that SM X, the general partner of SVP X, may be deemed to have sole dispositive power and Healy and Katabi, the managing members of SM X, may be deemed to have shared power to dispose of these shares.	
	10	SHARED DISPOSITIVE POWER See response to row 9.	
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON		2,222,222
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW 11 EXCLUDES CERTAIN SHARES		<input type="checkbox"/>
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 11		4.3%
14	TYPE OF REPORTING PERSON		PN

1	NAME OF REPORTING PERSON I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY) Sofinnova Management X, L.L.C. ("SM X")		
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP <span style="float: right;">(a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/></span>		
3	SEC USE ONLY		
4	SOURCE OF FUNDS AF		
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>		
6	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 2,222,222 Ordinary Shares (including 2,222,222 Ordinary Shares represented by 2,222,222 American Depositary Shares), all of which are owned directly by SVP X. SM X, the general partner of SVP X, may be deemed to have sole voting power, and Healy and Katabi, the managing members of SM X, may be deemed to have shared power to vote these shares.	
	8	SHARED VOTING POWER See response to row 7.	
	9	SOLE DISPOSITIVE POWER 2,222,222 Ordinary Shares (including 2,222,222 Ordinary Shares represented by 2,222,222 American Depositary Shares), all of which are owned directly by SVP X. SM X, the general partner of SVP X, may be deemed to have sole dispositive power, and Healy and Katabi, the managing members of SM X, may be deemed to have shared power to dispose of these shares.	
	10	SHARED DISPOSITIVE POWER See response to row 9.	
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON		2,222,222
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW 11 EXCLUDES CERTAIN SHARES		<input type="checkbox"/>
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 11		4.3%
14	TYPE OF REPORTING PERSON		OO

**Statement on Schedule 13D**

This Amendment No. 2 (“Amendment No. 2”) amends and restates the Statement on Schedule 13D that was originally filed on October 11, 2017 and amended on October 5, 2020 (as amended, the “Original Schedule 13D”). This Amendment No. 2 relates to the beneficial ownership of Ordinary Shares, nominal value £0.04 per share (“Ordinary Shares”) represented by American Depositary Shares (“ADSs”), of NuCana plc, a public limited company incorporated in England and Wales (“Issuer”). This Amendment No. 2 is being filed by Sofinnova Venture Partners VIII, L.P., a Delaware limited partnership (“SVP VIII”), Sofinnova Management VIII, L.L.C., a Delaware limited liability company (“SM VIII”), Sofinnova Venture Partners X, L.P., a Delaware limited partnership (“SVP X”), Sofinnova Management X, L.L.C., a Delaware limited liability company (“SM X”), Dr. James I. Healy (“Healy”), and Dr. Maha Katabi (“Katabi” and collectively with SVP VIII, SM VIII, SVP X, SM X, and Healy, the “Reporting Persons”). This Amendment No. 2 is being filed to update the aggregate percentage of the class of securities of the Issuer owned by the Reporting Persons due to dilution caused by the Issuer’s additional sales of Ordinary Shares from time to time since the date of the filing of the Original Schedule 13D. The Issuer reported outstanding Ordinary Shares in the Issuer’s Form 6-K (File No. 001-38215) filed on November 18, 2021 causing a decrease in aggregate percentage ownership by the Reporting Persons of one percent (1%) or more from the percentages reported in the Original Schedule 13D.

**ITEM 1. SECURITY AND ISSUER.**

- (a) The class of equity securities to which this statement relates is the Ordinary Shares of the Issuer.
- (b) The Issuer’s principal executive offices are located at 3 Lochside Place, Edinburgh, EH12 9DT, United Kingdom.

**ITEM 2. IDENTITY AND BACKGROUND.**

(a) The persons and entities filing this Schedule 13D are SVP VIII, SM VIII, SVP X, SM X, Healy, and Katabi. SM VIII, the general partner of SVP VIII, may be deemed to have sole power to vote and sole power to dispose of shares of the Issuer directly owned by SVP VIII. SM X, the general partner of SVP X, may be deemed to have sole power to vote and sole power to dispose of shares of the Issuer directly owned by SVP X. Healy may be deemed to have sole power to vote and sole power to dispose of shares of the Issuer directly owned by Healy. Dr. Michael F. Powell, a reporting person on the Original Schedule 13D, is no longer a managing member of SM VIII and SM X, and accordingly, is no longer a reporting person on this Amendment No. 2.

