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

SCHEDULE 13G

Under the Securities Exchange Act of 1934
(Amendment No. 2)*

Nightstar Therapeutics plc

(Name of Issuer)

Ordinary Shares, nominal value £0.01 per share

(Title of Class of Securities)

65413A101

(CUSIP Number)

March 4, 2019

(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*).

SCHEDULE 13G/A

CUSIP No. 65413A101

1	Names of Reporting Person: 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 0
	6 Shared Voting Power 13,203,922 (1)
	7 Sole Dispositive Power 0
	8 Shared Dispositive Power 13,203,922 (1)
9	Aggregate Amount Beneficially Owned by Each Reporting Person 13,203,922 (1)
10	Check box if the aggregate amount in row (9) excludes certain shares (See Instructions)
11	Percent of class represented by amount in row (9) 39.0% (2)
12	Type of Reporting Person (See Instructions) CO

- (1) Consists of 11,203,922 ordinary shares and 2,000,000 American Depository Share (“ADS”) held directly by Syncona Portfolio Limited. Each ADS represents one ordinary share, nominal value 0.01 GBP per share, of the Issuer. 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 33,844,103 Ordinary Shares reported to be outstanding as of October 2, 2018 immediately following the Issuer’s recent public offering, pursuant to the Issuer’s prospectus filed under Rule 424(b)(4), filed with the SEC on September 28, 2018.

SCHEDULE 13G/A

CUSIP No. 65413A101

1		Names of Reporting Person: 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 0
	6	Shared Voting Power 13,203,922 (1)
	7	Sole Dispositive Power 0
	8	Shared Dispositive Power 13,203,922 (1)
9	Aggregate Amount Beneficially Owned by Each Reporting Person 13,203,922 (1)	
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SCHEDULE 13G/A

CUSIP No. 65413A101

1	Names of Reporting Person: Syncona Investment Management 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 United Kingdom	
Number of Shares Beneficially Owned by Each Reporting Person With:	5	Sole Voting Power 0
	6	Shared Voting Power 13,203,922 (1)
	7	Sole Dispositive Power 0
	8	Shared Dispositive Power 13,203,922 (1)
9	Aggregate Amount Beneficially Owned by Each Reporting Person 13,203,922 (1)	
10	Check box if the aggregate amount in row (9) excludes certain shares (See Instructions)	
11	Percent of class represented by amount in row (9) 39.0% (2)	
12	Type of Reporting Person (See Instructions) CO	

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SCHEDULE 13G/A

CUSIP No. 65413A101

1	Names of Reporting Person: 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 0
	6	Shared Voting Power 13,203,922 (1)
	7	Sole Dispositive Power 0
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SCHEDULE 13G/A

CUSIP No. 65413A101

The following constitutes Amendment No. 2 (“Amendment No. 2”) to the Schedule 13G originally filed on February 2, 2018 (the “Original Schedule 13G”), as further amended on February 13, 2019 (“Amendment No. 1”), filed by the Reporting Persons with the Securities and Exchange Commission (“SEC”) with respect to their ownership of Ordinary Shares, nominal value 0.01 GBP per share (consisting of ordinary shares and American Depositary Share (“ADS”), with each ADS representing one ordinary share), of Nightstar Therapeutics plc, a company incorporated in England and Wales (the “Issuer”). This Amendment No. 2 amends the Original Schedule 13G, as amended by Amendment No. 1, as specifically set forth herein. Except as specifically set forth herein, this Amendment No. 2 does not modify any of the information previously reported on the Schedule 13G (including Amendment No. 1 thereto).

This Amendment No. 2 is being filed to solely to voluntarily disclose that on March 4, 2019, the Issuer entered into an implementation agreement (the “Implementation Agreement”) by and among the Issuer, Biogen Switzerland Holdings GmbH (“Biogen”) and Tungsten Bidco Limited (“Bidco”) whereby Bidco agreed to acquire the entire issued and to be issued share capital of the Issuer for \$25.50 in cash per share (the “Scheme”). In connection with the closing of the transaction contemplated by the Implementation Agreement, the Issuer and Biogen entered into a Shareholder’s Irrevocable Undertaking (the “Undertaking”) with Syncona Portfolio Limited (“Syncona”) and New Enterprise Associates 15, L.P. to vote or procure votes in favor of the resolutions relating to the Scheme in respect of their entire beneficial holdings. The Undertaking will terminate if the Scheme lapses or is withdrawn in accordance with its terms and Bidder or Bidco publicly confirms that it does not intend to proceed with the acquisition or if the Scheme lapses or has not become effective by 11:59pm (London time) on September 4, 2019.

