

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

**Form F-1  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

**Nightstar Therapeutics plc**

(Exact name of registrant as specified in its charter)

**England and Wales**  
(State or other jurisdiction of  
incorporation or organization)

**2836**  
(Primary Standard Industrial  
Classification Code Number)

**Not applicable**  
(I.R.S. Employer  
Identification Number)

**10 Midford Place, 2nd Floor  
London W1T 5BJ  
United Kingdom  
Tel: +44 (0)20 7062 2777**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Cogency Global Inc.  
10 East 40th Street, 10th Floor  
New York, New York 10016  
+1 212-947-7200**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

**Copies of all communications, including communications sent to agent for service, should be sent to:**

**Brian A. Johnson  
Wilmer Cutler Pickering Hale and  
Dorr LLP  
7 World Trade Center  
250 Greenwich Street  
New York, New York 10007  
+1 212 230 8800**

**Jonathan King  
Osborne Clarke LLP  
One London Wall  
London EC2Y 5EB  
United Kingdom  
+44 20 7105 7000**

**Simon Amies  
James Gubbins  
Covington & Burling LLP  
265 Strand  
London WC2R 1BH  
United Kingdom  
+44 20 7067 2000**

**Eric W. Blanchard  
Brian K. Rosenzweig  
Covington & Burling LLP  
The New York Times Building  
620 Eighth Avenue  
New York, New York 10018  
+1 212 841 1000**

**Approximate date of commencement of proposed sale to public:** As soon as practicable after this registration statement becomes effective.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act.

Emerging growth company

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards† provided pursuant to Section 7(a)(2)(B) of the Securities Act.

† The term "new or revised financial accounting standards" refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

**CALCULATION OF REGISTRATION FEE**

TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED	AMOUNT TO BE REGISTERED(1)	PROPOSED MAXIMUM OFFERING PRICE PER SHARE(2)	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE(2)	AMOUNT OF REGISTRATION FEE
Ordinary shares, nominal value £0.01 per share(3)(4)	4,600,000	\$21.31	\$98,026,000	\$12,204.24

(1) Includes 600,000 ordinary shares represented by American Depositary Shares, or ADSs, that the underwriters have the option to purchase.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) under the Securities Act of 1933, as amended. The proposed maximum offering price per share and proposed maximum aggregate offering price are calculated on the basis of \$21.31, the average of the high and low sale price of the ADSs on the Nasdaq Global Select Market on September 24, 2018, in accordance with Rule 457(c) under the Securities Act of 1933, as amended.

(3) These ordinary shares are represented by ADSs, each of which represents one ordinary share of the Registrant.

(4) ADSs issuable upon deposit of the ordinary shares registered hereby have been registered pursuant to a separate registration statement on Form F-6 (File No. 333-220343).

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to such Section 8(a), may determine.

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The information contained in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is declared effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting an offer to buy these securities in any jurisdiction where such offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED SEPTEMBER 25, 2018

PRELIMINARY PROSPECTUS

**4,000,000 American Depositary Shares**



**Representing 4,000,000 Ordinary Shares**

We are offering 4,000,000 American Depositary Shares, or ADSs. Each ADS represents one ordinary share. The ADSs may be evidenced by American Depositary Receipts, or ADRs.

The public offering price is \$ \_\_\_\_\_ per ADS. Our ADSs are listed on the Nasdaq Global Select Market under the symbol "NITE." On September \_\_\_\_\_, 2018, the last reported sale price of our ADSs on the Nasdaq Global Select Market was \$ \_\_\_\_\_ per share.

Investing in our ADSs involves a high degree of risk. Before buying any ADSs, you should carefully read the discussion of material risks of investing in our ADSs in "[Risk Factors](#)" beginning on page 13 of this prospectus.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and a "foreign private issuer" under applicable U.S. federal securities laws. As such, we have elected to comply with certain reduced public company reporting requirements. See "Prospectus Summary—Implications of Being an Emerging Growth Company and Foreign Private Issuer" for additional information.

Neither the U.S. Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

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	PER ADS	TOTAL
Public offering price	\$ _____	\$ _____
Underwriting discounts and commissions(1)	\$ _____	\$ _____
Proceeds to Nightstar Therapeutics plc before expenses	\$ _____	\$ _____

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(1) See "Underwriting" for additional information regarding total underwriter compensation.

Delivery of the ADSs is expected to be made on or about \_\_\_\_\_, 2018. We have granted the underwriters an option for a period of 30 days to purchase an additional 600,000 ADSs. If the underwriters exercise the option to purchase additional ADSs in full, the total underwriting discounts and commissions payable by us will be \$ \_\_\_\_\_, and the total proceeds to us, before expenses, will be \$ \_\_\_\_\_.

**Jefferies**

**Barclays**

**UBS Investment Bank**

Prospectus dated \_\_\_\_\_, 2018

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**We have not, and the underwriters have not, authorized anyone to provide you with any information other than that contained in this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information others may give you. We are not, and the underwriters are not, making an offer to sell our ADSs in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or the sale of any ADSs.**

For investors outside the United States: Neither we nor the underwriters have done anything that would permit this public offering of the ADSs or possession or distribution of this prospectus in any jurisdiction, other than the United States, where action for that purpose is required. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the ADSs and the distribution of this prospectus outside the United States.

We are incorporated under the laws of England and Wales. Under the rules of the U.S. Securities and Exchange Commission, or the SEC, we are currently eligible for treatment as a “foreign private issuer.” As a foreign private issuer, we will not be required to file periodic reports and financial statements with the SEC as frequently or as promptly as domestic registrants whose securities are registered under the Securities Exchange Act of 1934, as amended, or the Exchange Act. See “Prospectus Summary—Implications of Being an Emerging Growth Company and Foreign Private Issuer” in this prospectus for more information.

## ABOUT THIS PROSPECTUS

On September 11, 2017, we completed the first step of a corporate reorganization pursuant to which NightstaRx Limited became a wholly owned subsidiary of Nightstar Therapeutics Limited, a holding company with nominal assets and liabilities formed to effect the corporate reorganization. On September 15, 2017, as the second step in the corporate reorganization, Nightstar Therapeutics Limited re-registered as a public limited company and our name was changed from Nightstar Therapeutics Limited to Nightstar Therapeutics plc. For more details on the corporate reorganization, see Note 7 to our audited consolidated financial statements included in our Annual Report on Form 20-F for the year ended December 31, 2017 incorporated herein by reference.

Unless otherwise indicated or the context otherwise requires, all references in this prospectus to the terms “NightstaRx Limited,” “Nightstar Therapeutics Limited,” “Nightstar Therapeutics plc,” “the company,” “we,” “us” and “our” refer to (i) NightstaRx Limited and its wholly owned U.S. subsidiary prior to the acquisition of NightstaRx Limited by Nightstar Therapeutics Limited on September 11, 2017, (ii) Nightstar Therapeutics Limited and its subsidiaries after the acquisition of NightstaRx Limited by Nightstar Therapeutics Limited on September 11, 2017, and (iii) Nightstar Therapeutics plc and its subsidiaries after the re-registration of Nightstar Therapeutics Limited as a public limited company on September 15, 2017. See Note 7 to our audited consolidated financial statements included in our Annual Report on Form 20-F for the fiscal year ended December 31, 2017 incorporated herein by reference.

We own various trademark registrations and applications, and unregistered trademarks, including Nightstar Therapeutics plc and our corporate logo. All other trade names, trademarks and service marks of other companies appearing in this prospectus are the property of their respective holders. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend to use or display other companies’ trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

The representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference into it contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that involve substantial risks and uncertainties. All statements other than statements of historical fact, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. In some cases, you can identify forward-looking statements by the words “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “intend,” “goal,” “plan,” “objective,” “target,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue” and “ongoing,” or the negative of these terms, or other comparable terminology intended to identify statements about the future, although not all forward-looking statements contain these identifying words. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. The forward-looking statements and opinions contained in this prospectus are based upon information available to us as of the date of this prospectus and, while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. Forward-looking statements include statements about:

- the development of NSR-REP1, NSR-RPGR and any of our other product candidates, including statements regarding the timing of initiation, completion and the outcome of clinical studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- our ability to obtain and maintain regulatory approval of our product candidates in the indications for which we plan to develop them, and any related restrictions, limitations or warnings in the label of an approved drug or therapy;
- our plans to research, develop, manufacture and commercialize our product candidates;
- our ability to acquire or in-license additional product candidates and technologies;
- the timing of our regulatory filings for our product candidates, along with regulatory developments in the United States, European Union and other foreign countries or jurisdictions;
- the size and growth potential of the markets for our product candidates and the rate and degree of market acceptance of our product candidates, including reimbursement that may be received from payors;
- our ability to raise additional capital;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our expectations regarding our ability to obtain and maintain intellectual property protection;
- our ability to attract and retain qualified employees and key personnel;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our expectations related to the use of proceeds from this offering; and
- our estimates regarding future expenses, revenues and needs for additional financing and the accuracy thereof.

You should refer to the important factors in the cautionary statements included in this prospectus and in other documents incorporated herein, for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements included or incorporated by reference in this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

You should read this prospectus and the documents that we reference in this prospectus, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

## **MARKET, INDUSTRY AND OTHER DATA**

This prospectus contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from our own internal estimates and research as well as from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

In addition, assumptions and estimates of our and our industry's future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section titled "Risk Factors" in this prospectus as well as those risk factors that are incorporated by reference in this prospectus. These and other factors could cause our future performance to differ materially from our assumptions and estimates. See "Special Note Regarding Forward-Looking Statements."

## PRESENTATION OF FINANCIAL INFORMATION

We maintain our books and records in pounds sterling, our results are subsequently converted to U.S. dollars and we prepare our consolidated financial statements in accordance with generally accepted accounting principles in the United States, or U.S. GAAP, as issued by the Financial Accounting Standards Board, or FASB. All references in this prospectus to "\$" are to U.S. dollars and all references to "£" are to pounds sterling. Our consolidated financial statements as at and for the years ended December 31, 2017, 2016 and 2015 have been translated from pounds sterling into U.S. dollars at the rate of £1.00 to \$1.3529, £1.00 to \$1.2337 and £1.00 to \$1.4746, respectively, which was the noon buying rate of the Federal Reserve Bank of New York on the last business day of our years ended December 31, 2017, 2016 and 2015, respectively. Our condensed consolidated financial statements as at and for the three-month and six-month periods ended June 30, 2018 and 2017 have been translated from pounds sterling into U.S. dollars at the rate of £1.00 to \$1.3197 and £1.00 to \$1.2995, respectively, which was the noon buying rate of the Federal Reserve Bank of New York on the last business day of the three months ended June 30, 2018 and 2017, respectively. These translations should not be considered representations that any such amounts have been, could have been or could be converted into U.S. dollars at that or any other exchange rate as of that or any other date. See "Exchange Rate Information" for more information.

We have made rounding adjustments to some of the figures included in this prospectus. Accordingly, numerical figures shown as totals in some tables may not be an arithmetic aggregation of the figures that preceded them. We have historically conducted our business through NightstaRx Limited and our U.S. subsidiary, and therefore our historical consolidated financial statements previously presented the consolidated results of operations of NightstaRx Limited. Following the completion of our reorganization on September 15, 2017 discussed above, our consolidated financial statements present the consolidated results of operations of Nightstar Therapeutics plc.

**PROSPECTUS SUMMARY**

*The following summary highlights information contained elsewhere in this prospectus and in the documents we incorporate herein by reference. This summary does not contain all of the information you should consider before investing in our American Depositary Shares, or ADSs. You should read the entire prospectus carefully, including the section titled “Risk Factors” contained in this prospectus, any related free writing prospectus and the section titled “Risk Factors” in our Report of Foreign Private Issuer on Form 6-K, furnished to the U.S. Securities and Exchange Commission, or SEC, on September 25, 2018, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus.*

**Overview**

We are a leading clinical-stage gene therapy company focused on developing and commercializing novel one-time treatments for patients suffering from rare inherited retinal diseases that would otherwise progress to blindness. Leveraging our expertise in ophthalmology, gene therapy and drug development, we are developing a pipeline of proprietary product candidates that are designed to substantially modify or halt the progression of inherited retinal diseases for which there are no currently approved treatments.

Our lead product candidate, NSR-REP1, is in Phase 3 clinical development for the treatment of choroideremia, or CHM, and represents the most clinically advanced product candidate for this indication worldwide. In data from 32 patients treated with NSR-REP1 across four open-label clinical trials, over 90% of treated patients maintained their visual acuity, or VA, over a two-year follow-up period. In some cases, we also observed substantial improvements in visual acuity. In June 2018, the U.S. Food and Drug Administration, or FDA, granted Regenerative Medicine Advanced Therapy, or RMAT, designation for NSR-REP1 in CHM.