(b) The address of the principal place of business for each of the Reporting Persons is c/o Sofinnova Investments, Inc., 3000 Sand Hill Road, Bldg 4, Suite 250, Menlo Park, California 94025.

(c) The principal occupation of each of the Reporting Persons is the venture capital investment business. The principal business of SVP VIII and SVP X is to make investments in private and public companies. The principal business of SM VIII is to serve as the general partner of SVP VIII, and the principal business of SM X is to serve as the general partner of SVP X. Healy is the managing member of SM VIII. Healy and Katabi are the managing members of SM X. Healy is a director of the Issuer.

(d) During the last five years, none of the Reporting Persons has been convicted in any criminal proceeding (excluding traffic violations or similar misdemeanors).

(e) During the last five years, none of the Reporting Persons has been a party to a civil proceeding of a judicial or administrative body of competent jurisdiction and as a result of such proceeding was or is subject to a judgment, decree or final order enjoining future violations of, or prohibiting or mandating activities subject to, federal or state securities laws or finding any violation with respect to such laws.

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(f) SVP VIII is a Delaware limited partnership. SM VIII is a Delaware limited liability company. SVP X is a Delaware limited partnership. SM X is a Delaware limited liability company. Healy is a U.S. citizen. Katabi is a Canadian citizen.

**ITEM 3. SOURCE AND AMOUNT OF FUNDS OR OTHER CONSIDERATION.**

On April 11, 2014, SVP VIII purchased an aggregate of 16,000,000 series B convertible participating shares (“Series B Shares”), at a price of £1.00 per share for an aggregate subscription price of £16,000,000. On September 14, 2017, the Issuer completed a one-for-four reverse share split. This had the effect of consolidating every four Series B Shares of £0.001 to one Series B Share of £0.004. As further described in the Issuer’s Prospectus filed pursuant to Rule 424(b)(4) on September 29, 2017 with the Securities and Exchange Commission (the “Prospectus”) under the heading “Series B Convertible Participating Shares,” immediately prior to the completion of the Issuer’s initial public offering of ADSs (the “Offering”), each Series B Share automatically converted into one Ordinary Share.

On December 12, 2016, the Issuer granted Healy options to purchase Ordinary Shares pursuant to the Issuer’s 2016 Share Option Scheme. Healy exercised such options prior to the Offering, and accordingly, immediately following the Offering, holds 45,750 Ordinary Shares through the Healy Family Trust. Such Ordinary Shares are subject to repurchase by the Issuer if Healy ceases to be a director of the Issuer during the four years following the grant date with 100% of such Ordinary Shares subject to repurchase during the first year following the grant date, 75% of such Ordinary Shares subject to repurchase during the second year following the grant date, 50% of such Ordinary Shares subject to repurchase during the third year following the grant date, and 25% of such Ordinary Shares subject to repurchase during the fourth year following the grant date. The Issuer’s 2016 Share Option Scheme is described more fully in the Prospectus.

In connection with the Offering, SVP VIII purchased 666,666 ADSs at \$15.00 per ADS, or \$9,999,990.00 in the aggregate. Such purchase occurred pursuant to and on the terms set forth in the Prospectus. Each ADS represents one Ordinary Share.

On May 15, 2019, the Issuer granted Healy options to purchase 25,000 Ordinary Shares at an exercise price of £11.26 per share pursuant to the Issuer’s 2016 Share Option Scheme. The shares underlying this option vest in four annual installments, subject to Healy’s continuous service as a director of the Issuer as of such vesting date.

On June 10, 2020, the Issuer granted Healy options to purchase 47,832 Ordinary Shares at an exercise price of £4.78 per share pursuant to the Issuer’s 2016 Share Option Scheme. The shares underlying this option vest in four annual installments, subject to Healy’s continuous service as a director of the Issuer as of such vesting date.