As a result of the Undertaking, the Reporting Persons may be deemed to be members of a “group” with the parties of the Undertaking. Syncona, together with New Enterprise Associates 15, L.P. is the beneficial owner of 19,866,454 Ordinary Shares, in aggregate, representing approximately 59.3% of the issued share capital of the Issuer as reported as of February 28, 2019 on the Issuer’s 8-K filed with the Securities and Exchange Commission (“SEC”) on March 4, 2019 (the “8-K”).

The foregoing description of the Undertaking is qualified in its entirety by reference to the Form of Shareholder’s Irrevocable Undertaking, which is attached hereto as Exhibit 99.2.

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: March 14, 2019

SYNCONA PORTFOLIO LIMITED

By: /s/ Nick Moss

Name: Nick Moss

Title: Director

SYNCONA HOLDINGS LIMITED

By: /s/ Nick Moss

Name: Nick Moss

Title: Director

SYNCONA INVESTMENT MANAGEMENT LIMITED

By: /s/ Martin Murphy

Name: Martin Murphy

Title: Director

SYNCONA LIMITED

By: /s/ Nick Moss

Name: Nick Moss

Title: Director

Exhibit(s):

Exhibit 99.1: Joint Filing Statement

Exhibit 99.2 Form of Shareholder's Irrevocable Undertaking

AGREEMENT

In accordance with Rule 13d-1(k) under the Securities Exchange Act of 1934, as amended, the persons named below 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 (represented by ADS, each of which represents one Ordinary Share) of Nightstar Therapeutics plc and further agree that this Joint Filing Agreement be included as an Exhibit to such joint filings. It is understood and agreed that the joint filing of the Schedule 13G shall not be construed as an admission that the persons named herein constitute a group for purposes of Regulation 13D-G of the Securities Exchange Act of 1934, as amended.

Dated: March 14, 2019

SYNCONA PORTFOLIO LIMITED

By: /s/ Nick Moss

Name: Nick Moss

Title: Director

SYNCONA HOLDINGS LIMITED

By: /s/ Nick Moss

Name: Nick Moss

Title: Director

SYNCONA INVESTMENT MANAGEMENT LIMITED

By: /s/ Martin Murphy

Name: Martin Murphy

Title: Director

SYNCONA LIMITED

By: /s/ Nick Moss

Name: Nick Moss

Title: Director

SHAREHOLDER'S IRREVOCABLE UNDERTAKING

To: Biogen Switzerland Holdings GmbH (the "Offeror")
Neuhofstrasse 30,
6340 Baar,
Switzerland

From: [●]

4 March 2019

Dear Sirs,

Proposed acquisition of Nightstar Therapeutics plc ("NST") – Deed of Irrevocable Undertaking

1. We understand that the Offeror intends to make an offer to acquire the entire issued and to be issued share capital of NST (other than treasury shares and Deferred Shares (as defined in the articles of association of NST)) (the "Acquisition") which is proposed to be implemented by way of a scheme of arrangement (the "Scheme") under Part 26 of the Companies Act 2006 (the "Act") substantially on the terms and conditions set out in the press announcement, a draft of which is annexed to this undertaking (the "Press Announcement").
2. We understand that the Offeror may, subject to the consent of NST, elect to implement the Acquisition by means of a takeover offer within the meaning of section 974 of the Act (as announced by the Offeror with consent of NST, an "Offer"). In this undertaking, an "Offer" shall also include any extended, increased or revised offer by the Offeror made with consent of NST in respect of the Acquisition.
3. This undertaking sets out the terms and conditions on which we will exercise, or procure the exercise of, the votes attaching to the securities in NST in which we have an interest as set out in Schedule 1 in favour of the Scheme at any relevant meeting of the members of NST or, if an Offer is made, accept the Offer when it is made (as applicable).
4. Notwithstanding any other provision of this undertaking, our obligations in this undertaking are conditional on the terms and conditions of the Scheme and any Offer being substantially as set out in the Press Announcement and (in either case), subject thereto, or otherwise as may be agreed between the Offeror and NST or as may be required to comply with the requirements of the High Court of Justice in England and Wales (the "Court"), the Act or any other legal or regulatory authority or body.
5. Notwithstanding any other provision in this undertaking, the Offeror agrees that we will have no liability to it or anyone else in connection with any failure by Citibank, N.A., as depositary in respect of the NST ADRs (as defined below) (the "Depositary") to act in accordance with any instructions we give to the Depositary in connection with the NST ADRs pursuant to this undertaking.