Our second product candidate, NSR-RPGR, is in Phase 1/2 clinical development for the treatment of X-linked retinitis pigmentosa, or XLRP. On September 22, 2018, we announced positive preliminary safety and efficacy data from this trial for the first five cohorts (combined n=15) of the dose escalation study of our Phase 1/2 clinical trial, known as the XIRIUS trial, at the EURETINA medical meeting, as described further below. The safety data and efficacy signals observed in the higher dose groups of the dose escalation study provided the basis for an early clinical proof of concept for the XIRIUS trial to progress to a pre-planned expansion study, for which we expect to initiate enrollment during the fourth quarter of 2018. The expansion study is intended to enroll approximately 30 patients at a therapeutic dose informed by the dose escalation study and is anticipated to include a low-dose control group of approximately 15 patients. We also have product candidates in preclinical development for a number of inherited retinal diseases for which there are no approved treatments, such as Stargardt disease and Best vitelliform macular dystrophy, or Best disease.

We have the worldwide commercial rights to our entire pipeline of retinal gene therapy product candidates, summarized in the table below.

<b>PROGRAM</b>	<b>INDICATION</b>	<b>STAGE OF DEVELOPMENT</b>	<b>PLANNED MILESTONES</b>
<b>NSR-REP1</b>	Choroideremia	Phase 3 STAR trial	Complete Phase 3 Enrollment: 1H 2019
<b>NSR-RPGR</b>	X-linked Retinitis Pigmentosa	Phase 1/2 XIRIUS trial	Initiate Expansion Study Enrollment in XIRIUS: Q4 2018  Six-Month Data from Dose Escalation Study: Q2 2019
<b>NSR-ABCA4</b>	Stargardt Disease	Preclinical	N/A
<b>NSR-BEST1</b>	Best Disease	Preclinical	N/A



**Recent Developments: Preliminary Data from Dose Escalation Study in Phase 1/2 XIRIUS Trial of NSR-RPGR in X-linked Retinitis Pigmentosa**

On September 22, 2018, we announced that positive preliminary safety and efficacy data of NSR-RPGR from the dose escalation study in the Phase 1/2 XIRIUS trial was presented at the EURETINA 2018 Congress.

Enrollment of the dose escalation study in the XIRIUS trial was completed in August 2018, consisting of six cohorts of three patients each for a total of 18 adult patients. Each patient in the trial received a single sub-retinal injection of NSR-RPGR. Doses ranged from  $5 \times 10^9$  genome particles, or gp, in cohort 1 up to  $5 \times 10^{11}$  gp in cohort 6. One-year follow-up data on all 18 patients in the dose escalation study is expected to be available in the second half of 2019.

Data were presented for each of cohorts 1 through 5 from the one-month follow-up, the latest clinical timepoint for which the complete set of safety and efficacy data was available for all patients. In addition, microperimetry data were presented for cohort 3 through the six-month follow-up visit.

Based on the totality of results announced at the EURETINA medical meeting, we expect to initiate enrollment of the expansion study in the XIRIUS trial in the fourth quarter of 2018. The expansion study is intended to enroll approximately 30 adult and pediatric patients at a therapeutic dose informed by the dose escalation study and a low-dose control group of approximately 15 patients. Preliminary efficacy data from the expansion study is expected to be available in mid-2019, with one-year follow-up data expected to be available in 2020.

**Efficacy Summary**

At the one-month follow-up after treatment with NSR-RPGR, all three patients in cohort 3 ( $5 \times 10^{10}$  gp), one of three patients in cohort 4 ( $1 \times 10^{11}$  gp) and one of three patients in cohort 5 ( $2.5 \times 10^{11}$  gp) experienced an improvement in microperimetry, as discussed further below. Among the patients in cohorts 4 and 5, improvements in microperimetry in the treated eyes were observed in those patients receiving a second course of steroids. The safety data and efficacy signals observed in the higher dose groups provided the basis for an early clinical proof of concept for the XIRIUS trial to progress to the expansion study.

All patients in cohort 3 showed an improvement in microperimetry endpoints at one, three and six months of follow-up after treatment with NSR-RPGR with general concordance across the various analyses described below. Efficacy signals were generally observed within one month and maintained through the six-month follow-up visit for patients in this cohort.

**Baseline Demographics**

The following table provides the baseline demographics of the 15 patients in cohorts 1 through 5.

COHORT	DOSE (GP)	# OF PATIENTS	MEAN AGE	BASELINE MEAN RETINAL SENSITIVITY (dB)		BASELINE MEAN BCVA (LETTERS)		BASELINE MEAN EZ WIDTH (MICRONS)	
				TREATED EYE	UNTREATED EYE	TREATED EYE	UNTREATED EYE	TREATED EYE	UNTREATED EYE
				1	$5 \times 10^9$	3	37	-0.2	-0.4
2	$1 \times 10^{10}$	3	34	+0.2	+1.5	50	57	1375	1384
3	$5 \times 10^{10}$	3	30	+0.2	+1.5	64	66	248	250
4	$1 \times 10^{11}$	3	33	+2.2	+2.3	64	63	462	792
5	$2.5 \times 10^{11}$	3	25	+8.9	+9.1	71	73	2411	3341

**Microperimetry (MP)**

Microperimetry measures changes in visual function by gauging the ability to detect varying levels of light stimulus projected across the macula, the central part of the retina responsible for visual acuity. In the XIRIUS

trial, microperimetry was measured on a grid of 68 points across the macula. Comparisons are made to baseline measurements in the treated eye as well as in comparison to the untreated eye.

- **Overall Macula Sensitivity:** Change in the mean retinal sensitivity measured in decibels, or dB, of all 68 test loci. A responder analysis was also completed with a threshold of at least 2dB.
- **Central 16 Sensitivity:** Change in the mean retinal sensitivity (in dB) from the 16 test loci closest to the center of the macula.
- **Number of Improved Loci:** The number of patients with at least a 5dB improvement in over 10% of loci (>= 7 loci).

The following table provides a summary of the microperimetry data observed in cohorts 1 through 5 at the one-month follow-up visit. Microperimetry data from the latest available timepoints for cohorts 1 through 5 (ranging from one month in cohort 5 through 12 months in cohort 1) were generally consistent with the one-month data presented below.

	OVERALL MACULA SENSITIVITY (MEAN CHANGE (dB) / # OF PATIENTS WITH ≥2dB INCREASE)				CENTRAL 16 SENSITIVITY (MEAN CHANGE (dB))		IMPROVED LOCI (# OF PATIENTS WITH ≥5dB INCREASE AT ≥7 LOCI)	
	TREATED EYE		UNTREATED EYE		TREATED EYE	UNTREATED EYE	TREATED EYE	UNTREATED EYE
	<b>Cohort 1 (n=3)</b>	+0.1 dB / 0 pts	+0.2 dB / 0 pts	+0.5 dB	+0.4 dB	0 pts	0 pts	
<b>Cohort 2* (n=2)</b>	+0.2 dB / 0 pts	-0.8 dB / 0 pts	-0.1 dB	-0.8 dB	1 pts	0 pts		
<b>Cohort 3 (n=3)</b>	+2.4 dB / 3 pts	-0.1 dB / 0 pts	+6.1 dB	-1.0 dB	3 pts	0 pts		
<b>Cohort 4 (n=3)</b>	+0.1 dB / 1 pts	-0.1 dB / 0 pts	+1.2 dB	-0.2 dB	1 pts	0 pts		
<b>Cohort 5 (n=3)</b>	+0.6 dB / 1 pts	+1.2 dB / 1 pts	-0.6 dB	+1.4 dB	1 pts	1 pts		

\* One patient in cohort 2 was excluded from the analysis because triplicate testing was not performed at baseline.

The following table summarizes the changes in microperimetry observed from baseline through the six-month follow-up visit for cohort 3 using the three microperimetry analyses described above:

	OVERALL MACULA SENSITIVITY (MEAN CHANGE (dB) FROM BASELINE)				CENTRAL 16 SENSITIVITY (MEAN CHANGE (dB))		IMPROVED LOCI (# OF PATIENTS WITH ≥5dB INCREASE AT ≥7 LOCI)	
	TREATED EYE		UNTREATED EYE		TREATED EYE	UNTREATED EYE	TREATED EYE	UNTREATED EYE
	<b>Month 1</b>	+2.4 dB	-0.1 dB	+6.1 dB	-1.0 dB	3 pts	0 pts	
<b>Month 3</b>	+2.4 dB	-0.3 dB	+5.6 dB	-1.1 dB	3 pts	0 pts		
<b>Month 6</b>	+2.3 dB	-0.5 dB	+5.1 dB	-1.2 dB	3 pts	0 pts		

The efficacy data for cohort 3 was further analyzed using a histogram analysis, which revealed that the mean number of loci with retinal sensitivity improvements was consistently greater in the treated eyes as compared to the untreated eyes. Conversely, the mean number of loci with worsening retinal sensitivity was consistently greater in the untreated eyes as compared to the treated eyes for cohort 3.

**Ellipsoid Zone (EZ)**

Ellipsoid zone, or EZ, measurements use optical coherence tomography to quantify the extent of undamaged photoreceptors remaining in the retina. No significant decreases in EZ from baseline were observed through the last follow-up visit for which data were available (ranging from one month in cohort 5 to 12 months in cohort 1). Due to the advanced stage of disease of patients enrolled in this dose escalation study, only two patients

(one in cohort 2 and one in cohort 5) had a measurable baseline EZ that extended beyond the central 5 degrees of the macula. Prior natural history studies have shown that significant changes in EZ may require at least 1 year to 1.5 years to be detected, with follow-up visits on an annual basis being sufficient to detect progression. One-year follow-up data on all 18 patients in the dose escalation study is expected to be available in the second half of 2019. We plan to enroll patients into the expansion study with higher measurable baseline EZ to allow assessment and correlation of this anatomical endpoint with functional improvements in microperimetry.

#### **Visual Acuity (VA)**

VA was assessed using the clinically validated vision test chart developed for the Early Treatment of Diabetic Retinopathy Study, known as ETDRS. The mean baseline VA for treated eyes in patients in cohorts 1 through 5 ranged from 28 letters to 71 letters, while the mean baseline VA for untreated eyes ranged from 57 letters to 73 letters, respectively. At the latest follow-up timepoints for which data were available (ranging from three months in cohort 5 to 12 months in cohort 1), the VA of 93% of patients in cohorts 1 through 5 was maintained within five ETDRS letters, or one line, of baseline in both the treated and untreated eyes.

#### **Safety Summary**

Available safety data (ranging from three months in cohort 5 to 12 months in cohort 1) from the 15 treated patients in cohorts 1 through 5 indicates that NSR-RPGR was generally well-tolerated. The safety profile in the dose escalation study is generally consistent with that of surgical vitrectomy procedures and what has been observed in clinical trials of other ocular gene therapies. No serious adverse events related to treatment were reported and no early discontinuations or dose limiting toxicity were observed. Mild drug-related inflammation that potentially dampened efficacy was seen in the treated eyes of cohorts 4 and 5, with treatment efficacy observed to have been rescued in patients who received additional steroid treatment.

Adverse events of varying severity and duration related to the vitrectomy procedure or drug have been observed in the dose escalation study such as retinal changes, intraocular inflammation and visual disturbances.

The Data Monitoring Committee, or DMC, reviewed preliminary safety data for cohorts 1 through 5 and recommended escalation to cohort 6. The DMC also has not restricted pediatric enrollment in either the dose escalation study or expansion study.

#### **Our Lead Retinal Gene Therapy Product Candidate: NSR-REP1 for the Treatment of CHM**

Our lead retinal gene therapy product candidate, NSR-REP1, is in Phase 3 clinical development for the treatment of CHM and represents the most clinically advanced product candidate for this indication worldwide, potentially providing us with a significant industry first-mover advantage. We have received orphan drug designation for NSR-REP1 for the treatment of CHM from the FDA in the United States and from the European Medicines Agency, or EMA, in the European Union and RMAT designation from the FDA.

#### **CHM Disease Overview**

CHM is a rare, degenerative, X-linked genetic retinal disorder primarily affecting males, with no treatments currently available and represents a significant unmet medical need. CHM presents in childhood as night blindness, followed by progressive constriction of the visual fields, generally leading to vision loss in early adulthood and total blindness thereafter. Patients generally maintain good visual acuity until the degeneration encroaches onto the fovea, which is the central part of the retina responsible for detailed vision. The prevalence of CHM is estimated to be one in 50,000 people, implying a total population of approximately 13,000 patients in the United States and the five major European markets.

CHM is caused by mutations in the CHM gene, which encodes Rab escort protein-1, or REP1, a protein that plays a key role in intracellular protein trafficking and the elimination of waste products from retinal cells. Absence of functional REP1 leads to death of the retinal pigment epithelium, or RPE, cells and degeneration of the overlying retina, which contains the retinal photoreceptors required to convert light into visual signals. Thus, the loss of REP1 function in retinal cells caused by CHM results in progressive vision loss and blindness.

***Our Solution: NSR-REP1 for CHM***

Our lead retinal gene therapy product candidate, NSR-REP1, is comprised of an AAV2 vector containing recombinant human complementary DNA, or cDNA, that is designed to produce REP1 inside the eye. NSR-REP1 is comprised of a standard AAV vector combined with the human REP1 cDNA and a woodchuck hepatitis post-transcriptional regulatory element, or WPRE, sequence. In preclinical animal studies, the incorporation of the WPRE sequence resulted in a statistically significant, nearly two-fold increase in REP1 expression in the retina from baseline, which could provide a greater therapeutic effect than a REP1 vector without the WPRE sequence. The introduction of a functional CHM gene into patients is intended to allow expression of REP1, thereby slowing or stopping the progression of CHM and the decline in vision.