On September 9, 2020, the Issuer granted Healy options to purchase 9,567 Ordinary Shares at an exercise price of £0.04 per share pursuant to the Issuer’s 2020 Long-Term Incentive Plan. The shares underlying this option vest in four annual installments, subject to Healy’s continuous service as a director of the Issuer as of such vesting date. Healy exercised such portion of such options equal to 2,392 Ordinary Shares on September 9, 2021.

The Issuer filed a Prospectus Supplement pursuant to Rule 424(b)(5) on September 17, 2020 with the Securities and Exchange Commission (the “Prospectus Supplement”) that details the Issuer’s offering of 15,555,556 ADSs (the “Secondary Offering”). As further described in the Prospectus Supplement, each ADS represents one Ordinary Share.

In connection with the Secondary Offering, SVP VIII purchased 1,111,111 ADSs at \$4.50 per ADS, or \$4,999,999.50 in the aggregate, and SVP X purchased 2,222,222 ADSs at \$4.50 per ADS, or \$9,999,999 in the aggregate. Such purchases occurred pursuant to and on the terms set forth in the Prospectus Supplement.

On February 10, 2021, the Issuer granted Healy options to purchase 23,100 Ordinary Shares at an exercise price of £4.53 per share pursuant to the Issuer’s 2016 Share Option Scheme and 11,550 Ordinary Shares at an exercise price of £0.04 per share pursuant to the Issuer’s 2020 Long-Term Incentive Plan. The shares underlying these options vest in four equal installments, subject to Healy’s continuous service as a director of the Issuer as of such vesting date.

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On September 15, 2021, the Issuer granted Healy options to purchase 29,700 Ordinary Shares at an exercise price of £1.71 per share pursuant to the Issuer's 2016 Share Option Scheme and 14,850 Ordinary Shares at an exercise price of £0.04 per share pursuant to the Issuer's 2020 Long-Term Incentive Plan. The shares underlying these options vest in four equal installments, subject to Healy's continuous service as a director of the Issuer as of such vesting date.

Unless noted above, the source of the funds for all purchases and acquisitions by the Reporting Persons was from working capital. Certain purchases by SVP VIII and SVP X were made using their working capital funded partially through a line of credit with Silicon Valley Bank in the normal course of business and then paid down from the proceeds from investor capital calls.

Unless noted above, no part of the purchase price was borrowed by any Reporting Person for the purpose of acquiring any securities discussed in this Item 3.

#### **ITEM 4. PURPOSE OF TRANSACTION.**

The Reporting Persons hold their securities of the Issuer for investment purposes. Depending on the factors discussed herein, the Reporting Persons may, from time to time, acquire additional Ordinary Shares and/or retain and/or sell all or a portion of the Ordinary Shares held by the Reporting Persons in the open market or in privately negotiated transactions, block sales or otherwise or pursuant to ordinary stock exchange transactions effected through one or more broker-dealers whether individually or utilizing specific pricing or other instructions (including by means of Rule 10b5-1 programs), and/or may distribute the Ordinary Shares held by the Reporting Persons to their respective members or limited partners. Any actions the Reporting Persons might undertake will be dependent upon the Reporting Persons' review of numerous factors, including, among other things, the price levels of the Ordinary Shares, general market and economic conditions, ongoing evaluation of the Issuer's business, financial condition, operations and prospects; the relative attractiveness of alternative business and investment opportunities, and other future developments. Except as set forth above, the Reporting Persons have no present plans or intentions which would result in or relate to any of the transactions described in subparagraphs (a) through (j) of Item 4 of Schedule 13D.

#### **ITEM 5. INTEREST IN SECURITIES OF THE ISSUER.**

(a,b) Regarding aggregate beneficial ownership, see Row 11 of the cover page of each Reporting Person. Regarding percentage beneficial ownership, see Row 13 of the cover page of each Reporting Person. Regarding sole power to vote shares, see Row 7 of the cover page of each Reporting Person. Regarding shared power to vote shares, see Row 8 of the cover page of each Reporting Person. Regarding sole power to dispose of shares, see Row 9 of the cover page of each Reporting Person. Regarding shared power to dispose of shares, see Row 10 of the cover page of each Reporting Person. Percentage calculations were made using 52,180,000 as the number of shares of Ordinary Shares outstanding as of September 30, 2021 as reported by the Issuer in its Form 6-K (File No. 001-38215) filed on November 18, 2021.

