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

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**SCHEDULE 13D**

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

**Nightstar Therapeutics plc**

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(Name of Issuer)

**Ordinary Shares, nominal value £0.01  
(represented by American Depositary Shares)**

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(Title of Class of Securities)

**65413A101**

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(CUSIP Number)

**Louis S. Citron, Esq.  
New Enterprise Associates  
1954 Greenspring Drive, Suite 600, Timonium, MD 21093  
(410) 842-4000**

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(Name, Address and Telephone Number of Person Authorized to Receive Notices and Communications)

**March 4, 2019**

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(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 §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.

The 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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<b>1</b>	<b>NAMES OF REPORTING PERSONS I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)</b> New Enterprise Associates 15, L.P.	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP</b> (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	<b>SEC USE ONLY</b>	
<b>4</b>	<b>SOURCE OF FUNDS (SEE INSTRUCTIONS)</b> WC	
<b>5</b>	<b>CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E)</b> <input type="checkbox"/>	
<b>6</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> Delaware Limited Partnership	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>7</b>	<b>SOLE VOTING POWER</b> 0 shares
	<b>8</b>	<b>SHARED VOTING POWER</b> 6,662,532 shares
	<b>9</b>	<b>SOLE DISPOSITIVE POWER</b> 0 shares
	<b>10</b>	<b>SHARED DISPOSITIVE POWER</b> 6,662,532 shares
<b>11</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 6,662,532 shares (1)	
<b>12</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)</b> <input type="checkbox"/>	
<b>13</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)</b> 19.9%	
<b>14</b>	<b>TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)</b> PN	

- (1) Includes only shares directly held by New Enterprise Associates 15, L.P. ("NEA 15"). NEA 15 may be deemed to be part of a voting group and may be deemed to have beneficial ownership of the shares held by such voting group. See Item 3 and Item 5.

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> <b>I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)</b> NEA Partners 15, L.P.	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP</b> (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	SEC USE ONLY	
<b>4</b>	<b>SOURCE OF FUNDS (SEE INSTRUCTIONS)</b> AF	
<b>5</b>	<b>CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E)</b> <input type="checkbox"/>	
<b>6</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> Delaware Limited Partnership	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>7</b>	<b>SOLE VOTING POWER</b> 0 shares
	<b>8</b>	<b>SHARED VOTING POWER</b> 6,662,532 shares
	<b>9</b>	<b>SOLE DISPOSITIVE POWER</b> 0 shares
	<b>10</b>	<b>SHARED DISPOSITIVE POWER</b> 6,662,532 shares
<b>11</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 6,662,532 shares (1)	
<b>12</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)</b> <input type="checkbox"/>	
<b>13</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)</b> 19.9%	
<b>14</b>	<b>TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)</b> PN	

- (1) Includes only shares directly held by New Enterprise Associates 15, L.P. ("NEA 15"). NEA 15 may be deemed to be part of a voting group and may be deemed to have beneficial ownership of the shares held by such voting group. See Item 3 and Item 5.

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> <b>I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)</b> NEA 15 GP, LLC	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP</b> (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	SEC USE ONLY	
<b>4</b>	<b>SOURCE OF FUNDS (SEE INSTRUCTIONS)</b> AF	
<b>5</b>	<b>CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E)</b> <input type="checkbox"/>	
<b>6</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> Delaware Limited Liability Company	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>7</b>	<b>SOLE VOTING POWER</b> 0 shares
	<b>8</b>	<b>SHARED VOTING POWER</b> 6,662,532 shares
	<b>9</b>	<b>SOLE DISPOSITIVE POWER</b> 0 shares
	<b>10</b>	<b>SHARED DISPOSITIVE POWER</b> 6,662,532 shares
<b>11</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 6,662,532 shares (1)	
<b>12</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)</b> <input type="checkbox"/>	
<b>13</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)</b> 19.9%	
<b>14</b>	<b>TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)</b> OO	

- (1) Includes only shares directly held by New Enterprise Associates 15, L.P. ("NEA 15"). NEA 15 may be deemed to be part of a voting group and may be deemed to have beneficial ownership of the shares held by such voting group. See Item 3 and Item 5.