NSR-REP1 is administered by injection into the sub-retinal space, following a standard vitrectomy procedure to allow for better visualization of the injection site. NSR-REP1 is delivered using a two-step process to enhance surgical precision. The first step in this process involves the creation of a small bubble, or bleb, in the sub-retinal space with a small amount of balanced salt solution, followed by the second step in which NSR-REP1 is administered into this newly created sub-retinal bleb. Surgical precision is further enhanced by intra-operative optical coherence tomography, or iOCT, providing the surgeon with real-time, cross-sectional imaging of the precise location of NSR-REP1 administration.

***Clinical Development of NSR-REP1***

***Phase 1/2 Oxford Trial and Phase 2 Investigator-Sponsored Clinical Trials, or ISTs***

In data from 32 patients treated with NSR-REP1 across four open-label clinical trials, over 90% of treated patients maintained their visual acuity over a two-year follow up period. In some cases, we also observed substantial improvements in visual acuity, which we refer to as hyper-responders. The greatest proportion of hyper-responders was observed in patients with moderate to severe visual acuity loss. At one-year follow-up after treatment, four out of 19 treated patients in this group, or 21%, experienced a gain in visual acuity of at least 15 ETDRS letters from baseline as compared to 1% of all untreated patients in the prospective, natural history observational study, known as the NIGHT study.

In January 2014, the positive initial six-month proof-of-concept efficacy and safety data from the first cohort of six patients in a Phase 1/2 open-label, dose-escalation, single-eye IST conducted at the University of Oxford was published in the medical journal *The Lancet*. We refer to this trial as the Oxford Trial. Additional data supporting the long-term durability of treatment effect after 42 months of follow-up in the first cohort in the Oxford Trial was published in the *New England Journal of Medicine* in April 2016. Based on the initial positive efficacy and safety data generated from the Oxford Trial, a second cohort of eight patients was treated at the University of Oxford with a higher dose of NSR-REP1. Subsequently, three other open-label, single-center, single-eye Phase 2 ISTs were initiated in the United States, Canada and Germany, treating six patients at each clinical site with the same higher dose of NSR-REP1 as was used to treat the second cohort in the Oxford Trial.

As of the date of this prospectus, available clinical data from the 32 treated patients in the completed ISTs indicates that NSR-REP1 was well tolerated. The safety profile in the completed ISTs is consistent with that of surgical vitrectomy procedures generally and what has been observed in clinical trials of other ocular gene therapies. Adverse events of varying severity and duration related to the vitrectomy procedure or drug have been observed in the completed ISTs such as retinal changes, intraocular inflammation and visual disturbances, which generally resolved within one week after surgery. The adverse events observed in our ongoing clinical trials of NSR-REP1 have also generally been consistent with the adverse events seen in the completed ISTs and other ocular gene therapy clinical trials.

Based on these results, our understanding of the progression of CHM and our experience treating CHM patients, we have designed our ongoing Phase 3 STAR trial to allow these findings to be replicated in a prospective, randomized, controlled clinical trial setting.

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*NIGHT Natural History Observational Study*

We are conducting a prospective, natural history observational study in CHM called the NIGHT study and have enrolled over 250 CHM patients. NIGHT provides important evidence regarding the disease state and rate of progression in untreated patients and provides a benchmark against which to compare the effects of NSR-REP1. In the NIGHT study, we observed that 68 out of the 308 eyes assessed, or 22%, experienced a loss in visual acuity of five or more ETDRS letters at the 20-month follow-up period. In the NIGHT study, the final evaluable time point is 20 months and some patients were eligible to have both of their eyes assessed based on the entry visual acuity criteria. We are recruiting participants for our Phase 3 STAR trial primarily from the NIGHT study to significantly accelerate enrollment from this well-characterized patient population.

*RMAT Designation*

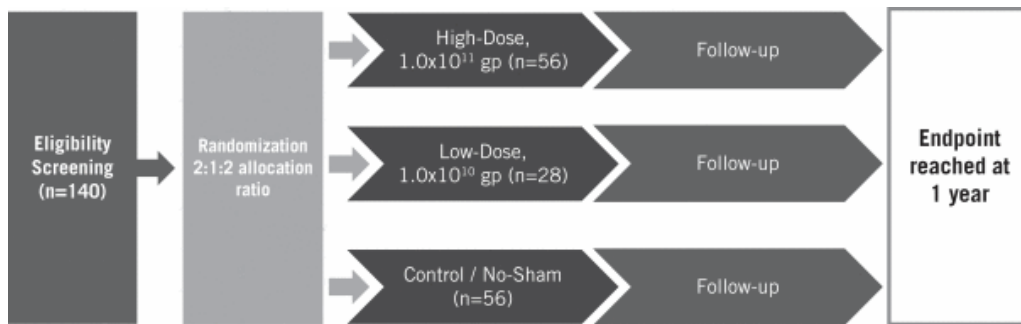
In June 2018, the FDA granted RMAT designation to NSR-REP1 based on clinical data supporting the maintenance and improvement of visual acuity from the four completed ISTs in CHM patients treated with NSR-REP1 and disease progression in untreated patients in the ongoing NIGHT natural history observational study. Established under the 21st Century Cures Act, the RMAT designation is an expedited program for the advancement and approval of regenerative medicine products. A regenerative medicine is eligible for the designation if it is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. RMAT designation allows companies developing regenerative medicine and gene therapies to work more closely and frequently with the FDA, and grants all of the benefits of Breakthrough Therapy Designation, including eligibility for priority review, rolling review and accelerated approval.

*STAR Phase 3 Registrational Trial*

In March 2018, we announced the initiation of our Phase 3 STAR registrational trial of NSR-REP1 in CHM. The trial is designed to study the safety and efficacy of NSR-REP1 in patients with a diagnosis of CHM due to REP1 mutations, as confirmed by genetic testing. The primary endpoint of the STAR trial is to measure the proportion of patients with an improvement of at least 15 ETDRS letters from baseline in visual acuity at 12 months post-treatment. Secondary endpoints include both anatomical and functional endpoints of efficacy and safety similar to the endpoints assessed in earlier clinical trials for NSR-REP1.

In the STAR trial, we intend to enroll approximately 140 patients across 18 clinical sites in the United States, Europe, Canada and South America, of which six sites are surgical centers. In order to be eligible to enter the STAR trial, patients must have a Moderate to Severe Visual Acuity Loss classification. The eligible patients will be randomized into one of three study arms: 56 patients receiving a high-dose NSR-REP1 in one eye ( $1.0 \times 10^{11}$  genome particles, or gp); 28 patients receiving a low-dose NSR-REP1 in one eye ( $1.0 \times 10^{10}$  gp); and 56 patients in an untreated, no-sham parallel-control arm. The primary endpoint will be assessed by comparing patients in the high-dose treatment arm with patients in the control arm. We are primarily recruiting patients in the STAR trial from the NIGHT study in order to significantly accelerate Phase 3 enrollment from this well-characterized patient population. We anticipate that the STAR Phase 3 registrational trial will be fully enrolled in the first half of 2019 and expect the one-year follow-up results of the STAR trial to be available in 2020.

The following chart summarizes the design of the STAR Phase 3 registrational trial:



We designed the STAR trial, including the statistical analyses, based on data from patients treated with NSR-REP1 in our earlier clinical trials and ISTs, and untreated patients from our NIGHT study. The doses in the STAR trial are equivalent to those studied in the earlier Phase 1/2 and Phase 2 ISTs. To achieve a statistical significance level of  $p < 0.05$ , between six and ten patients out of the 56 patients in the high-dose group, or 11% to 18% (assuming zero and two responses from patients in the control arm, respectively), will need to meet the primary endpoint criteria of a 15-letter improvement in visual acuity. This result would compare favorably to the 21% of patients who met the same criteria in the subgroup of the Phase 1/2 and Phase 2 ISTs previously conducted.

*Other Clinical Programs of NSR-REP1 in CHM*

NSR-REP1 is also currently being studied in the REGENERATE trial, an open-label, exploratory, single-eye Phase 2 clinical trial intended to enroll up to 30 patients with an early-stage diagnosis of CHM. NSR-REP1 is also currently being studied in an ongoing Phase 2 clinical trial known as the GEMINI trial to evaluate the safety of bilateral administration of a single dose of NSR-REP1 in both eyes of CHM patients.

**NSR-RPGR for the Treatment of XLRP**

NSR-RPGR is in Phase 1/2 clinical development for XLRP, known as the XIRIUS trial. Enrollment of the dose escalation study in the XIRIUS trial was completed in August 2018, consisting of six cohorts of three patients each for a total of 18 adult patients. On September 22, 2018, we announced positive preliminary safety and efficacy data from the XIRIUS trial for the first five cohorts (combined  $n=15$ ) of the dose escalation study at the EURETINA medical meeting. We have received orphan drug designation for NSR-RPGR for the treatment of XLRP from the EMA in the European Union.

***XLRP Disease Overview***

XLRP, a form of retinitis pigmentosa, is a rare inherited X-linked recessive genetic retinal disorder primarily affecting males. The disease is characterized by a lack of protein transport that leads to a loss of photoreceptors, resulting in rapid disease progression and severe retinal dysfunction. Approximately 70% of XLRP cases are due to variants in the genes responsible for the production of RPGR. RPGR is involved in the transport of proteins necessary for the maintenance of photoreceptor cells. Loss of RPGR function in the retinal cells causes the progressive loss of rod and cone photoreceptors, leading to the loss of vision experienced by patients. The estimated worldwide prevalence of XLRP due to RPGR variants is approximately one in 40,000 people, which implies approximately 17,000 patients in the United States and the five major European markets. There are no treatments currently available for XLRP.

The onset, progression, severity and clinical manifestations of XLRP vary from patient to patient. Typically, male patients first experience increasing symptoms of night blindness in the first decade, followed by a narrowing of their peripheral vision, and progressive loss of central vision in the patient's second or third decade. Legal or total blindness commonly occurs when the patient reaches his forties.

***Our Solution: NSR-RPGR for XLRP***

NSR-RPGR is comprised of a standard AAV8 vector containing codon-optimized cDNA that is designed to produce human RPGR inside the eye. We have developed a codon-optimized gene that features higher RPGR protein expression levels than with a wild-type RPGR coding sequence. In addition, codon optimization provides greater sequence stability, which results in the consistent production of an identical protein product. NSR-RPGR is designed to produce RPGR-ORF15, the form of RPGR preferentially expressed in the retina.

Based on preclinical findings indicating the potential for safety and efficacy with a significant rescue of photoreceptors, we believe NSR-RPGR has the ability to slow or stop retinal degeneration of photoreceptors and to restore or maintain vision in patients affected by these mutations. In two mouse models of XLRP in which the mice lacked RPGR-ORF15 expression in the retina, treatment with NSR-RPGR resulted in a statistically significant rescue of photoreceptor cell function in the treated eyes, but not in the untreated eyes. A single treatment in both eyes of wild-type mice with NSR-RPGR indicated a favorable safety profile, without inducing any toxic effects.

### **Clinical Development of NSR-RPGR**

#### *Phase 1/2 XIRIUS Clinical Trial*

We are conducting a Phase 1/2, open-label, dose-ranging, single-eye clinical trial, which we refer to as the XIRIUS trial, to evaluate the safety and efficacy of NSR-RPGR for the treatment of XLRP in patients with the RPGR mutation. The XIRIUS trial is a multicenter trial consisting of a dose escalation study and an expansion study that will be enrolling patients in both the United States and the United Kingdom.

We have completed enrollment of the dose escalation study in the XIRIUS trial, consisting of six cohorts of three patients each for a total of 18 patients. Each patient in the trial received a single sub-retinal injection of NSR-RPGR. The primary goal of the trial is to assess the safety and tolerability of NSR-RPGR over a two-year period. On September 22, 2018, we announced positive preliminary safety and efficacy data from the XIRIUS trial for the first five cohorts (combined n=15) of the dose escalation study at the EURETINA medical meeting.

We expect to begin enrollment of the expansion study in the XIRIUS trial in the fourth quarter of 2018. The expansion study is intended to enroll approximately 30 patients at a therapeutic dose informed by the dose escalation study and a low-dose control group of approximately 15 patients. Preliminary efficacy data from the expansion study is expected to be available in mid-2019, with one-year follow-up data expected to be available in 2020.

#### *XOLARIS Natural History Observational Study*

We are conducting a prospective, natural history observational study, which we refer to as the XOLARIS study, to better understand the progression of untreated XLRP in up to approximately 100 patients. We also believe the study will assist us in identifying a pool of well-characterized patients for subsequent clinical trials of NSR-RPGR.

