
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

SCHEDULE 13G

**Under the Securities Exchange Act of 1934
(Amendment No. __)***

Nightstar Therapeutics plc

(Name of Issuer)

Ordinary Shares (represented by American Depositary Shares)
(Title of Class of Securities)

65413A101
(CUSIP Number)

December 31, 2017
(Date of Event which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

- Rule 13d-1(b)
- Rule 13d-1(c)
- Rule 13d-1(d)

* 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 the disclosures provided in a prior cover page.

The information required in 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*).

1.	Names of Reporting Persons Syncona Portfolio Limited	
2.	Check the appropriate box if a member of a Group (see instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC Use Only	
4.	Citizenship or Place of Organization Guernsey	
Number of Shares Beneficially Owned by Each Reporting Person With:	5.	Sole Voting Power 12,203,922 (1)
	6.	Shared Voting Power 0
	7.	Sole Dispositive Power 12,203,922 (1)
	8.	Shared Dispositive Power 0
9.	Aggregate Amount Beneficially Owned by Each Reporting Person 12,203,922 (1)	
10.	Check box if the aggregate amount in Row (9) excludes certain shares (See Instructions) <input type="checkbox"/>	
11.	Percent of class represented by amount in row (9) 42.2% (2)	
12.	Type of Reporting Person (See Instructions) CO	

- (1) Consists of 11,203,922 Ordinary Shares and 1,000,000 American Depositary Shares (“ADS”) each representing one Ordinary Share, in each case owned directly by Syncona Portfolio Limited. The Ordinary Shares and the ADS are collectively referred to as the “**Ordinary Shares**”.
- (2) The percentage of outstanding Ordinary Shares of the Issuer beneficially owned by Syncona Portfolio Limited is set forth on Line 11 above. Such percentage was calculated based on (i) the 28,100,714 Ordinary Shares reported to be outstanding immediately following the offering on the Issuer’s prospectus filed under Rule 424(b)(4), filed with the SEC on September 28, 2017 and (ii) the 804,000 Ordinary Shares reported by the Issuer, in the Issuer’s press release dated October 2, 2017, to have been issued upon the exercise in full by the underwriters to purchase additional ADSs.

1.	Names of Reporting Persons Syncona Holdings Limited	
2.	Check the appropriate box if a member of a Group (see instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC Use Only	
4.	Citizenship or Place of Organization Guernsey	
Number of Shares Beneficially Owned by Each Reporting Person With:	5.	Sole Voting Power 12,203,922 (1)
	6.	Shared Voting Power 0
	7.	Sole Dispositive Power 12,203,922 (1)
	8.	Shared Dispositive Power 0
9.	Aggregate Amount Beneficially Owned by Each Reporting Person 12,203,922 (1)	
10.	Check box if the aggregate amount in Row (9) excludes certain shares (See Instructions) <input type="checkbox"/>	
11.	Percent of class represented by amount in row (9) 42.2% (2)	
12.	Type of Reporting Person (See Instructions) CO	

- (1) Consists of 11,203,922 Ordinary Shares and 1,000,000 American Depositary Shares (“ADS”) each representing one Ordinary Share, in each case owned directly by Syncona Portfolio Limited. The Ordinary Shares and the ADS are collectively referred to as the “**Ordinary Shares**”.
- (2) The percentage of outstanding Ordinary Shares of the Issuer which may be deemed to be beneficially owned by Syncona Holdings Limited is set forth on Line 11 above. Such percentage was calculated based on (i) the 28,100,714 Ordinary Shares reported to be outstanding immediately following the offering on the Issuer’s prospectus filed under Rule 424(b)(4), filed with the SEC on September 28, 2017 and (ii) the 804,000 Ordinary Shares reported by the Issuer, in the Issuer’s press release dated October 2, 2017, to have been issued upon the exercise in full by the underwriters to purchase additional ADSs.

1.	Names of Reporting Persons Syncona Limited	
2.	Check the appropriate box if a member of a Group (see instructions) (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC Use Only	
4.	Citizenship or Place of Organization Guernsey	
Number of Shares Beneficially Owned by Each Reporting Person With:	5.	Sole Voting Power 12,203,922 (1)
	6.	Shared Voting Power 0
	7.	Sole Dispositive Power 12,203,922 (1)
	8.	Shared Dispositive Power 0
9.	Aggregate Amount Beneficially Owned by Each Reporting Person 12,203,922 (1)	
10.	Check box if the aggregate amount in Row (9) excludes certain shares (See Instructions) <input type="checkbox"/>	
11.	Percent of class represented by amount in row (9) 42.2% (2)	
12.	Type of Reporting Person (See Instructions) CO	

- (1) Consists of 11,203,922 Ordinary Shares and 1,000,000 American Depositary Shares (“ADS”) each representing one Ordinary Share, in each case owned directly by Syncona Portfolio Limited. The Ordinary Shares and the ADS are collectively referred to as the “**Ordinary Shares**”.
- (2) The percentage of outstanding Ordinary Shares of the Issuer which may be deemed to be beneficially owned by Syncona Limited is set forth on Line 11 above. Such percentage was calculated based on (i) the 28,100,714 Ordinary Shares reported to be outstanding immediately following the offering on the Issuer’s prospectus filed under Rule 424(b)(4), filed with the SEC on September 28, 2017 and (ii) the 804,000 Ordinary Shares reported by the Issuer, in the Issuer’s press release dated October 2, 2017, to have been issued upon the exercise in full by the underwriters to purchase additional ADSs.