(c) Except as set forth in Item 3 above, the Reporting Persons have not effected any transaction in the Ordinary Shares of the Issuer during the past 60 days.

(d) Under certain circumstances set forth in the limited partnership agreement of SVP VIII, the general partner and limited partners of SVP VIII may be deemed to have the right to receive dividends from, or the proceeds from, the sale of shares of the Issuer owned by such entity of which they are a partner. Under certain circumstances set forth in the limited partnership agreement of SVP X, the general partner and limited partners of SVP X may be deemed to have the right to receive dividends from, or the proceeds from, the sale of shares of the Issuer owned by such entity of which they are a partner.

(e) Not applicable.

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**ITEM 6. CONTRACTS, ARRANGEMENTS, UNDERSTANDINGS OR RELATIONSHIPS WITH RESPECT TO SECURITIES OF THE ISSUER.**

Certain of the Reporting Persons have entered into a registration rights agreement with the Issuer to be effective upon the completion of the Offering and pursuant to which the Issuer has agreed under specified circumstances to file a registration statement to register the resale of the Ordinary Shares held by such Reporting Persons and other shareholders, as well as to cooperate in specified public offerings of such shares. The Form of Registration Rights Agreement is incorporated herein by reference to Exhibit 1.9 to the Issuer's Amendment No. 1 to Form F-1 Registration Statement (File No. 333-220321).

Healy, in his capacity as a director of the Issuer, along with the other directors of the Issuer, entered into a Deed of Indemnity with the Issuer, as more fully described in the Prospectus. Such description and form of Deed of Indemnity is incorporated herein by reference to Exhibit 10.10 to the Issuer's Amendment No. 2 to Form F-1 Registration Statement (File No. 333-220321).

SVP VIII and Healy have agreed that, subject to specified limited exceptions, for a period of 180 days from the date of the Prospectus, they will not, without the prior written consent of Citigroup Global Markets Inc., 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 their Ordinary Shares, ADSs, or any securities convertible into, or exercisable or exchangeable for Ordinary Shares; provided, that these restrictions do not apply to ADSs purchased in this offering, among other exceptions. Citigroup Global Markets Inc., Jefferies LLC and Cowen and Company, LLC in their sole discretion may release any of the securities subject to these lock-up agreements at any time, which, in the case of officers and directors, shall be with notice. The Form of Lock-up Agreement is incorporated herein by reference to Exhibit A to Exhibit 1.1 to the Issuer's Amendment No. 1 to Form F-1 Registration Statement (File No. 333-220321).

In connection with the Secondary Offering, SVP VIII has agreed that for a period of 60 days from the date of the Prospectus Supplement and Healy has agreed that for a period of 90 days from the date of the Prospectus Supplement, subject to specified exceptions, not to directly or indirectly: (i) sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, (ii) otherwise dispose of any Ordinary Shares or ADSs, options or warrants to acquire Ordinary Shares or ADSs, or securities exchangeable or exercisable for or convertible into Ordinary Shares or ADSs currently or hereafter owned either of record or beneficially, or (iii) publicly announce an intention to do any of the foregoing without the prior written consent of Jefferies LLC, Cowen and Company LLC and William Blair & Company, L.L.C. The Form of Lock-up Agreement is incorporated herein by reference to Exhibit A to Exhibit 1.1 to the Issuer's Form 6-K (File No. 001-38215) filed on September 18, 2020.

**ITEM 7. MATERIAL TO BE FILED AS EXHIBITS.**

EXHIBIT A Agreement of Joint Filing.

EXHIBIT B Power of Attorney.

EXHIBIT C Form of Lock-Up Agreement described in Item 6, filed as Exhibit A to Exhibit 1.1 to the Issuer's Amendment No. 1 to Form F-1 Registration Statement (File No. 333-220321) and incorporated herein by reference.