### **NSR-ABCA4 for the Treatment of Stargardt Disease**

Our retinal gene therapy product candidate, NSR-ABCA4, is in preclinical development for the treatment of Stargardt disease in patients with mutations in the gene encoding ATP-binding cassette, sub-family A member 4, or ABCA4. Stargardt disease is the most common form of inherited juvenile macular dystrophy, with a prevalence estimated to be approximately one in 10,000 people. The form of Stargardt disease we are targeting is an autosomal recessive disease that is linked to mutations in the ABCA4 gene that are inherited from both parents of an affected individual. The progressive central vision loss associated with Stargardt disease is caused by the degeneration of photoreceptor cells in the central portion of the retina called the macula. Stargardt disease typically develops during childhood and adolescence, and can lead to blindness in patients by their twenties. There are no treatments currently available for Stargardt disease.

Due to the large size of the ABCA4 cDNA, we have developed a dual vector approach to address the size limitations associated with the AAV packaging capacity based on optimizing the length of DNA overlap between the two vectors. In mouse models of Stargardt disease, NSR-ABCA4 has shown expression of full length ABCA4 protein in photoreceptor outer segments, leading to significant reductions in toxic metabolic byproducts associated with Stargardt disease.

### **Our Strategy**

Our goal is to become the leading commercial-stage gene therapy company focused on delivering life-altering therapies for inherited retinal diseases. The key elements of our strategy to achieve this goal are to:

- Complete the clinical development and obtain regulatory approval for NSR-REP1 for the treatment of CHM.
- Advance the clinical development of NSR-RPGR for the treatment of XLRP.
- Continue to build and commercialize a pipeline of gene therapy treatments, such as NSR-ABCA4 and NSR-BEST1, for rare inherited retinal diseases for which there are no currently approved treatments.
- Improve procedural success through surgical training and collaborations with surgical delivery innovators.

- Continue to leverage relationships with retinal disease key opinion leaders and global gene therapy centers to ensure clinical trial success and enhance future commercialization.
- Develop manufacturing expertise for gene therapy products utilizing a hybrid model that retains in-house process development and quality assurance expertise while relying on outsourced manufacturing facilities.
- Establish a global commercial infrastructure.

#### **Risks Associated with Our Business**

Our business is subject to a number of risks of which you should be aware before making an investment decision. You should carefully consider all of the information set forth in this prospectus. In particular, you should evaluate the specific factors set forth in the section titled "Risk Factors" included in this prospectus and in our Report of Foreign Private Issuer on Form 6-K, furnished to the SEC on September 25, 2018, and incorporated by reference herein before deciding whether to invest in our ADSs. Among these important risks are, but not limited to, the following:

- We have incurred net losses since inception and may never achieve or maintain profitability.
- We will need additional funding to complete the development of our product candidates, which may not be available on acceptable terms, if at all.
- Our limited operating history may make it difficult to evaluate the success of our business to date and to assess our future viability.
- Our gene therapy product candidates are based on novel technologies, which makes it difficult to predict the timing and costs of development and of subsequently obtaining regulatory approvals, and only a limited number of gene replacement therapy products have been approved by regulatory agencies to date.
- We may encounter substantial delays or difficulties in our clinical trials.
- We may fail to demonstrate safety and efficacy of our product candidates to the satisfaction of applicable regulatory authorities.
- Success in preclinical studies or clinical trials may not be indicative of results in future clinical trials, and interim results of clinical trials may not be indicative of the final results of such clinical trials.
- Our product candidates and the process for administering our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval.
- We utilize, and expect to continue to utilize, third parties to conduct our preclinical studies, clinical trials, and product manufacturing for the foreseeable future, and these third parties may not perform satisfactorily.
- We face significant competition in an environment of rapid technological change and the possibility that our competitors may achieve regulatory approval before us or develop therapies that are more advanced or effective than ours.
- If we are unable to obtain and maintain patent protection for our current product candidates, any future product candidates we may develop and our technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours.
- If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.
- Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize our product candidates and the approval may be for a more narrow indication than we seek.



- Delays in obtaining regulatory approval of our manufacturing process and facility or disruptions in our manufacturing process may delay or disrupt our product development and commercialization efforts.

#### **Implications of Being an Emerging Growth Company and Foreign Private Issuer**

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies. These provisions include:

- reductions in the number of years of required audited financial statements in addition to any required interim financial statements and correspondingly reduced Management’s Discussion and Analysis of Financial Condition and Results of Operations disclosure; and
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002.

We may take advantage of these provisions for up to five years from the date of our initial public offering or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company upon the earlier to occur of: (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.07 billion or more; (ii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; or (iii) the date on which we are deemed to be a large accelerated filer under the rules of the SEC. We may choose to take advantage of some, but not all of, the available benefits under the JOBS Act. We have taken advantage of some reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

In addition, under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

We are a “foreign private issuer” under the rules and regulations of the SEC. As a result, we have made our annual filings on Form 20-F, rather than on Form 10-K; we have not been required to file quarterly reports on Form 10-Q or current reports on Form 8-K; and we have not been subject to SEC rules governing the solicitation of proxies, consents or authorizations in respect of a security registered under the Securities Exchange Act of 1934, as amended, or Exchange Act, the provisions of Regulation Fair Disclosure, which regulate the selective disclosure of material information, or the sections of the Exchange Act requiring insiders to file public reports of their share ownership and trading activities and establishing insider liability for profits realized from any “short-swing” transactions in our equity securities. Further, we have been permitted to certain provisions of the rules and regulations of the Nasdaq Stock Market allowing us to follow English corporate law with regard to certain aspects of corporate governance.

We have determined that, as of June 30, 2018, we no longer qualify as a foreign private issuer. We made the determination based on the fact that, as of June 30, 2018, more than 50 percent of our outstanding voting securities were directly or indirectly owned of record by residents of the United States and a majority of our executive officers were U.S. citizens or residents. As a result, commencing on January 1, 2019, we will no longer be entitled to the “foreign private issuer” exemptions.

Both foreign private issuers and emerging growth companies are also exempt from certain more stringent executive compensation disclosure rules. Thus, even though we will cease to be a foreign private issuer effective January 1, 2019, we will continue to be exempt from the more stringent compensation disclosures required of companies that are not emerging growth companies.

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**Corporate Information**

Our registered office is located 10 Midford Place, 2nd Floor, London, W1T 5BJ, United Kingdom, and our telephone number is +44 (0)20 7062 2777. Our website address is [www.nightstartx.com](http://www.nightstartx.com). The reference to our website is an inactive textual reference only and the information contained in, or that can be accessed through, our website is not a part of this prospectus.

## THE OFFERING

ADSs offered by us	4,000,000 ADSs, each ADS representing one ordinary share.
Option to purchase additional ADSs	We have granted the underwriters an option for a period of 30 days from the date of this prospectus to purchase up to an additional 600,000 ADSs from us.
Ordinary shares to be outstanding immediately after this offering	32,884,103 ordinary shares (or 33,484,103 ordinary shares if the underwriters exercise in full their option to purchase an additional 600,000 ADSs).
American Depositary Shares	Each ADS represents one ordinary share, nominal value £0.01 per share. You will have the rights of an ADS holder or beneficial owner (as applicable) as provided in the deposit agreement among us, the depositary and holders and beneficial owners of ADSs from time to time. To better understand the terms of our ADSs, see "Description of American Depositary Shares." We also encourage you to read the deposit agreement, the form of which is filed as an exhibit to the registration statement of which this prospectus forms a part.
Depositary	Citibank, N.A.
Use of proceeds	We intend to use the net proceeds from this offering to fund the clinical development of NSR-REP1 for the treatment of CHM, including obtaining one-year follow-up data from our ongoing Phase 3 STAR trial of NSR-REP1; the clinical development of NSR-RPGR for XLRP, including obtaining one-year follow-up data from the expansion study of our ongoing Phase 1/2 XIRIUS trial of NSR-RPGR; and other research and development activities, working capital and other general corporate purposes. See "Use of Proceeds" for a more complete description of the intended use of proceeds from this offering.
Risk factors	See "Risk Factors" and the other information included in this prospectus and incorporated by reference for a discussion of factors you should carefully consider before deciding to invest in our ADSs.
Nasdaq Global Select Market Symbol	"NITE"

The number of ordinary shares to be outstanding after this offering includes 0.7 million shares of unvested restricted share awards as of August 31, 2018, that were previously granted to our officers, directors and employees.

The total number of ordinary shares to be outstanding after this offering is based on 28.9 million ordinary shares outstanding as of August 31, 2018. The number of ordinary shares to be outstanding after this offering excludes:

- 1.0 million ordinary shares issuable upon exercise of share options outstanding as of August 31, 2018 under our 2017 Equity Incentive Plan, or 2017 Plan, at a weighted-average exercise price of \$15.44 per share;
- 10,000 ordinary shares issuable upon the vesting of restricted stock units outstanding as of August 31, 2018, under our 2017 Plan; and
- 1.6 million ordinary shares reserved for future issuance as of August 31, 2018, under our 2017 Plan.

Unless otherwise indicated, all information contained in this prospectus also assumes:

- no exercise of the outstanding options described above; and
- no exercise of the option granted to the underwriters to purchase up to an additional 600,000 ADSs in connection with this offering.

## RISK FACTORS

*Investing in our American Depositary Shares, or ADSs, involves a high degree of risk. Before you invest in our ADSs, you should carefully consider the following risks, as well as general economic and business risks, including those set forth under the heading "Risk Factors" in our Report of Foreign Private Issuer on Form 6-K furnished to the U.S. Securities and Exchange Commission on September 25, 2018, incorporated by reference herein, and all of the other information contained in this prospectus and in the documents incorporated by reference herein. Any of the following risks, including those discussed in the documents incorporated by reference herein, could have a material adverse effect on our business, operating results and financial condition and cause the trading price of our ADSs to decline, which would cause you to lose all or part of your investment. When determining whether to invest, you should also refer to the other information contained or incorporated by reference in this prospectus, including our financial statements and the related notes thereto. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us may also adversely affect our business.*

### **Risks Related to this Offering and the Ownership of Our Securities**

#### ***If you purchase our ADSs in this offering, you will suffer immediate dilution of your investment.***

The assumed public offering price of our ADSs, which was the last reported sale price of our ADSs on the Nasdaq Global Select Market on September 25, 2018, is substantially higher than the net tangible book value per ADS. Therefore, if you purchase ADSs in this offering, you will pay a price per share that substantially exceeds our net tangible book value per ADS after this offering. In addition, as of August 31, 2018, we had outstanding share options to purchase an aggregate 1.0 million ADSs at a weighted average exercise price of \$15.44 per share. To the extent these outstanding options are exercised, there will be further dilution to investors in this offering. Based on an assumed public offering price of \$20.00 per ADS, you will experience immediate dilution of \$4.56 per share, representing the difference between our as-adjusted net tangible book value per ADS after giving effect to this offering and the assumed public offering price.

#### ***A significant portion of our total outstanding ADSs are restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our ADSs to drop significantly, even if our business is performing well.***

Sales of a substantial number of ADSs in the public market could occur at any time, subject to the restrictions and limitations described below. If our shareholders sell, or the market perceives that our shareholders intend to sell, substantial amounts of our ADSs in the public market, the market price of our ADSs could decline significantly.

As of August 31, 2018, we had 28.9 million shares outstanding. Of these shares, approximately 1.0 million shares are freely tradable upon the closing of this offering, subject, in the case of our affiliates, to the conditions of Rule 144 under the Securities Act of 1933, as amended, or the Securities Act. An additional 27.9 million shares are subject to a contractual lock-up with the underwriters for this offering for 90 days following this offering. Jefferies LLC and Barclays Capital Inc. may release these shareholders from their lock-up agreements at any time and without notice, which would allow for earlier sales of shares in the public market subject to the conditions of Rule 144 under the Securities Act.

#### ***Substantial future sales of our ADSs, or the perception that these sales could occur, could cause the price of the ADSs to decline.***

Additional sales of our ADSs, or the perception that these sales could occur, could cause the market price of the ADSs to decline. If any of our large shareholders or members of our management team sell substantial amounts of ADSs in the public market, or the market perceives that such sales may occur, the market price of our ADSs and our ability to raise capital through an issue of equity securities in the future could be adversely affected.

#### ***An active trading market for our ADSs may not be sustained.***

Our ADSs began trading on the Nasdaq Global Select Market in September 2017. Given the limited trading history of our shares, there is a risk that an active trading market may not continue to develop or be sustained. If an active market for our ADSs does not continue to develop or is not sustained, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares, or at all.

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***The significant share ownership position of our executive officers, directors and principal shareholders may limit your ability to influence corporate matters.***

Upon the closing of the offering, our executive officers and directors, combined with our shareholders who owned more than 5% of our outstanding ADSs or ordinary shares and their respective affiliates, will, in the aggregate, beneficially own ordinary shares representing approximately \_\_\_\_\_% of our outstanding share capital (assuming no exercise of the underwriters' option to purchase additional ADSs). As a result, if these security holders were to choose to act together, they would be able to control all matters submitted to our shareholders for approval, as well as our management and affairs. Depending on the level of attendance at our general meetings of shareholders, these shareholders either alone or voting together as a group may be in a position to determine or significantly influence the outcome of decisions taken at any such general meeting. Any shareholder or group of shareholders controlling more than 50% of the share capital present and voting at our general meetings of shareholders may control any shareholder resolution requiring a simple majority, including the appointment of board members, certain decisions relating to our capital structure, the approval of certain significant corporate transactions and amendments to our Articles of Association. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and the board of directors; or
- impede a merger, consolidation, takeover or other business combination involving us that other shareholders may desire.