Shareholdings

6. We irrevocably and unconditionally undertake and warrant to the Offeror that:
 - (a) we are the sole beneficial and, where indicated in the first column of each of the tables set out in Schedule 1, the sole registered holder of:
 - (i) the number of ordinary shares of £0.01 each in the capital of NST shown in Schedule 1 (collectively, the "NST Shares"); and
 - (ii) the number of American depositary receipts, each representing an interest in one ordinary share of £0.01 in the capital of NST, shown in Schedule 1 (collectively, the "NST ADRs" and, together with the NST Shares, the "NST Securities")

and have full power and authority to vote (in the case of the NST ADRs, to the extent they carry any right to vote) and sell or procure the sale of the NST Securities with full title guarantee, free from any lien, charge, option, equity encumbrance, rights of pre-emption, legal or other restrictions, together with all rights (including but not limited to any voting rights and the right to receive and retain in full all dividends of any nature and other distributions (if any) hereafter declared, made or paid subject to the matters referred to in the Press Announcement) attaching to or enjoyed by them as envisaged by the terms of the Acquisition;

(b) the information set out in Schedule 1 regarding the NST Securities is complete and accurate and, other than as set out in Schedule 1, we do not have any interest in any securities or shares of NST or any rights to subscribe for, purchase or otherwise acquire any securities or shares of NST; and

(c) we have full power and authority to enter into this undertaking and to perform the obligations under it in respect of the NST Securities.

For the purposes of this paragraph 6, a person will be treated as having an interest in securities if:

(i) he owns them;

(ii) he has the right (whether conditional or absolute) to exercise or direct the exercise of the voting rights attaching to them or has general control of them;

(iii) by virtue of any agreement to purchase, option or derivative he:

(1) has the right or option to acquire them or call for their delivery; or

(2) is under an obligation to take delivery of them,

whether the right, option or obligation is conditional or absolute and whether it is in the money or otherwise; or

(iv) he is party to any derivative:

(1) whose value is determined by reference to their price; and

(2) which results, or may result, in his having a long position in them.

Dealings

7. Subject to paragraph 14 below, we undertake to the Offeror that before the earliest to occur of (i) the Scheme becoming effective and (ii) an Offer, if made by the Offeror, being declared unconditional in all respects, we shall not ourselves or permit any registered holder (if different) to:

(a) sell, transfer, loan, charge, encumber, grant any option over or otherwise dispose of any NST Securities or any other shares or securities in NST issued, allotted or transferred to us or otherwise acquired by us before then (“**Further NST Securities**”) other than pursuant to the Scheme, or an acceptance of the Offer if made;

(b) accept any other offer (whether such offer is to be implemented by way of a takeover offer, scheme of arrangement, merger or other business combination of any nature whatsoever) in respect of the shares or securities referred to in paragraph 7(a); or

(c) (other than pursuant to the Scheme or the Offer, if made) enter into any agreement or arrangement or incur any obligation:

(i) to do any of the acts referred to in paragraphs 7(a) or 7(b) in relation to, or operating by reference to, the NST Securities or any Further NST Securities; or

(ii) which, in relation to the NST Securities or any Further NST Securities, would or might restrict or impede our complying with the terms of this undertaking,

and for the avoidance of doubt, references in paragraphs 7(b) and 7(c) to any acceptance of an offer or any agreement, arrangement or obligation includes any acceptance of an offer or agreement, arrangement or obligation whether or not legally binding or subject to any condition or which is to take effect if the Scheme is withdrawn, if the Offer closes or lapses or if this undertaking ceases to be binding or upon or following any other event.