<b>1</b>	<b>NAMES OF REPORTING PERSONS I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)</b>  Peter J. Barris	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP</b> (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	<b>SEC USE ONLY</b>	
<b>4</b>	<b>SOURCE OF FUNDS (SEE INSTRUCTIONS)</b>  AF	
<b>5</b>	<b>CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E)</b> <input type="checkbox"/>	
<b>6</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b>  United States citizen	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>7</b>	<b>SOLE VOTING POWER</b>  0 shares
	<b>8</b>	<b>SHARED VOTING POWER</b>  6,662,532 shares
	<b>9</b>	<b>SOLE DISPOSITIVE POWER</b>  0 shares
	<b>10</b>	<b>SHARED DISPOSITIVE POWER</b>  6,662,532 shares
<b>11</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b>  6,662,532 shares (1)	
<b>12</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)</b> <input type="checkbox"/>	
<b>13</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)</b>  19.9%	
<b>14</b>	<b>TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)</b>  IN	

- (1) Includes only shares directly held by New Enterprise Associates 15, L.P. ("NEA 15"). NEA 15 may be deemed to be part of a voting group and may be deemed to have beneficial ownership of the shares held by such voting group. See Item 3 and Item 5.

<b>1</b>	<b>NAMES OF REPORTING PERSONS I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)</b> Forest Baskettt	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP</b> (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	<b>SEC USE ONLY</b>	
<b>4</b>	<b>SOURCE OF FUNDS (SEE INSTRUCTIONS)</b> AF	
<b>5</b>	<b>CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E)</b> <input type="checkbox"/>	
<b>6</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> United States citizen	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>7</b>	<b>SOLE VOTING POWER</b> 0 shares
	<b>8</b>	<b>SHARED VOTING POWER</b> 6,662,532 shares
	<b>9</b>	<b>SOLE DISPOSITIVE POWER</b> 0 shares
	<b>10</b>	<b>SHARED DISPOSITIVE POWER</b> 6,662,532 shares
<b>11</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 6,662,532 shares (1)	
<b>12</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)</b> <input type="checkbox"/>	
<b>13</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)</b> 19.9%	
<b>14</b>	<b>TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)</b> IN	

- (1) Includes only shares directly held by New Enterprise Associates 15, L.P. ("NEA 15"). NEA 15 may be deemed to be part of a voting group and may be deemed to have beneficial ownership of the shares held by such voting group. See Item 3 and Item 5.

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> <b>I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)</b>  Anthony A. Florence, Jr.	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP</b> (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	<b>SEC USE ONLY</b>	
<b>4</b>	<b>SOURCE OF FUNDS (SEE INSTRUCTIONS)</b>  AF	
<b>5</b>	<b>CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E)</b> <input type="checkbox"/>	
<b>6</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b>  United States citizen	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>7</b>	<b>SOLE VOTING POWER</b>  0 shares
	<b>8</b>	<b>SHARED VOTING POWER</b>  6,662,532 shares
	<b>9</b>	<b>SOLE DISPOSITIVE POWER</b>  0 shares
	<b>10</b>	<b>SHARED DISPOSITIVE POWER</b>  6,662,532 shares
<b>11</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b>  6,662,532 shares (1)	
<b>12</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)</b> <input type="checkbox"/>	
<b>13</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)</b>  19.9%	
<b>14</b>	<b>TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)</b>  IN	

- (1) Includes only shares directly held by New Enterprise Associates 15, L.P. ("NEA 15"). NEA 15 may be deemed to be part of a voting group and may be deemed to have beneficial ownership of the shares held by such voting group. See Item 3 and Item 5.

<b>1</b>	<b>NAMES OF REPORTING PERSONS I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)</b> Mohamad Makhzoumi	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP</b> (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	<b>SEC USE ONLY</b>	
<b>4</b>	<b>SOURCE OF FUNDS (SEE INSTRUCTIONS)</b> AF	
<b>5</b>	<b>CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E)</b> <input type="checkbox"/>	
<b>6</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> United States citizen	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>7</b>	<b>SOLE VOTING POWER</b> 0 shares
	<b>8</b>	<b>SHARED VOTING POWER</b> 6,662,532 shares
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	<b>10</b>	<b>SHARED DISPOSITIVE POWER</b> 6,662,532 shares
<b>11</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 6,662,532 shares (1)	
<b>12</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)</b> <input type="checkbox"/>	
<b>13</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)</b> 19.9%	
<b>14</b>	<b>TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)</b> IN	

- (1) Includes only shares directly held by New Enterprise Associates 15, L.P. ("NEA 15"). NEA 15 may be deemed to be part of a voting group and may be deemed to have beneficial ownership of the shares held by such voting group. See Item 3 and Item 5.