Any of these consequences could adversely affect the market price of our ADSs.

***We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.***

Our management will have broad discretion in the use of the net proceeds from this offering and could spend those proceeds in ways that do not improve our results of operations or enhance the value of our ADSs. The failure by our management to apply these proceeds effectively could result in financial losses that could cause the price of our ADSs to decline and delay the development and commercialization of our product candidates. We may invest the net proceeds from this offering, pending their use, in a manner that does not produce income or that loses value.

***Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be our ADS holders' and shareholders' sole source of gains and they may never receive a return on their investment.***

Under current U.K. law, a company's accumulated realized profits must exceed its accumulated realized losses (on a non-consolidated basis) before dividends can be paid. Therefore, we must have distributable profits before issuing a dividend. We have not paid dividends in the past on our ordinary shares. We intend to retain earnings, if any, for use in our business and do not anticipate paying any cash dividends in the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, on our ADSs will be our ADS holders' sole source of gains for the foreseeable future, and they will suffer a loss on their investment if they are unable to sell their ADSs at or above the price at which they purchased the ADSs.

## EXCHANGE RATE INFORMATION

Our functional currency is the pound sterling. However, for financial reporting purposes, our financial statements, which are prepared using the functional currency, have been translated into U.S. dollars. Fluctuations in the exchange rate between the pound sterling and the U.S. dollar will affect the U.S. dollar amounts received by owners of our American Depositary Shares, or ADSs, on conversion of dividends, if any, paid in pounds sterling on the ordinary shares and will affect the U.S. dollar price of our ADSs on Nasdaq. The table below shows the period end, average, high and low exchange rates of U.S. dollars per pound sterling for the periods shown. Average rates are computed by using the noon buying rate of the Federal Reserve Bank of New York for the U.S. dollar on the last business day of each month during the relevant year indicated or each business day during the relevant month indicated. The rates set forth below are provided solely for your convenience and may differ from the actual rates used in the preparation of our consolidated financial statements incorporated by reference in this prospectus and other financial data appearing or incorporated by reference in this prospectus.

Year Ended December 31:	PERIOD-END <sup>(1)</sup>	AVERAGE FOR PERIOD <sup>(2)</sup> (\$ per £1.00)	LOW	HIGH
2013	1.6574	1.5641	1.4837	1.6574
2014	1.5578	1.6484	1.5517	1.7165
2015	1.4746	1.5284	1.4648	1.5882
2016	1.2337	1.3555	1.2155	1.4800
2017	1.3529	1.2890	1.2118	1.3578
2018 (through September, 2018)				

- (1) In the event that the period end fell on a day for which data are not available, the exchange rate on the prior most recent business day is given.  
(2) The average of the noon buying rate for pounds sterling on the last day of each full month during the relevant year or each business day during the relevant month indicated.

Month Ended:	LOW	HIGH
	(\$ per £1.00)	
March 2018	1.3755	1.4236
April 2018	1.3751	1.4332
May 2018	1.3258	1.3611
June 2018	1.3095	1.3429
July 2018	1.2987	1.3266
August 2018	1.2685	1.3120
September 2018 (through September, 2018)		

Unless otherwise indicated, certain U.S. dollar amounts contained in this prospectus have been translated into pounds sterling at the rate in effect at December 29, 2017, the last business day of the year ended December 31, 2017, of £1.00 to \$1.3529.

On September, 2018, the noon buying rate of the Federal Reserve Bank of New York for the U.S. dollar was £1.00 to \$.

## USE OF PROCEEDS

We estimate that the net proceeds from the sale of 4,000,000 ADSs in this offering will be approximately \$ \_\_\_\_\_ million, based on an assumed public offering price of \$ \_\_\_\_\_ per ADS, which was the last reported sale price of our ADSs on the Nasdaq Global Select Market on September \_\_\_\_\_, 2018, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional ADSs in full, we estimate that the net proceeds to us from this offering will be approximately \$ \_\_\_\_\_ million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

As of June 30, 2018, we had cash, cash equivalents and marketable securities of approximately \$111.4 million. We expect to use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, to advance our clinical pipeline, including specifically:

- approximately \$ \_\_\_\_\_ million to fund the clinical development of NSR-REP1 for the treatment of CHM, including obtaining one-year follow-up data from our ongoing Phase 3 STAR trial of NSR-REP1 for the treatment of CHM;
- approximately \$ \_\_\_\_\_ million to fund the clinical development of NSR-RPGR for XLRP, including obtaining one-year follow-up data from the expansion study of our ongoing Phase 1/2 XIRIUS trial of NSR-RPGR for the treatment of XLRP; and
- the remainder to fund other research and development activities, working capital and other general corporate purposes.

The amount and timing of our actual expenditures will depend upon numerous factors, including the status and results of our ongoing and planned clinical trials, the design of our clinical trials, the pace of patient enrollment, the occurrence of adverse events, feedback from regulatory agencies, the timing of approval of any of our product candidates, any collaborations that we may enter into with third parties for complementary businesses, technologies, products or assets and any unforeseen cash needs. Based on our current plans, we believe that our existing cash, cash equivalents and marketable securities, together with the net proceeds from this offering, will be sufficient to fund our operating expenses and capital expenditure requirements for at least the next 12 months. Our existing cash, cash equivalents and marketable securities, together with the net proceeds from this offering, may not be sufficient to enable us to submit our applications for marketing authorization or receive marketing authorization for NSR-REP1 for the treatment of CHM or complete clinical development of NSR-RPGR for the treatment of XLRP.

Our expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. Predicting the cost necessary to develop product candidates can be difficult and the amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including those described in "Risk Factors" or incorporated by reference in this prospectus, and any unforeseen cash needs. As a result, our management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds of this offering. We may also use a portion of the remaining net proceeds to in-license, acquire, or invest in complementary businesses, technologies, products or assets. However, we have no current commitments or obligations to do so. In addition, we might decide to postpone or not pursue clinical trials or preclinical activities if the net proceeds from this offering and any other sources of cash are less than expected.

Pending these uses, we plan to invest these net proceeds in short-term, interest bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the United States.

**MARKET PRICE OF ORDINARY SHARES**

Our ADSs began trading on the Nasdaq Global Select Market under the symbol "NITE" on September 28, 2017. Prior to that date, there was no public trading market for ADSs or our ordinary shares. The following table sets forth for the periods indicated the reported high and low sales prices per ADS as reported on the Nasdaq Global Select Market:

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	PRICE PER ADS	
	HIGH	LOW
	\$	\$
<b>Annual:</b>		
2017 (beginning September 28, 2017)	24.94	11.99
2018 (through September , 2018)		
<b>Quarterly:</b>		
Third Quarter 2017 (beginning September 28, 2017)	24.94	14.56
Fourth Quarter 2017	23.47	11.99
First Quarter 2018	15.24	10.05
Second Quarter 2018	17.73	10.01
Third Quarter 2018 (through September , 2018)		
<b>Month Ended:</b>		
October 2017	21.95	16.28
November 2017	23.47	17.42
December 2017	18.86	11.99
January 2018	15.24	12.73
February 2018	14.80	10.05
March 2018	14.85	12.22
April 2018	15.40	10.01
May 2018	14.98	12.82
June 2018	17.73	13.80
July 2018	21.96	15.41
August 2018	22.90	14.99
September 2018 (through September , 2018)		

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On September , 2018, the last reported sale price of the ADSs on the Nasdaq Global Select Market was \$ per ADS. As of September , 2018, we had approximately 10 holders of record of our ordinary shares. The actual number of holders is greater than these numbers of record holders and includes beneficial owners whose ordinary shares are held in street name by brokers and other nominees. This number of holders of record also does not include holders whose shares may be held in trust by other entities.



## DIVIDEND POLICY

We have never declared or paid a dividend, and we do not anticipate declaring or paying dividends in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. See *“Risk Factors—Risks Related to this Offering and the Ownership of Our Securities.”*

Under English law, among other things, we may only pay dividends if we have sufficient distributable reserves (on a non-consolidated basis), which are our accumulated realized profits that have not been previously distributed or capitalized less our accumulated realized losses, so far as such losses have not been previously written off in a reduction or reorganization of capital.

## CAPITALIZATION

The following table sets forth our cash, cash equivalents and marketable securities and capitalization as of June 30, 2018 on:

- an actual basis; and
- an as adjusted basis to give effect to the sale of 4,000,000 ADSs in this offering.

The as adjusted calculations are based on an assumed public offering price of \$ \_\_\_\_\_ per ADS, which was the last reported sale price of our ADSs on the Nasdaq Global Select Market on September \_\_\_\_\_, 2018, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information together with our unaudited consolidated financial statements, audited consolidated financial statements and related notes incorporated by reference in this prospectus and the information set forth under the sections titled "Selected Consolidated Financial Data," "Exchange Rate Information" and "Use of Proceeds" in this prospectus, and the section titled "Operating and Financial Review and Prospects" included in our Annual Report on Form 20-F for the year ended December 31, 2017 incorporated herein by reference.

	AS OF JUNE 30, 2018	
	ACTUAL	AS ADJUSTED
	(in thousands, except share and per share data)	
Cash, cash equivalents and marketable securities	\$ 111,361	\$ _____
Shareholders' equity:		
Ordinary shares, nominal value £0.01 per share; 100,000,000 shares authorized, actual and as adjusted; 28,888,205 shares issued and outstanding, actual; 32,888,205 shares issued and outstanding, as adjusted	1	
Additional paid-in capital	187,987	
Accumulated other comprehensive income	5,555	5,555
Accumulated deficit	(84,476)	(84,476)
Total shareholders' equity	109,067	_____
Total capitalization	\$ 109,067	\$ _____

The number of ordinary shares to be outstanding in the table above includes 0.9 million shares of unvested restricted share awards as of June 30, 2018 that were previously granted to our officers, directors and employees.

The number of ordinary shares outstanding on an as adjusted basis in the table above exclude:

- 1.0 million ordinary shares issuable upon exercise of share options outstanding as of June 30, 2018, under our 2017 Equity Incentive Plan, or 2017 Plan, at a weighted-average exercise price of \$15.39 per share;
- 10,000 ordinary shares issuable upon the vesting of restricted stock units, or RSUs, outstanding as of June 30, 2018, under our 2017 Plan; and
- 1.6 million ordinary shares reserved for future issuance under our 2017 Plan.

## DILUTION

If you invest in our ADSs in this offering, your interest will be immediately diluted to the extent of the difference between the public offering price per ADS in this offering and the as adjusted net tangible book value per ADS immediately after this offering. Dilution results from the fact that the public offering price per ADS is substantially in excess of the net tangible book value per ADS. As of June 30, 2018, we had a historical net tangible book value of \$109.1 million, or \$3.78 per ordinary share (equivalent to \$3.78 per ADS). Our net tangible book value per share represents total tangible assets less total liabilities, divided by the number of ordinary shares outstanding on June 30, 2018.

After giving effect to the sale of 4,000,000 ADSs in this offering at an assumed public offering price of \$ \_\_\_\_\_ per ADS, which was the last reported sale price of our ADSs on the Nasdaq Global Select Market on September \_\_\_\_\_, 2018, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value at June 30, 2018 would have been \$ \_\_\_\_\_ million, or \$ \_\_\_\_\_ per ordinary share (equivalent to \$ \_\_\_\_\_ per ADS). This represents an immediate increase in as adjusted net tangible book value of \$ \_\_\_\_\_ per ADS and immediate dilution of \$ \_\_\_\_\_ per ADS to new investors. The following table illustrates this dilution to new investors purchasing ADSs in this offering:

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Assumed public offering price per ADS	\$
Historical net tangible book value per ADS as of June 30, 2018	\$3.78
Effect attributable to new investors purchasing ADSs in this offering	
As adjusted net tangible book value per ADS as of June 30, 2018	
Dilution per share to new investors purchasing ADSs in this offering	\$

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If the underwriters exercise their option to purchase additional ADSs in full, you will experience further dilution. The as adjusted net tangible book value per ADS after the offering would be \$ \_\_\_\_\_, the increase in net tangible book value per ADS to existing shareholders would be \$ \_\_\_\_\_ and the immediate dilution in net tangible book value per ADS to new investors in this offering would be \$ \_\_\_\_\_.

The number of ordinary shares to be outstanding in the discussion above includes 0.9 million shares of unvested restricted share awards as of June 30, 2018 that were previously granted to our officers, directors and employees.

The table and discussion above exclude:

- 1.0 million ordinary shares issuable upon exercise of share options outstanding as of June 30, 2018, under our 2017 Plan, at a weighted-average exercise price of \$15.39 per share;
- 10,000 ordinary shares issuable upon the vesting of RSUs outstanding as of June 30, 2018, under our 2017 Plan; and
- 1.6 million ordinary shares reserved for future issuance under our 2017 Plan.

To the extent that options are issued under our 2017 Plan, or we issue additional ordinary shares or ADSs in the future, there will be further dilution to investors participating in this offering.