EXHIBIT D Form of Registration Rights Agreement described in Item 6, filed as Exhibit 1.9 to the Issuer's Amendment No. 1 to Form F-1 Registration Statement (File No. 333-220321) and incorporated herein by reference.

EXHIBIT E Form of Deed of Indemnity for directors and executive officers, filed as Exhibit 10.10 to the Issuer's Amendment No. 2 to Form F-1 Registration Statement (File No. 333-220321) and incorporated herein by reference.

EXHIBIT F Form of Lock-Up Agreement described in Item 6, filed as Exhibit A to Exhibit 1.1 to the Issuer's Form 6-K (File No. 001-38215) on September 18, 2020 and incorporated herein by reference.

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SIGNATURES

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Date: February 25, 2022

SOFINNOVA VENTURE PARTNERS VIII, L.P., a Delaware Limited Partnership

By: SOFINNOVA MANAGEMENT VIII, L.L.C., a Delaware Limited Liability Company  
Its: General Partner

By: /s/ Nathalie Auber  
Nathalie Auber  
Attorney-in-Fact

SOFINNOVA MANAGEMENT VIII, L.L.C., a Delaware Limited Liability Company

By: /s/ Nathalie Auber  
Nathalie Auber  
Attorney-in-Fact

SOFINNOVA VENTURE PARTNERS X, L.P., a Delaware Limited Partnership

By: SOFINNOVA MANAGEMENT X, L.L.C., a Delaware Limited Liability Company  
Its: General Partner

By: /s/ Nathalie Auber  
Nathalie Auber  
Attorney-in-Fact

SOFINNOVA MANAGEMENT X, L.L.C., a Delaware Limited Liability Company

By: /s/ Nathalie Auber  
Nathalie Auber  
Attorney-in-Fact

DR. JAMES I. HEALY  
DR. MAHA KATABI

By: /s/ Nathalie Auber  
Nathalie Auber  
Attorney-in-Fact

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EXHIBIT INDEX

<u>Exhibit</u>	<u>Description</u>
A	Agreement of Joint Filing.
B	Power of Attorney.
C	Form of Lock-Up Agreement described in Item 6, filed as Exhibit A to Exhibit 1.1 to the Issuer's Amendment No. 1 to Form F-1 Registration Statement (File No. 333-220321) and incorporated herein by reference.
D	Form of Registration Rights Agreement described in Item 6, filed as Exhibit 1.9 to the Issuer's Amendment No. 1 to Form F-1 Registration Statement (File No. 333-220321) and incorporated herein by reference.
E	Form of Deed of Indemnity for directors and executive officers, filed as Exhibit 10.10 to the Issuer's Amendment No. 2 to Form F-1 Registration Statement (File No. 333-220321) and incorporated herein by reference.
F	Form of Lock-Up Agreement described in Item 6, filed as Exhibit A to Exhibit 1.1 to the Issuer's Form 6-K (File No. 001-38215) on September 18, 2020 and incorporated herein by reference.

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EXHIBIT A

Agreement of Joint Filing

The undersigned hereby agree that a single Schedule 13D (or any amendment thereto) relating to the Ordinary Shares of NuCana plc shall be filed on behalf of each of the undersigned and that this Agreement shall be filed as an exhibit to such Schedule 13D.

Date: February 25, 2022

SOFINNOVA VENTURE PARTNERS VIII, L.P., a Delaware Limited Partnership

By: SOFINNOVA MANAGEMENT VIII, L.L.C., a Delaware Limited Liability Company  
Its: General Partner

By: /s/ Nathalie Auber  
Nathalie Auber  
Attorney-in-Fact

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SOFINNOVA VENTURE PARTNERS X, L.P., a Delaware Limited Partnership

By: SOFINNOVA MANAGEMENT X, L.L.C., a Delaware Limited Liability Company  
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By: /s/ Nathalie Auber  
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DR. JAMES I. HEALY  
DR. MAHA KATABI

By: /s/ Nathalie Auber  
Nathalie Auber  
Attorney-in-Fact

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EXHIBIT BPower of Attorney

Nathalie Auber has signed this Schedule 13D as Attorney-In-Fact. Note that copies of the applicable Power of Attorney are already on file with the appropriate agencies.

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