<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> <b>I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)</b> Joshua Makower	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP</b> (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	<b>SEC USE ONLY</b>	
<b>4</b>	<b>SOURCE OF FUNDS (SEE INSTRUCTIONS)</b> AF	
<b>5</b>	<b>CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E)</b> <input type="checkbox"/>	
<b>6</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> United States citizen	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>7</b>	<b>SOLE VOTING POWER</b> 0 shares
	<b>8</b>	<b>SHARED VOTING POWER</b> 6,662,532 shares
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	<b>10</b>	<b>SHARED DISPOSITIVE POWER</b> 6,662,532 shares
<b>11</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 6,662,532 shares (1)	
<b>12</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)</b> <input type="checkbox"/>	
<b>13</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)</b> 19.9%	
<b>14</b>	<b>TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)</b> IN	

(1) Includes only shares directly held by New Enterprise Associates 15, L.P. ("NEA 15"). NEA 15 may be deemed to be part of a voting group and may be deemed to have beneficial ownership of the shares held by such voting group. See Item 3 and Item 5.

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> <b>I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)</b> David M. Mott	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP</b> (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	SEC USE ONLY	
<b>4</b>	<b>SOURCE OF FUNDS (SEE INSTRUCTIONS)</b> AF	
<b>5</b>	<b>CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E)</b> <input type="checkbox"/>	
<b>6</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> United States citizen	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>7</b>	<b>SOLE VOTING POWER</b> 0 shares
	<b>8</b>	<b>SHARED VOTING POWER</b> 6,662,532 shares
	<b>9</b>	<b>SOLE DISPOSITIVE POWER</b> 0 shares
	<b>10</b>	<b>SHARED DISPOSITIVE POWER</b> 6,662,532 shares
<b>11</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 6,662,532 shares (1)	
<b>12</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)</b> <input type="checkbox"/>	
<b>13</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)</b> 19.9%	
<b>14</b>	<b>TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)</b> IN	

- (1) Includes only shares directly held by New Enterprise Associates 15, L.P. ("NEA 15"). NEA 15 may be deemed to be part of a voting group and may be deemed to have beneficial ownership of the shares held by such voting group. See Item 3 and Item 5.

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> <b>I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)</b> Scott D. Sandell	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP</b> (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	<b>SEC USE ONLY</b>	
<b>4</b>	<b>SOURCE OF FUNDS (SEE INSTRUCTIONS)</b> AF	
<b>5</b>	<b>CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E)</b> <input type="checkbox"/>	
<b>6</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> United States citizen	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>7</b>	<b>SOLE VOTING POWER</b> 0 shares
	<b>8</b>	<b>SHARED VOTING POWER</b> 6,662,532 shares
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	<b>10</b>	<b>SHARED DISPOSITIVE POWER</b> 6,662,532 shares
<b>11</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 6,662,532 shares (1)	
<b>12</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)</b> <input type="checkbox"/>	
<b>13</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)</b> 19.9%	
<b>14</b>	<b>TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)</b> IN	

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<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> <b>I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)</b>  Peter W. Sonsini	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP</b> (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	<b>SEC USE ONLY</b>	
<b>4</b>	<b>SOURCE OF FUNDS (SEE INSTRUCTIONS)</b>  AF	
<b>5</b>	<b>CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(D) OR 2(E)</b> <input type="checkbox"/>	
<b>6</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b>  United States citizen	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>7</b>	<b>SOLE VOTING POWER</b>  0 shares
	<b>8</b>	<b>SHARED VOTING POWER</b>  6,662,532 shares
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	<b>10</b>	<b>SHARED DISPOSITIVE POWER</b>  6,662,532 shares
<b>11</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b>  6,662,532 shares (1)	
<b>12</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)</b> <input type="checkbox"/>	
<b>13</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)</b>  19.9%	
<b>14</b>	<b>TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)</b>  IN	

- (1) Includes only shares directly held by New Enterprise Associates 15, L.P. ("NEA 15"). NEA 15 may be deemed to be part of a voting group and may be deemed to have beneficial ownership of the shares held by such voting group. See Item 3 and Item 5.