## SELECTED CONSOLIDATED FINANCIAL DATA

The following selected financial data for the three years ended December 31, 2017 are derived from the audited consolidated financial statements of Nightstar Therapeutics plc. The financial data for the six-month periods ended June 30, 2018 and 2017 are derived from unaudited condensed consolidated financial statements. The unaudited condensed consolidated financial statements include all adjustments, consisting of normal recurring accruals, which Nightstar Therapeutics plc considers necessary for a fair presentation of the financial position and the results of operations for these periods. Operating results for the six months ended June 30, 2018 are not necessarily indicative of the results that may be expected for the entire year ending December 31, 2018. The data should be read in conjunction with the consolidated financial statements, related notes and other financial information incorporated by reference herein.

Our functional currency is the pound sterling. However, for financial reporting purposes, our financial statements, which are prepared using the functional currency, have been translated into U.S. dollars. Our assets and liabilities are translated at the exchange rates at the balance sheet date, our revenue and expenses are translated at average exchange rates and shareholders' equity is translated based on historical exchange rates. Translation adjustments are not included in determining net loss but are included in foreign exchange translation adjustment to other comprehensive loss, a component of shareholders' equity.

Foreign currency transactions in currencies different from the functional currency are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange differences resulting from the settlement of such transactions and from the translation at period-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recorded in other income (expense), net in the statement of operations and comprehensive loss.

We were incorporated pursuant to the laws of England and Wales as Nightstar Therapeutics Limited in July 2017 to become a holding company for NightstarRx Limited. Subsequently, in September 2017, Nightstar Therapeutics Limited re-registered as a public limited company and its name was changed to Nightstar Therapeutics plc pursuant to our corporate reorganization. Prior to its incorporation, Nightstar Therapeutics Limited has only engaged in activities incidental to its formation. For more details on the corporate reorganization, see Note 7 to our audited financial statements included in our Annual Report on Form 20-F for the year ended December 31, 2017 incorporated herein by reference.

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	YEAR ENDED DECEMBER 31,			SIX MONTHS ENDED	
	2017	2016	2015	2018	2017
(in thousands, except per share data)					
<b>Consolidated Statement of Operations and Comprehensive Loss Data:</b>					
Operating expenses:					
Research and development	\$ 20,502	\$ 10,165	\$ 7,175	\$ 14,116	\$ 6,292
General and administrative	7,001	2,055	2,149	6,100	1,407
Total operating expenses	27,503	12,220	9,324	20,216	7,699
Other income (expense):					
Interest and other income	709	22	9	1,089	6
Other income (expense), net	(2,855)	—	—	(3,661)	—
Change in fair value tranche obligations	—	—	(4,333)	—	—
Total other income (expense), net	(2,146)	22	(4,324)	(2,572)	6
Loss before provision for (benefit from) income taxes	(29,649)	(12,198)	(13,648)	(22,788)	(7,693)
Provision for (benefit from) income taxes	37	—	—	(334)	—
Net loss	(29,686)	(12,198)	(13,648)	(22,454)	(7,693)
Other comprehensive income (loss)					
Foreign exchange translation adjustment	3,988	(1,385)	(541)	(269)	1,722
Unrealized holding gains on available-for-sale securities, net of tax expense of \$0.8 million for the six months ended June 30, 2018	—	—	—	3,934	—
Total comprehensive loss	\$(25,698)	\$(13,583)	\$(14,189)	\$(18,789)	\$(5,971)
Weighted-average ordinary shares outstanding—basic and diluted	18,187	8,954	5,539	27,957	23,336
Basic and diluted net loss per ordinary share	\$ (1.63)	\$ (1.36)	\$ (2.46)	\$ (0.80)	\$ (0.33)

	YEAR ENDED DECEMBER 31,			AS OF JUNE 30,
	2017	2016	2015	2018
(in thousands)				
<b>Consolidated Balance Sheet Data</b>				
Cash, cash equivalents and marketable securities	\$129,404	\$10,122	\$10,676	\$ 111,361
Working capital <sup>(1)</sup>	\$125,457	\$ 8,681	\$10,849	\$ 108,472
Total assets	\$135,197	\$14,595	\$14,072	\$ 121,188
Total shareholders' equity	\$125,812	\$ 9,044	\$11,102	\$ 109,067

(1) We define working capital as current assets less current liabilities.

## RELATED PARTY TRANSACTIONS

Since January 1, 2015, we have engaged in the following transactions with our directors, executive officers or holders of more than 5% of our outstanding share capital and their affiliates, which we refer to as our related parties. All of the historical share numbers in this section are as of dates prior to and do not reflect the conversion of each separate class of ordinary shares of Nightstar Therapeutics plc into a single class of ordinary shares, as described under Note 12 in the notes to our audited consolidated financial statements included in our Annual Report on Form 20-F for the year ended December 31, 2017, incorporated by reference in this prospectus.

### **Transactions with Entities Affiliated with Syncona**

#### ***Syncona***

We receive accounting and professional services from Syncona Partners LLP, Syncona Limited and their affiliates, which we refer to herein as Syncona. Syncona is a shareholder of ours, and the chairman of our board of directors serves as the chief investment officer and a managing partner of Syncona. We recorded accounting and professional fees totaling \$1,200, \$23,000 and \$52,000 for the years ended December 31, 2017, 2016 and 2015, respectively. We also recorded accounting and professional fees totaling \$9,000 for the six months ended June 30, 2018. As of June 30, 2018, we had a payment of \$10,000 outstanding to Syncona, which is recorded in the accounts payable line in the condensed consolidated balance sheet.

#### ***The Wellcome Trust***

In June 2015, we entered into a lease agreement with The Wellcome Trust Limited, as trustee of The Wellcome Trust, the prior holding company of Syncona. We leased approximately 900 square feet of office space to serve as our corporate headquarters on a quarter-by-quarter basis. Under the terms of the lease, we are billed for certain office costs in addition to the leased space. We recorded general and administrative expenses totaling \$152,000 and \$182,000 for the years ended December 31, 2016 and 2015, respectively. As of December 31, 2016, there was \$44,000 outstanding to the Wellcome Trust. Subsequent to December 31, 2016, The Wellcome Trust is no longer considered an affiliated entity of our company.

#### ***Freeline Therapeutics***

In August 2015, we entered into a consultancy services agreement with Freeline Therapeutics Limited, or Freeline, a majority-owned portfolio company of Syncona. Under the terms of the agreement, we agreed to provide Freeline with certain materials as specified in the agreement. Freeline provided certain ancillary research and development services to us through a consulting contract in 2018, 2017 and 2016. We recorded research and development expenses totaling \$11,000, \$30,000 and \$0 for the years ended December 31, 2017, 2016 and 2015, respectively, and \$31,000 for the six months ended June 30, 2018. As of June 30, 2018, we had a payment of \$32,000 outstanding to Freeline.

#### ***Gyroscope Therapeutics***

In January 2018, we entered into an agreement with Gyroscope Therapeutics Limited, or Gyroscope, an entity controlled by Syncona. Pursuant to the agreement, we provided Gyroscope with certain clinical manuals and other documents. We recorded \$36,000 as other income during the six months ended June 30, 2018.

#### ***MacLaren Consulting Relationship***

In November 2013 and as amended in 2016, we entered into a consulting agreement with Oxford University Innovation Ltd., which we refer to as the Prior Consulting Agreement, for consulting services of Prof. Robert MacLaren. Prof. MacLaren was a member of our board of directors until April 15, 2018. Under the terms of the Prior Consulting Agreement, Prof. MacLaren provided us with advice and expertise in relation to regulatory submissions, prepared for and attended meetings of our clinical advisory board, prepared for and attended regulatory meetings, provided scientific and medical advice in relation to the preparation of medical education materials and provided consulting services to us.

Under the terms of the Prior Consulting Agreement, we agreed to pay consulting fees for Prof. MacLaren's services subject to a minimum annual fee of approximately \$134,000. In October 2017, our board of directors awarded Prof. MacLaren 58,000 restricted stock units, or RSUs, which are scheduled to vest annually over a four-year period from

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the date of award. Prof. MacLaren submitted his resignation from the board of directors on March 29, 2018 and his resignation became effective as of April 15, 2018. In connection with Prof. MacLaren's resignation from the board of directors, the board of directors agreed to allow for immediate vesting of 29,000 of the RSUs awarded in October 2017, with the remainder being forfeited as of the same date. The board of directors also agreed to pay a bonus to Prof. MacLaren for services provided in the year ended December 31, 2017 in the amount of \$26,000.

Under the Prior Consulting Agreement, we recorded consulting fees totaling \$107,000, \$150,000 and \$90,000, for the years ended December 31, 2017, 2016 and 2015, respectively. We also recorded consulting fees of \$50,000 for the six months ended June 30, 2018. As of June 30, 2018, there was a payment obligation of \$46,000 outstanding to Oxford.

In August 2018, we and Oxford University Innovation Ltd. mutually agreed to terminate the Prior Consulting Agreement. Simultaneously, we entered into a consulting agreement directly with Prof. MacLaren.

### **Subscriptions of Our Class A Ordinary Shares**

#### ***May 2014 and June 2015 Financings***

In May 2014, we amended and restated the subscription and shareholders agreement entered into in November 2013, or the Amended 2013 Agreement, whereby certain of our shareholders elected to subscribe for an aggregate of 7,000,000 of our Class A ordinary shares at a price of £1.00 per share. Under the Amended 2013 Agreement, we issued 6,000,000 of our Class A ordinary shares in May 2014 and 1,000,000 of our Class A ordinary shares in June 2015. The Amended 2013 Agreement was terminated in November 2015.

6,500,000 of the Class A ordinary shares issued pursuant to the Amended 2013 Agreement were issued to Syncona LLP, a holder of more than 5% of our share capital.

#### ***November 2015 and September 2016 Financings***

In November 2015, we entered a subscription and shareholders agreement, or the 2015 Agreement, pursuant to which certain of our shareholders elected to subscribe for an aggregate of 11,830,242 of our Class A ordinary shares as follows: 7,153,929 of our Class A ordinary shares at a price of £1.00 per share and 4,676,313 of our Class A ordinary shares at a price of £2.0737 per share. The 2015 Agreement was terminated in March 2017.

The following table sets forth the aggregate number of Class A ordinary shares issued to our related parties pursuant to these transactions:

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<b>PARTICIPANTS</b>	<b>CLASS A ORDINARY SHARES (#)</b>
Syncona LLP <sup>(1)</sup>	8,074,191
Entities affiliated with New Enterprise Associates <sup>(2)</sup>	3,294,256
David Fellows <sup>(3)</sup>	64,354

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(1) Dr. Hollowood, the chairman of our board of directors, is the Chief Investment Officer and Managing Partner of Syncona Investment Management Limited.

(2) Mr. Mott, a member of our board of directors, is a General Partner of New Enterprise Associates.

(3) Mr. Fellows is our Chief Executive Officer and a member of our board of directors.

#### ***Management Rights Letter***

In November 2015, in connection with the 2015 Agreement, we entered into a management rights letter with New Enterprise Associate 15, L.P. and NEA Ventures 2015, L.P., collectively, NEA, which holds more than 5% of our share capital. Pursuant to this management rights letter, NEA was entitled to consult and advise our management on significant business issues. The management rights letter terminated in October 2017 upon the completion of our initial public offering, or IPO.

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**March and June 2017 Financings**

In March 2017, we entered in to a subscription and shareholders' agreement, or the March SSA, whereby certain shareholders elected to subscribe for an aggregate of 8,070,314 Class A ordinary shares as follows: 1,846,071 Class A ordinary shares at a price of £1.00 per share and 6,224,243 Class A ordinary shares at a price of £2.0737 per share. We issued all 8,070,314 Class A ordinary shares pursuant to the March SSA on June 27, 2017. The March SSA was terminated in June 2017.

In June 2017, we entered in to a subscription and shareholders' agreement, or the June SSA, pursuant to which we issued an aggregate of 11,203,837 Class A ordinary shares at a price of \$4.01648 per share. The June SSA terminated in October 2017 in connection with our corporate reorganization.

The following table sets forth the aggregate number of our Class A ordinary shares issued to our related parties in these transactions:

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<b>PARTICIPANTS</b>	<b>CLASS A ORDINARY SHARES (#)</b>
Syncona Portfolio Limited(1)	6,609,574
Entities affiliated with New Enterprise Associates(2)	7,496,889
David Fellows(3)	85,646

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(1) Dr. Hollowood, the chairman of our board of directors, is the Chief Investment Officer and Managing Partner of Syncona Investment Management Limited.

(2) Mr. Mott, a member of our board of directors, is a General Partner of New Enterprise Associates.

(3) Mr. Fellows is our Chief Executive Officer and a member of our board of directors.

**Participation in Our Initial Public Offering**

In October 2017, entities affiliated with Syncona Portfolio Limited and New Enterprise Associates purchased 1,000,000 and 714,285 ADSs, respectively, in our IPO.