Undertaking to vote in favour of the Scheme

8. In consideration of the Offeror agreeing to be bound by the Scheme in the event that the Scheme becomes effective, we undertake to the Offeror to attend (either in person or by proxy) any meeting of NST's shareholders convened by order of the Court pursuant to section 896 of the Act to consider and approve the Scheme ("**Court Meetings**") and any general or class meeting of NST convened in order to consider and approve measures required to implement the Scheme ("**Shareholders' Meetings**") and, from the time the Scheme is announced until this undertaking terminates in accordance with paragraph 14 below, will exercise and procure the exercise of the votes (whether on a show of hands, a poll or otherwise) attaching to the NST Shares (and any other shares in NST which we acquire and which are capable of voting at the Court Meetings and/or the Shareholders' Meetings ("**Further NST Shares**")) in favour of the Scheme at any Court Meeting and in order to give effect to any measures required to implement the Scheme. In particular, but without limiting the foregoing, we undertake to the Offeror that we shall or shall procure that, after the posting of the circular to be issued by NST to its shareholders containing, inter alia, the Scheme (the "**Scheme Document**") (and without prejudice to any right to attend and vote in person at any Court Meeting and any Shareholders' Meeting), we shall return or shall procure the return of the signed forms of proxy accompanying the Scheme Document (completed and signed and voting in favour of the resolutions to approve the Scheme and any measures required to implement the Scheme) as soon as possible and in any event within seven days after the posting of the Scheme Document.
9. In respect of the NST ADRs we undertake to instruct the Depository to exercise the votes (whether on a show of hands, a poll or otherwise) attaching to the underlying NST ordinary shares which are represented by the NST ADRs in favour of the Scheme at any Court Meeting and any measures required to implement the Scheme and to return forms of proxy on the same basis as set forth in paragraph 8 above.

Undertaking to accept the Offer

10. In consideration of the Offeror's agreement to make the Acquisition, we irrevocably and unconditionally undertake that if an Offer is made by the Offeror:
 - (a) we shall accept or procure acceptance of the Offer in respect of the NST Securities in accordance with the procedure for acceptance set out in the formal document containing the Offer (the "**Offer Document**", including any additional document reflecting any extended, increased or revised terms) not later than seven days after the Offeror posts the Offer Document to NST Shareholders;
 - (b) we shall accept or procure the acceptance of the Offer in respect of any Further NST Securities in accordance with the procedure for acceptance set out in the Offer Document not later than seven days after the date we first become able so to accept or procure acceptance of the Offer;
 - (c) we shall promptly forward or procure the forwarding of, in respect of any NST Securities or Further NST Securities held in certificated form, the relevant certificate(s) to the Offeror or its nominated representative (or a form of indemnity acceptable to the directors of the Company in respect of any lost certificate(s)) at the time of acceptance and, in respect of any NST Securities or Further NST Securities held in uncertificated form, shall promptly take any action which may be reasonably required by the Offeror or its nominated representative in accordance with normal market practice in a takeover;
 - (d) notwithstanding that the terms of an Offer will confer a right of withdrawal on accepting shareholders, I will not, and, to the extent that I am not the registered holder of the NST Securities, will procure that such registered holder will not, withdraw acceptances in respect of the NST Securities; and
 - (e) the Offeror shall acquire the NST Securities and any Further NST Securities from us with full title guarantee, free from any lien, charge, option, equity encumbrance, rights of pre-emption, legal or other restrictions, together with all rights (including but not limited to any voting rights and the right to receive and retain in full all dividends of any nature and other distributions (if any) hereafter declared, made or paid subject to the matters referred to in the Press Announcement) attaching to or enjoyed by them as envisaged by the terms of the Offer.

Documentation

11. We irrevocably and unconditionally consent to:
 - (a) the inclusion of references to us and particulars of this irrevocable undertaking and our legal and beneficial holdings of the relevant securities of NST in any press announcement or other document issued by or on behalf of the Offeror or NST in connection with the Acquisition; and

(b) this undertaking being published on a website.

12. We irrevocably and unconditionally shall:

- 12.1.1 promptly give you all information and any assistance as you may reasonably require for the preparation of any such announcement or document in order to comply with the requirements of the Court, the Act and any other legal or regulatory requirement or body (but will not be required to take responsibility for any information or other matters other than factual information relating solely to ourselves); and
- 12.1.2 immediately notify you in writing of any material change in the accuracy or impact of any information previously given to you or in the event of any breach of the undertakings, representations or warranties set out herein.