## Schedule 13D

**Item 1. Security and Issuer.**

This Amendment No. 2 ("Amendment No. 2") to Schedule 13D amends and restates the statement on Schedule 13D originally filed on October 6, 2017 and Amendment No. 1 thereto filed on October 9, 2018, relating to the ordinary shares, nominal value £0.01 per share (the "Ordinary Shares"), including Ordinary Shares represented by American Depositary Shares (the "ADSs"), with each ADS representing one Ordinary Share, of Nightstar Therapeutics plc (the "Issuer") having its principal executive office at 10 Midford Place, 2<sup>nd</sup> Floor, London W1T 5BJ, United Kingdom.

Certain terms used but defined in this Amendment No. 2 have the meanings assigned thereto in the Schedule 13D (including Amendment No. 1 thereto). Except as specifically provided herein, this Amendment No. 1 does not modify any of the information previously reported on the Schedule 13D (including Amendment No. 1 thereto).

**Item 2. Identity and Background.**

This statement is being filed by:

(a) New Enterprise Associates 15, L.P. ("NEA 15"); NEA Partners 15, L.P. ("NEA Partners 15"), which is the sole general partner of NEA 15; and NEA 15 GP, LLC ("NEA 15 LLC" and, together with NEA Partners 15, the "Control Entities"), which is the sole general partner of NEA Partners 15; and

(b) Peter J. Barris ("Barris"), Forest Baskett ("Baskett"), Anthony A Florence, Jr. ("Florence"), Mohamad Makhzoumi ("Makhzoumi"), Joshua Makower ("Makower"), David M. Mott ("Mott"), Scott D. Sandell ("Sandell"), Peter W. Sonsini ("Sonsini") (together, the "Managers") and Ravi Viswanathan ("Viswanathan"). The Managers are the managers of NEA 15 LLC.

The persons named in this Item 2 are referred to individually herein as a "Reporting Person" and collectively as the "Reporting Persons."

The address of the principal business office of NEA 15 and each Control Entity is New Enterprise Associates, 1954 Greenspring Drive, Suite 600, Timonium, MD 21093. The address of the principal business office of each of Barris and Mott is New Enterprise Associates, 5425 Wisconsin Avenue, Suite 800, Chevy Chase, MD 20815. The address of the principal business office of Baskett, Makhzoumi, Makower, Sandell and Sonsini is New Enterprise Associates, 2855 Sand Hill Road, Menlo Park, California 94025. The address of the principal business office of Florence is New Enterprise Associates, 104 5<sup>th</sup> Avenue, 19<sup>th</sup> Floor, New York, NY 10001.

The principal business of NEA 15 is to invest in and assist growth-oriented businesses located principally in the United States. The principal business of NEA Partners 15 is to act as the sole general partner of NEA 15. The principal business of NEA 15 LLC is to act as the sole general partner of NEA Partners 15. The principal business of each of the Managers is to manage the Control Entities, and a number of affiliated partnerships with similar businesses.

During the five years prior to the date hereof, none of the Reporting Persons has been convicted in a criminal proceeding or has been a party to a civil proceeding ending in 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.

NEA 15 LLC is a limited liability company organized under the laws of the State of Delaware. NEA 15 and NEA Partners 15 are limited partnerships organized under the laws of the State of Delaware. Each of the Managers is a United States citizen.

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**Item 3. Source and Amount of Funds or Other Consideration.**

The Reporting Persons are filing this Schedule 13D amendment because they may be deemed to be a member of a "group," within the meaning of Section 13(d)(3) of the Act as a result of NEA 15 having entered into a Shareholder's Irrevocable Undertaking, dated March 4, 2019, as described in Item 4 below.

**Item 4. Purpose of Transaction.**

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 has 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 NEA 15 and Syncona Portfolio Limited ("Syncona") 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. NEA 15, together with Syncona, 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 as Exhibit 99.1 to the 8-K and incorporated herein by reference.

Depending on market conditions, its continuing evaluation of the business and prospects of the Issuer and other factors, NEA 15 and other Reporting Persons may dispose of or acquire additional shares of the Issuer. Except as set forth above, none of the Reporting Persons has any present plans which relate to or would result in:

- (a) The acquisition by any person of additional securities of the Issuer, or the disposition of securities of the Issuer;
  - (b) An extraordinary corporate transaction, such as a merger, reorganization or liquidation, involving the Issuer or any of its subsidiaries;
  - (c) A sale or transfer of a material amount of assets of the Issuer or any of its subsidiaries;
  - (d) Any change in the present board of directors or management of the Issuer, including any plans or proposals to change the number or term of directors or to fill any existing vacancies on the board;
  - (e) Any material change in the present capitalization or dividend policy of the Issuer;
  - (f) Any other material change in the Issuer's business or corporate structure;
  - (g) Changes in the Issuer's charter, bylaws or instruments corresponding thereto or other actions which may impede the acquisition of control of the Issuer by any person;
  - (h) Causing a class of securities of the Issuer to be delisted from a national securities exchange or to cease to be authorized to be quoted in an inter-dealer quotation system of a registered national securities association;
  - (i) A class of equity securities of the Issuer becoming eligible for termination of registration pursuant to Section 12(g)(4) of the Securities Exchange Act of 1934; or
  - (j) Any action similar to any of those enumerated above.
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**Item 5. Interest in Securities of the Issuer.**

- (a) NEA 15 is the record owner of the NEA 15 Shares. As the general partner of NEA 15, NEA Partners 15 may be deemed to own beneficially the NEA 15 Shares. As the sole general partner of NEA Partners 15, NEA 15 LLC may be deemed to own beneficially the NEA 15 Shares. As members of NEA 15 LLC, each of the Managers may be deemed to own beneficially the NEA 15 Shares.

Each Reporting Person disclaims beneficial ownership of the NEA 15 Shares other than those shares which such person owns of record.

The percentage of outstanding Ordinary Shares of the Issuer which may be deemed to be beneficially owned by each Reporting Person is set forth on Line 13 of such Reporting Person's cover sheet. Such percentage was calculated based on the 33,533,714 Ordinary Shares reported to be outstanding on the Issuer's 8-K.

- (b) Regarding the number of shares as to which such person has:
- (i) sole power to vote or to direct the vote: See line 7 of cover sheets
  - (ii) shared power to vote or to direct the vote: See line 8 of cover sheets
  - (iii) sole power to dispose or to direct the disposition: See line 9 of cover sheets
  - (iv) shared power to dispose or to direct the disposition: See line 10 of cover sheets
- (c) Except as set forth in Item 3 above, none of the Reporting Persons has effected any transaction in the Ordinary Shares during the last 60 days.
- (d) No other person is known to have the right to receive or the power to direct the receipt of dividends from, or any proceeds from the sale of, Shares beneficially owned by any of the Reporting Persons.
- (e) Viswanathan has ceased to own beneficially five percent (5%) or more of the Issuer's Ordinary Shares as a result of ceasing to be a Manager of NEA 15 LLC.

**Item 6. Contracts, Arrangements, Undertakings or Relationships with Respect to Securities of the Issuer.**

As described in Item 4, above, NEA 15 is subject to the terms of the Undertaking.

**Item 7. Material to be Filed as Exhibits.**

Exhibit 1 – Agreement regarding filing of joint Schedule 13D.

Exhibit 2 – Power of Attorney regarding filings under the Securities Exchange Act of 1934, as amended.

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SIGNATURE

After reasonable inquiry and to the best of its knowledge and belief, each of the undersigned certifies that the information set forth in this statement is true, complete and correct.

EXECUTED this 13<sup>th</sup> day of March, 2019.

NEW ENTERPRISE ASSOCIATES 15, L.P.

By: NEA PARTNERS 15, L.P.  
General Partner

By: NEA 15 GP, LLC  
General Partner

By: \_\_\_\_\_\*  
Louis S. Citron  
Chief Legal Officer

NEA PARTNERS 15, L.P.

By: NEA 15 GP, LLC  
General Partner

By: \_\_\_\_\_\*  
Louis S. Citron  
Chief Legal Officer

NEA 15 GP, LLC

By: \_\_\_\_\_\*  
Louis S. Citron  
Chief Legal Officer

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Peter J. Barris

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Forest Baskett

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Anthony A. Florence, Jr.

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Mohamad Makhzoumi

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\_\_\_\_\_  
Joshua Makower

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\_\_\_\_\_  
David M. Mott

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\_\_\_\_\_  
Scott D. Sandell

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\_\_\_\_\_  
Peter W. Sonsini

\*/s/ Sasha O. Keough

Sasha O. Keough  
As attorney-in-fact

This Amendment No. 2 to Schedule 13D was executed by Sasha O. Keough on behalf of the individuals listed above pursuant to a Power of Attorney a copy of which is attached as Exhibit 2.

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## AGREEMENT

Pursuant to Rule 13d-1(k)(1) under the Securities Exchange Act of 1934, the undersigned hereby agree that only one statement containing the information required by Schedule 13D need be filed with respect to the ownership by each of the undersigned of shares of stock of Nightstar Therapeutics plc.