Item 1. Issuer

(a) **Name of Issuer:** Nightstar Therapeutics plc (the “Issuer”)

(b) **Address of Issuer’s Principal Executive Offices:**

215 Euston Road, London NW1 2BE, United Kingdom

Item 2. Filing Person

(a) – (c) **Name of Persons Filing; Address; Citizenship:**

- (i) Syncona Portfolio Limited;
- (ii) Syncona Holdings Limited; and
- (iii) Syncona Limited

The address of the principal business office of each of the reporting persons is PO Box 255, Trafalgar Court, Les Banques, St Peter Port, Guernsey GY1 3QL, Channel Islands. Each filing person’s citizenship is Guernsey.

(d) **Title of Class of Securities:** Ordinary Shares

(e) **CUSIP No.:** 65413A101

Item 3. If this statement is filed pursuant to §§ 240.13d-1(b) or 240.13d-2(b) or (c), check whether the person filing is a:

- (a) Broker or dealer registered under Section 15 of the Act;
- (b) Bank as defined in Section 3(a)(6) of the Act;
- (c) Insurance company as defined in Section 3(a)(19) of the Act;
- (d) Investment company registered under Section 8 of the Investment Company Act of 1940;
- (e) An investment adviser in accordance with Rule 13d-1(b)(1)(ii)(E);
- (f) An employee benefit plan or endowment fund in accordance with Rule 13d-1(b)(1)(ii)(F);
- (g) A parent holding company or control person in accordance with Rule 13d-1(b)(1)(ii)(G);
- (h) A savings associations as defined in Section 3(b) of the Federal Deposit Insurance Act (12 U.S.C. 1813);
- (i) A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment Company Act of 1940;
- (j) A non-U.S. institution in accordance with Rule 240.13d-1(b)(1)(ii)(J);
- (k) Group, in accordance with Rule 240.13d-1(b)(1)(ii)(K). If filing as a non-U.S. institution in accordance with Rule 240.13d-1(b)(1)(ii)(J), please specify the type of institution:

Item 4. Ownership**For Syncona Portfolio Limited:**

(a) **Amount Beneficially Owned:** 12,203,922 Ordinary Shares

(b) **Percent of Class:** 42.2%

(c) Number of shares as to which such person has:

- (i) Sole power to vote or to direct the vote: 12,203,922
- (ii) Shared power to vote or to direct the vote: 0
- (iii) Sole power to dispose or to direct the disposition of: 12,203,922
- (iv) Shared power to dispose or to direct the disposition of: 0

For Syncona Holdings Limited:**(a) Amount Beneficially Owned:** 12,203,922 Ordinary Shares**(b) Percent of Class:** 42.2%**(c) Number of shares as to which such person has:**

- (i) Sole power to vote or to direct the vote: 12,203,922
- (ii) Shared power to vote or to direct the vote: 0
- (iii) Sole power to dispose or to direct the disposition of: 12,203,922
- (iv) Shared power to dispose or to direct the disposition of: 0

For Syncona Limited:**(a) Amount Beneficially Owned:** 12,203,922 Ordinary Shares**(b) Percent of Class:** 42.2%**(c) Number of shares as to which such person has:**

- (i) Sole power to vote or to direct the vote: 12,203,922
- (ii) Shared power to vote or to direct the vote: 0
- (iii) Sole power to dispose or to direct the disposition of: 12,203,922
- (iv) Shared power to dispose or to direct the disposition of: 0

Item 5. Ownership of Five Percent or Less of a Class.

If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than five percent of the class of securities, check the following [].

Item 6. Ownership of more than Five Percent on Behalf of Another Person.

Not applicable

Item 7. Identification and classification of the subsidiary which acquired the security being reported on by the parent holding company or control person.

Not applicable

Item 8. Identification and classification of members of the group.

Not applicable

Item 9. Notice of Dissolution of Group.

Not applicable

Item 10. Certifications.

Not applicable

SIGNATURE

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.

Dated: February 2, 2018

SYNCONA PORTFOLIO LIMITED

By: /s/ Martin Murphy
Name: Martin Murphy
Title: Director

SYNCONA HOLDINGS LIMITED

By: /s/ Martin Murphy
Name: Martin Murphy
Title: Director

SYNCONA LIMITED

By: /s/ Jeremy Tighe
Name: Jeremy Tighe
Title: Director

JOINT FILING AGREEMENT

In accordance with Rule 13d-1(k) under the Securities Exchange Act of 1934, as amended, the undersigned agree to the joint filing on behalf of each of them of a statement on Schedule 13G (including amendments thereto) with respect to the Ordinary Shares and the American Depositary Shares representing Ordinary Shares, in each case of Nightstar Therapeutics plc, and further agree that this agreement be included as an exhibit to such filing. Each party to the agreement expressly authorizes each other party to file on its behalf any and all amendments to such statement. Each party to this agreement agrees that this joint filing agreement may be signed in counterparts.

Dated: February 2, 2018

SYNCONA PORTFOLIO LIMITED

By: /s/ Martin Murphy
Name: Martin Murphy
Title: Director

SYNCONA HOLDINGS LIMITED

By: /s/ Martin Murphy
Name: Martin Murphy
Title: Director

SYNCONA LIMITED

By: /s/ Jeremy Tighe
Name: Jeremy Tighe
Title: Director