**Subscriptions for Our Ordinary Shares by Certain Related Parties**

**Subscriptions by David Fellows**

From March 2014 to August 2017, we issued a total of 1,985,975 ordinary shares, consisting of 29,411 Class B ordinary shares, 261,642 Class C ordinary shares, 367,281 Class D ordinary shares, 180,100 Class E1 ordinary shares, 180,000 Class E2 ordinary shares, 180,000 Class E3 ordinary shares, 180,000 Class E4 ordinary shares and 607,541 Class F shares, to Mr. Fellows, our Chief Executive Officer and a member of our board of directors, for aggregate consideration of £19.90. This paragraph excludes Class A ordinary shares issued and sold to Mr. Fellows pursuant to the subscription and shareholders agreements as described above.

**Subscription by David Lubner**

In August 2017, we issued a total of 133,498 Class F ordinary shares to Mr. Lubner, a member of our board of directors, for aggregate consideration of £1.33.

**Subscriptions by Robert MacLaren**

From March 2015 to June 2017, we issued a total of 97,760 ordinary shares, consisting of 2,363 Class D ordinary shares and 95,397 Class E1 ordinary shares, to Prof. MacLaren, who was a member of our board of directors until April 2018, for aggregate consideration of £0.98.

**Subscriptions by James McArthur**

From November 2016 to August 2017, we issued a total of 133,498 ordinary shares, consisting of 86,000 Class E1 ordinary shares and 47,498 Class F ordinary shares, to Dr. McArthur, a member of our board of directors, for aggregate consideration of £1.33.

**Subscription by Tuyen Ong**

In August 2017, we issued a total of 597,000 Class F ordinary shares to Dr. Ong, our Chief Development Officer, for aggregate consideration of £5.97.



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***Subscriptions by Gregory Robinson***

From September 2016 to August 2017, we issued a total of 533,994 ordinary shares, consisting of 108,500 Class E1 ordinary shares, 108,500 Class E2 ordinary shares, 108,500 Class E3 ordinary shares, 108,500 Class E4 ordinary shares and 99,994 Class F shares, to Dr. Robinson, our Chief Scientific Officer, for aggregate consideration of £5.36.

***Subscriptions by Senthil Sundaram***

From April 2017 to August 2017, we issued a total of 443,598 ordinary shares, consisting of 87,000 Class E1 ordinary shares, 87,000 Class E2 ordinary shares, 87,000 Class E3 ordinary shares, 87,000 Class E4 ordinary shares and 95,598 Class F ordinary shares, to Mr. Sundaram, our Chief Financial Officer, for aggregate consideration of £4.44.

***Subscriptions by Scott Whitcup***

From April 2017 to August 2017, we issued a total of 266,997 ordinary shares, consisting of 173,000 Class E1 ordinary shares and 93,997 Class F ordinary shares, to Dr. Whitcup, a member of our board of directors, for aggregate consideration of £2.67.

**Agreements with Our Executive Officers and Directors**

We have entered into employment agreements with our executive officers and service agreements with our non-executive directors. These agreements contain customary provisions and representations, including confidentiality, non-competition, non-solicitation and inventions assignment undertakings by the executive officers. However, the enforceability of the non-competition provisions may be limited under applicable law.

**Indemnification Agreements**

We have entered into a deed of indemnity with each of our directors and executive officers. These agreements and our Articles of Association require us to indemnify our directors and executive officers to the fullest extent permitted by law.

**Related Person Transactions Policy**

We have adopted a related person transaction policy. Our related person transaction policy sets forth our procedures for the identification, review, consideration and approval or ratification of related person transactions. For the purposes of our policy only, for so long as we are a foreign private issuer, a related person transaction will be a transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we and any related person are, were or will be participants in which the amount involved exceeds \$120,000 or which is unusual in its nature or conditions; thereafter, a related person transaction will be a transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we and any related person are, were or will be participants in which the amount involved exceeds \$120,000. Transactions involving remuneration for services provided to us as an employee or director will not be covered by this policy.

For so long as we are a foreign private issuer, a related person will be any:

- enterprise that directly or indirectly controls or is controlled by or is under common control with us;
- enterprise over which we have a significant influence or which has significant influence over us;
- individual owning, directly or indirectly, an interest in our voting power that gives them significant influence over us, and close members of any such individual's family;
- persons having authority or responsibility for planning, directing or controlling our activities, including directors and senior management and close members of such individuals' families; or
- enterprise in which a substantial interest in our voting power is owned, directly or indirectly, by any person described above or over which such a person is able to exercise significant influence, including enterprises owned by our directors or major shareholders and enterprises that have a member of key management in common with us.

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If we cease to be a foreign private issuer, then, under our policy, a related person will be any:

- person who is, or at any time since the beginning of our last fiscal year was, a director or executive officer of us or a nominee to become a director of us;
- security holder known by us to be the beneficial owner of more than 5% of any class of our voting securities;
- immediate family member of any of the foregoing; and
- firm, corporation or other entity in which any of the foregoing persons is an executive, partner or principal or similar control position or in which such person has a 5% or greater beneficial ownership interest.

Under the policy, if a transaction has been identified as a related person transaction, including any transaction that was not a related person transaction when originally consummated or any transaction that was not initially identified as a related person transaction prior to consummation, our management must present information regarding the related person transaction to our audit committee, or, if audit committee approval would be inappropriate, to another independent body of our board of directors for review, consideration and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related persons, the benefits to us of the transaction and whether the transaction is on terms that are comparable to the terms available to or from, as the case may be, an unrelated third party or to or from employees generally. Under the policy, we will collect information that we deem reasonably necessary from each director, executive officer and, to the extent feasible, significant shareholder to enable us to identify any existing or potential related person transactions and to effectuate the terms of the policy. In addition, under our Code of Business Conduct and Ethics, our employees, executive officers and directors have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest.

## IDENTITY OF DIRECTORS AND SENIOR MANAGEMENT

The following table sets forth information with respect to each of our directors and executive officers, who share a business address at 10 Midford Place, 2nd Floor, London W1T 5BJ, United Kingdom.

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<u>NAME</u>	<u>POSITION(S)</u>
<b><i>Executive Officers:</i></b>	
David Fellows	Chief Executive Officer and Director
Tuyen Ong, M.D., MRCOphth, MBA	Chief Development Officer
Gregory Robinson, Ph.D.	Chief Scientific Officer
Senthil Sundaram	Chief Financial Officer
Bryan Yoon, Esq.	General Counsel and Secretary
<b><i>Non-Executive Directors:</i></b>	
Chris Hollowood, Ph.D.	Chairman of the Board of Directors
Paula K. Cobb	Director
David C. Lubner	Director
James McArthur, Ph.D.	Director
David M. Mott	Director
Scott M. Whitcup, M.D.	Director

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## PRINCIPAL SHAREHOLDERS

The following table sets forth information with respect to the beneficial ownership of our ordinary shares as of August 31, 2018 by:

- each beneficial owner of 5% or more of our outstanding ordinary shares;
- each of our directors and executive officers; and
- all of our directors and executive officers as a group.

Beneficial ownership is determined in accordance with the rules of the U.S. Securities and Exchange Commission, or SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities and include ordinary shares that can be acquired within 60 days of August 31, 2018. These ordinary shares, however, are not included in the computation of the percentage ownership of any other person.

The percentages in the column entitled “Shares Beneficially Owned Before Offering” is based on 28,884,103 ordinary shares outstanding as of August 31, 2018. The percentages in the column entitled “Shares Beneficially Owned After Offering” is based on 32,884,103 ordinary shares to be outstanding after this offering, including the 4,000,000 ordinary shares underlying ADSs that we are selling in this offering. The percentages in the column entitled “Shares Beneficially Owned After Offering Assuming Underwriters Exercise Option in Full” give further effect to the exercise in full by the underwriters of their option to purchase an additional 600,000 ADSs. The information set forth in the columns entitled “Shares Beneficially Owned After Offering” and “Shares Beneficially Owned After Offering Assuming Underwriters Exercise Option in Full” does not give effect to the issuance of any additional shares issuable upon exercise of outstanding options as of August 31, 2018.

Except as otherwise indicated, all of the shares reflected in the table are ordinary shares and all persons listed below have sole voting and investment power with respect to the shares beneficially owned by them, subject to applicable community property laws. The information is not necessarily indicative of beneficial ownership for any other purpose.

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Except as otherwise indicated in the table below, addresses of the directors, executive officers and named beneficial owners are in care of Nightstar Therapeutics plc, 10 Midford Place, 2nd Floor, London W1T 5BJ United Kingdom.

NAME OF BENEFICIAL OWNER	ORDINARY SHARES BENEFICIALLY OWNED PRIOR TO OFFERING	PERCENTAGE OF SHARES BENEFICIALLY OWNED		SHARES BENEFICIALLY OWNED AFTER OFFERING IF UNDERWRITERS EXERCISE OPTION IN FULL
	NUMBER(1)	BEFORE OFFERING	AFTER OFFERING	PERCENT
<i>5% or Greater Shareholders:</i>				
Syncona Portfolio Limited(2)	12,203,922	42.3%	37.1%	36.4%
Entities affiliated with New Enterprise Associates(3)	6,164,358	21.3%	18.7%	18.4%
Entities affiliated with Wellington Management Company(4)	1,814,737	6.3%	5.5%	5.4%
Entities affiliated with Redmile Group(5)	1,772,843	6.1%	5.4%	5.3%
Point72 Asset Management, L.P.(6)	1,502,193	5.2%	4.6%	4.5%
<i>Executive Officers and Directors:(7)</i>				
David Fellows	651,453	2.3%	2.0%	1.9%
Senthil Sundaram	128,131	*	*	*
Tuyen Ong, M.D. MRCOphth, MBA	97,681	*	*	*
Gregory Robinson, Ph.D.	139,898	*	*	*
Bryan Yoon, Esq.	—	—	—	—
Chris Hollowood, Ph.D.(8)	12,203,922	42.3%	37.1%	36.4%
Paula K. Cobb(9)	—	—	—	—
David C. Lubner	29,124	*	*	*
James McArthur, Ph.D.	37,237	*	*	*
David M. Mott(10)	6,164,358	21.3%	18.7%	18.4%
Scott M. Whitcup, M.D.	74,568	*	*	*
All current directors and executive officers as a group (11 persons)	19,526,372	67.6%	59.4%	58.3%

\* Represents beneficial ownership of less than one percent.

- (1) Number of ordinary shares beneficially owned, as shown both in this table and the accompanying footnotes, and percentage ownership are based on 28,884,103 ordinary shares outstanding as of August 31, 2018.
- (2) Consists of ordinary shares and ADSs held by Syncona Portfolio Limited reported on a Schedule 13G filed with the SEC on February 2, 2018. Syncona Portfolio Limited is a controlled subsidiary of Syncona Holdings Limited, which in turn is a controlled subsidiary of Syncona Limited, a publicly-listed closed-end investment fund. Each of Syncona Holdings Limited and Syncona Limited may be deemed to have voting and dispositive power over the shares held by Syncona Portfolio Limited. Investment and voting decisions with respect to these shares are made by Syncona Portfolio Limited acting upon the recommendation of an investment committee of Syncona Investment Management Limited, also a subsidiary of Syncona Holdings Limited. The members of this investment committee consist of Nigel Keen, Martin Murphy, Chris Hollowood (a member of our board of directors) and Toby Sykes. The share numbers in the table above also include 1,000,000 ADSs that were purchased in our IPO. The address for Syncona Portfolio Limited is PO Box 255, Trafalgar Court, Les Banques, St Peter Port, Guernsey, GY1 3QL, Channel Islands.
- (3) Consists of ordinary shares and ADSs directly held by New Enterprise Associates 15, L.P., or NEA 15, and NEA Ventures 2015, L.P., or NEA Ventures. The shares directly held by NEA 15 are indirectly held by NEA Partners 15, L.P., or NEA Partners 15, the sole general partner of NEA 15, NEA 15 GP, LLC, or NEA 15 LLC, the sole general partner of NEA Partners 15 and each of the individual managers of NEA 15 LLC. The individual managers, or collectively, the managers, of NEA 15 LLC are Peter J. Barris, Forest Baskett, Anthony A. Florence, Jr., Joshua Makower, David M. Mott (a member of our board of directors), Scott D. Sandell, Peter Sonsini and Ravi Viswanathan. The managers share voting and dispositive power with regard to the shares held by NEA 15. Karen P. Welsh, the general partner of NEA Ventures, shares voting and dispositive power with regard to the shares held by NEA Ventures. All indirect holders of the above referenced shares disclaim beneficial ownership of all applicable ordinary shares, except to the extent of their actual pecuniary interest therein. The share numbers in the table above also include 714,285 ADSs that were purchased in our IPO. The principal business address of NEA 15 and NEA Ventures is 1954 Greenspring Drive, Suite 600, Timonium, MD 21093.