EXECUTED this 13<sup>th</sup> day of March, 2019.

NEW ENTERPRISE ASSOCIATES 15, L.P.

By: NEA PARTNERS 15, L.P.  
General Partner

By: NEA 15 GP, LLC  
General Partner

By: \_\_\_\_\_  
\*  
Louis S. Citron  
Chief Legal Officer

NEA PARTNERS 15, L.P.

By: NEA 15 GP, LLC  
General Partner

By: \_\_\_\_\_  
\*  
Louis S. Citron  
Chief Legal Officer

NEA 15 GP, LLC

By: \_\_\_\_\_  
\*  
Louis S. Citron  
Chief Legal Officer

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Peter J. Barris

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Forest Baskett

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Anthony A. Florence, Jr.

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Mohamad Makhzoumi

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Joshua Makower

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David M. Mott

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\_\_\_\_\_  
Scott D. Sandell

\*

\_\_\_\_\_  
Peter W. Sonsini

\*/s/ Sasha O. Keough \_\_\_\_\_

Sasha O. Keough  
As attorney-in-fact

This Agreement relating to Schedule 13D was executed by Sasha O. Keough on behalf of the individuals listed above pursuant to a Power of Attorney a copy of which is attached hereto as Exhibit 2.

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EXHIBIT 2

## POWER OF ATTORNEY

KNOW ALL MEN BY THESE PRESENTS, that the undersigned hereby constitutes and appoints Louis S. Citron, Timothy Schaller, Sasha Keough and Stephanie Brecher, and each of them, with full power to act without the others, his or her true and lawful attorney-in-fact, with full power of substitution, to sign any and all instruments, certificates and documents that may be necessary, desirable or appropriate to be executed on behalf of himself as an individual or in his or her capacity as a direct or indirect general partner, director, officer or manager of any partnership, corporation or limited liability company, pursuant to section 13 or 16 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and any and all regulations promulgated thereunder, and to file the same, with all exhibits thereto, and any other documents in connection therewith, with the Securities and Exchange Commission, and with any other entity when and if such is mandated by the Exchange Act or by the Financial Industry Regulatory Authority, granting unto said attorney-in-fact full power and authority to do and perform each and every act and thing necessary, desirable or appropriate, fully to all intents and purposes as he or she might or could do in person, thereby ratifying and confirming all that said attorney-in-fact, or his or her substitutes, may lawfully do or cause to be done by virtue hereof.

IN WITNESS WHEREOF, this Power of Attorney has been signed as of the 13th day of March, 2017.

/s/ M. James Barrett  
M. James Barrett

/s/ Peter J. Barris  
Peter J. Barris

/s/ Forest Baskett  
Forest Baskett

/s/ Ali Behbahani  
Ali Behbahani

/s/ Colin Bryant  
Colin Bryant

/s/ Carmen Chang  
Carmen Chang

/s/ Anthony A. Florence, Jr.  
Anthony A. Florence, Jr.

/s/ Carol G. Gallagher  
Carol G. Gallagher

/s/ Dayna Grayson  
Dayna Grayson

/s/ Patrick J. Kerins  
Patrick J. Kerins

/s/ P. Justin Klein  
P. Justin Klein

/s/ Vanessa Larco  
Vanessa Larco

/s/ Joshua Makower  
Joshua Makower

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/s/ Mohamad H. Makhzoumi  
Mohamad H. Makhzoumi

/s/ Edward T. Mathers  
Edward T. Mathers

/s/ David M. Mott  
David M. Mott

/s/ Sara M. Nayeem  
Sara M. Nayeem

/s/ Jason R. Nunn  
Jason R. Nunn

/s/ Gregory Papadopoulos  
Gregory Papadopoulos

/s/ Chetan Puttagunta  
Chetan Puttagunta

/s/ Jon Sakoda  
Jon Sakoda

/s/ Scott D. Sandell  
Scott D. Sandell

/s/ A. Brooke Seawell  
A. Brooke Seawell

/s/ Peter W. Sonsini  
Peter W. Sonsini

/s/ Melissa Taunton  
Melissa Taunton

/s/ Frank M. Torti  
Frank M. Torti

/s/ Ravi Viswanathan  
Ravi Viswanathan

/s/ Paul E. Walker  
Paul E. Walker

/s/ Rick Yang  
Rick Yang