Confidentiality and Market Conduct

13. Subject to and save to the extent required by law or regulation or by any court of competent jurisdiction or any stock exchange in accordance with whose regulations we or NST or the Offeror is required to comply, we shall keep confidential the possibility, terms and conditions of the Acquisition and the existence and terms of this undertaking until the Press Announcement is released or the information is otherwise in the public domain, provided that we may disclose the same to NST, the Offeror and their respective advisers. The obligations in this paragraph shall survive termination of this undertaking.

Termination

14. The undertakings, warranties, consents, waivers, agreements and obligations in this undertaking are conditional upon the issue of the Press Announcement by noon (London time) on 5 March 2019 or such later time or date as we may agree and (save as expressly provided for herein) will only lapse and cease to have effect to the extent not already undertaken and without prejudice to any liability for antecedent breach:
- (a) if the Scheme or Offer (as applicable) does not become effective, lapses or is withdrawn without becoming or being declared unconditional in accordance with its terms; or
 - (b) if the Offeror announces, with the consent of any relevant authority (if required) and before the Scheme Document or Offer Document is posted, that it does not intend to proceed with the Acquisition and no new, revised or replacement Scheme or Offer is announced by the Offeror at the same time or within 28 days thereafter; or
 - (c) if the Scheme or Offer (as applicable) does not become effective by 4 September 2019 but will extend to such later date as we agree in writing; or
 - (d) if the implementation agreement entered into between Bidder, Tungsten Bidco Limited and the NST in connection with the Acquisition has been terminated in accordance with its terms.
15. We hereby acknowledge that we have not entered into this undertaking relying on any statement or representation, whether or not made by the Offeror or its advisers (or any of their respective directors, officers, employees or agents) and we acknowledge that nothing in this undertaking obliges the Offeror to despatch the Press Announcement or the Scheme Document or the Offer Document. This undertaking contains the whole agreement between the Offeror and us relating to the subject matter of this undertaking at the date hereof, to the exclusion of any terms implied by law which may be executed by contract.
16. The Offeror undertakes to be bound by the Scheme in the event that the Scheme becomes effective. The obligations on the Offeror hereunder are conditional upon receipt by the Offeror of:
- (a) undertakings substantially in the terms agreed with the Offeror from each of the directors of NST in respect of their respective shares in the capital of NST, by noon (London time) on 4 March 2019 (or such later time and/or date as the Offeror may determine); and
 - (b) confirmation in terms satisfactory to the Offeror that the board of directors of NST has unanimously approved the issue of the Press Announcement including a statement that the board of directors of NST intends unanimously to recommend that its shareholders vote in favour of the Scheme and such approval and recommendation not having been withdrawn or qualified prior to publication of the Scheme Document.

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17. This undertaking shall not oblige the Offeror to proceed with the Acquisition.
 18. We acknowledge that, except to the extent otherwise specified, our obligations, undertakings, representations and warranties set out in this undertaking are unconditional and irrevocable. Time shall be of the essence in connection with any deadline or time for performance referred to in this undertaking.
 19. We acknowledge that damages would not be an adequate remedy for breach of the obligations contained in this undertaking and we further undertake that we will not assert otherwise in any proceeds relating hereto. We acknowledge that the Offeror shall be entitled to seek the remedies of specific performance, injunctive relief or other equitable relief and no proof of special damages shall be necessary for the enforcement by the Offeror of its rights hereunder by such remedies.

Governing Law and Jurisdiction

20. This undertaking and any claim, dispute or difference (including non-contractual claims, disputes or differences) arising out of or in connection with it or its subject matter shall be governed by, and construed in accordance with, English law.
21. We irrevocably agree to submit to the exclusive jurisdiction of the courts of England to settle any claim, legal action, proceeding, dispute or matter of difference (including non-contractual claims, disputes or differences) which may arise out of or in connection with this undertaking or its subject matter (including a dispute regarding the existence, validity, formation, effect, interpretation, performance or termination of this undertaking) and that accordingly any proceedings be brought in such courts.

SCHEDULE 1

INTERESTS IN NST

Interests in Shares

<u>Registered Holder</u>	<u>Beneficial Owner (if different)</u>	<u>Number of ordinary shares of £0.01 each</u>
<hr/>		

Interests in ADRs

<u>Registered Holder</u>	<u>Beneficial Owner (if different)</u>	<u>Number of American depository receipts, each representing ordinary shares of £0.01 each</u>
<hr/>		

ANNEX

Press Announcement