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- (4) Consists of ordinary shares and ADSs held by Wellington Management Group LLP reported on an amended Schedule 13G/A filed with the SEC on August 10, 2018. Wellington Management Group LLP, Wellington Group Holdings LLP and Wellington Investment Advisors Holdings LLP each report shared voting power over 1,662,133 ordinary shares and shared dispositive power over 1,814,737 ordinary shares. Wellington Management Company LLP reports shared voting power over 1,650,252 ordinary shares and shared dispositive power over 1,718,810 ordinary shares. Such Schedule 13G/A indicates that these shares are owned of record by clients of certain investment advisors owned, directly or indirectly, by Wellington Management Group LLP. Wellington Investment Advisors Holdings LLP controls, directly or indirectly, through Wellington Management Global Holdings, Ltd., the Wellington Investment Advisers. Wellington Investment Advisors Holdings LLP is owned by Wellington Group Holdings LLP. Wellington Group Holdings LLP is owned by Wellington Management Group LLP. The share numbers in the table above also include 800,000 ADSs that were purchased in our IPO. The business address of Wellington Management Company LLP and Wellington Management Group LLP is 280 Congress Street, Boston, MA 02110.
- (5) Consists of ordinary shares and ADSs reported on a Schedule 13G filed with the SEC on July 27, 2018 by Redmile Group LLC, or Redmile. Redmile serves as the general partner and/or investment manager to the limited partnerships and pooled investment vehicles that own the shares. Redmile, as the general partner and/or investment manager to the limited partnership(s), pooled investment vehicle(s), etc. and Jeremy Green, as the majority managing member and owner of Redmile, may therefore be deemed to beneficially own securities owned by such investment limited partnership, pooled investment vehicle, etc. for the purposes of Rule 13d-3 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, insofar as they may be deemed to have the power to direct the voting or disposition of the shares. As of December 31, 2017, Redmile and Mr. Green had shared dispositive power and voting power over 1,772,843 shares. Redmile and Mr. Green disclaim beneficial ownership of all shares held of record by Redmile in which they do not have an actual pecuniary interest. The share numbers in the table above also include 700,000 ADSs that were purchased in our IPO. The address of Redmile is One Letterman Drive, Bldg D, Ste D3-300, San Francisco, CA 94111.
- (6) Consists of ordinary shares represented by ADSs reported on a Schedule 13G filed with the SEC on August 7, 2018 by Point72 Asset Management L.P. Point72 Asset Management, L.P. and Point72 Capital Advisors, Inc. each report shared voting and dispositive power over 1,502,110 ordinary shares; Point72 Hong Kong Limited reports shared voting and dispositive power over 83 ordinary shares; and Steven A. Cohen ("Mr. Cohen") reports shared voting and dispositive power over 1,502,193 ordinary shares. Point72 Capital Advisors, Inc. is the general partner of Point72 Asset Management, L.P. Point72 Asset Management L.P. maintains investment and voting power with respect to the securities held by certain investment funds it manages. Point72 Hong Kong Limited maintains investment and voting power with respect to the securities held by certain investment funds it manages. Mr. Cohen controls each of Point72 Asset Management L.P., Point72 Capital Advisors, Inc. and Point72 Hong Kong Limited. By reason of the provisions of Rule 13d-3 of the Exchange Act, each of (i) Point72 Asset Management L.P., Point72 Capital Advisors, Inc. and Mr. Cohen may be deemed to beneficially own 1,502,110 shares and (ii) Point72 Hong Kong Limited and Mr. Cohen may be deemed to beneficially own 83 shares. Each of Point72 Asset Management L.P. Point72 Capital Advisors Inc, Point72 Hong Kong Limited, and Mr. Cohen disclaims beneficial ownership of any of these securities. The address of the principal business office of Point72 Asset Management L.P., Point72 Capital Advisors, Inc., and Steven A. Cohen is 72 Cummings Point Road, Stamford, CT 06902. The address of the principal business office of Point72 Hong Kong Limited is 12th Floor, Cater House, 8 Connaught Road Central, Hong Kong.
- (7) As of August 31, 2018, our executive officers and directors held an aggregate of 625,677 restricted share awards, of which an aggregate of 66,608 shares were vested or would have vested within 60 days. The restricted share awards, including the portions subject to forfeiture, provide voting rights and, as such, are included in the beneficial ownership table.
- (8) Consists of the ordinary shares and ADSs set forth in footnote (2) above held by Syncona Portfolio Limited. Dr. Hollowood, a member of our board of directors, is a member of the investment committee of Syncona Investment Management Limited, a subsidiary of Syncona Holdings Limited, the parent company of Syncona Portfolio Limited.
- (9) Ms. Cobb was elected to our board of directors on September 12, 2018.
- (10) Consists of the ordinary shares and ADSs set forth in footnote (3) above held by NEA 15. Mr. Mott, a member of our board of directors, is manager at NEA 15 LLC.

In October 2017, we completed our IPO and listed our ADSs on the Nasdaq Global Select Market. In the IPO, we issued and sold 6,164,000 ADSs, representing 6,164,000 ordinary shares and included the full exercise by the underwriters of their option to purchase additional ADSs. Upon the completion of our IPO, 28,904,714 ordinary shares were outstanding. While none of our existing shareholders sold ordinary shares in the IPO, the percentage ownership held by certain shareholders decreased as a result of the issuance of the ADSs sold by us in the IPO.

We have experienced significant changes in the percentage ownership held by major shareholders as a result of our IPO. Prior to our IPO in October 2017, our principal shareholders were Syncona Portfolio Limited, entities affiliated with New Enterprise Associates and entities affiliated with Wellington Management Company.

As of August 31, 2018, we estimate that approximately 19% of our outstanding ordinary shares (including ordinary shares underlying ADSs) were held in the United States by 2 holders of record. The actual number of holders is greater than these numbers of record holders, and includes beneficial owners whose ordinary shares are held in street name by brokers and other nominees. This number of holders of record also does not include holders whose shares may be held in trust by other entities.

## DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

*The following describes our issued share capital, summarizes the material provisions of our Articles of Association, or the Articles, and highlights certain differences in corporate law in the United Kingdom and the United States.*

We were incorporated pursuant to the laws of England and Wales as Nightstar Therapeutics Limited in July 2017 to become a holding company for NightstaRx Limited. Subsequently, in September 2017, Nightstar Therapeutics Limited re-registered as a public limited company and its name was changed to Nightstar Therapeutics plc.

We are registered with the Registrar of Companies in England and Wales under number 10852952, and our registered office is at 10 Midford Place, 2nd Floor, London W1T 5BJ, United Kingdom.

Certain resolutions have been passed by our shareholders in connection with our initial public offering, including resolutions:

- authorizing our directors, for the purposes of section 551 of the U.K. Companies Act 2006, or the Companies Act, to issue shares in the company and grant rights to subscribe for or convert any securities into shares in the company up to a maximum aggregate nominal amount of £1,000,000 for a period of five years; and
- empowering our directors, pursuant to sections 568 and 570 of the Companies Act, to issue equity securities for cash pursuant to the section 551 authority referred to above as if the preemption rights under the company's articles of association in effect prior to the offering and the statutory preemption rights under section 561(1) of the Companies Act did not apply to such allotments.

### Issued Share Capital

As of August 31, 2018, the issued share capital of Nightstar Therapeutics plc was 28.9 million ordinary shares with a nominal value of £0.01 per share.

### Ordinary Shares

In accordance with the Articles, the following summarizes the rights of holders of our ordinary shares:

- each holder of our ordinary shares is entitled to one vote per ordinary share on all matters to be voted on by shareholders generally;
- the holders of the ordinary shares are entitled to receive notice of, attend, speak and vote at our general meetings; and
- the holders of our ordinary shares are entitled to receive such dividends as are recommended by our directors and declared by our shareholders.

### Registered Shares

We are required by the Companies Act to keep a register of our shareholders. Under English law, the ordinary shares are deemed to be issued when the name of the shareholder is entered in our share register. The share register therefore is prima facie evidence of the identity of our shareholders, and the shares that they hold. The share register generally provides limited, or no, information regarding the ultimate beneficial owners of our ordinary shares.

Our share register is maintained by Computershare Investor Services plc.

Holders of our ADSs will not be treated as one of our shareholders and their names will therefore not be entered in our share register. The depositary, the custodian or their nominees will be the holder of the shares underlying our ADSs. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs. For discussion on our ADSs and ADS holder rights, see "Description of American Depositary Shares" in this prospectus.

Under the Companies Act, we must enter an allotment of shares in our share register as soon as practicable and in any event within two months of the allotment. We will perform all procedures necessary to update the share register to reflect the ordinary shares being sold in this offering, including updating the share register with the number of

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ordinary shares to be issued to the depositary upon the closing of this offering. We also are required by the Companies Act to register a transfer of shares (or give the transferee notice of and reasons for refusal as the transferee may reasonably request) as soon as practicable and in any event within two months of receiving notice of the transfer.

We, any of our shareholders or any other affected person may apply to the court for rectification of the share register if:

- the name of any person, without sufficient cause, is wrongly entered in or omitted from our register of members; or
- there is a default or unnecessary delay in entering on the register the fact of any person having ceased to be a member or on which we have a lien, provided that such delay does not prevent dealings in the shares taking place on an open and proper basis.

### **Preemptive Rights**

English law generally provides shareholders with preemptive rights when new shares are issued for cash; however, it is possible for the articles of association, or shareholders in general meeting, to exclude preemptive rights. Such an exclusion of preemptive rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the exclusion is contained in the articles of association, or from the date of the shareholder resolution, if the exclusion is by shareholder resolution. In either case, this exclusion would need to be renewed by our shareholders upon its expiration (i.e., at least every five years). On September 14, 2017, our shareholders approved the exclusion of preemptive rights in connection with the allotment of shares with an aggregate nominal value of up to £1,000,000 for a period of five years from the date of approval, which exclusion will need to be renewed upon expiration (i.e., at least every five years) to remain effective, but may be sought more frequently for additional five-year terms (or any shorter period). On September 14, 2017, our shareholders also approved the exclusion of preemptive rights for the allotment of ordinary shares in connection with this offering.

### **Articles of Association**

The Articles were approved by our shareholders on September 14, 2017 and were adopted with effect from the IPO. A summary of the terms of the Articles is set out below. The summary below is not a complete copy of the terms of the Articles.

The Articles contain no specific restrictions on our purpose and therefore, by virtue of section 31(1) of the Companies Act, our purpose is unrestricted.

The Articles contain, among other things, provisions to the following effect:

#### ***Share Capital***

Our share capital currently consists of ordinary shares. We may issue shares with such rights or restrictions as may be determined by ordinary resolution, including shares which are to be redeemed, or are liable to be redeemed at our option or the holder of such shares.

#### ***Voting***

The shareholders have the right to receive notice of, and to vote at, our general meetings. Each shareholder who is present in person (or, being a corporation, by representative) at a general meeting on a show of hands has one vote and, on a poll, every such holder who is present in person (or, being a corporation, by representative) or by proxy has one vote in respect of every share held by him.

#### ***Variation of Rights***

Whenever our share capital is divided into different classes of shares, the special rights attached to any class may be varied or abrogated either with the consent in writing of the holders of three-fourths in nominal value of the issued shares of that class or with the sanction of a special resolution passed at a general meeting of the holders of the shares of that class and may be so varied and abrogated whilst the company is a going concern.

#### ***Dividends***

We may, subject to the provisions of the Companies Act and the Articles, by ordinary resolution from time to time declare dividends to be paid to shareholders not exceeding the amount recommended by our board of directors.



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Subject to the provisions of the Companies Act, in so far as, in the board of directors' opinions, our profits justify such payments, the board of directors may pay interim dividends on any class of our shares.

Any dividend unclaimed after a period of 12 years from the date such dividend was declared or became payable shall, if the board of directors resolve, be forfeited and shall revert to us. No dividend or other moneys payable on or in respect of a share shall bear interest as against us.

### ***Transfer of Ordinary Shares***

Each member may transfer all or any of his shares which are in certificated form by means of an instrument of transfer in any usual form or in any other form which the board of directors may approve. Each member may transfer all or any of his shares which are in uncertificated form by means of a "relevant system" (i.e., the CREST System) in such manner provided for, and subject as provided in, the CREST Regulations.

The board may, in its absolute discretion, refuse to register a transfer of certificated shares unless:

- (i) it is for a share which is fully paid up;
- (ii) it is for a share upon which the company has no lien;
- (iii) it is only for one class of share;
- (iv) it is in favor of a single transferee or no more than four joint transferees;
- (v) it is duly stamped or is duly certificated or otherwise shown to the satisfaction of the board of directors to be exempt from stamp duty; and
- (vi) it is delivered for registration to the registered office of the company (or such other place as the board of directors may determine), accompanied (except in the case of a transfer by a person to whom the company is not required by law to issue a certificate and to whom a certificate has not been issued or in the case of a renunciation) by the certificate for the shares to which it relates and such other evidence as the board of directors may reasonably require to prove the title of the transferor (or person renouncing) and the due execution of the transfer or renunciation by him or, if the transfer or renunciation is executed by some other person on his behalf, the authority of that person to do so.

The board of directors may refuse to register a transfer of uncertificated shares in any circumstances that are allowed or required by the CREST Regulations and the CREST System.

### ***Allotment of Shares and Preemption Rights***

Subject to the Companies Act and to any rights attached to existing shares, any share may be issued with or have attached to it such rights and restrictions as the company may by ordinary resolution determine, or if no ordinary resolution has been passed or so far as the resolution does not make specific provision, as the board of directors may determine (including shares which are to be redeemed, or are liable to be redeemed at the option of the company or the holder of such shares).

In accordance with section 551 of the Companies Act, the board of directors may be generally and unconditionally authorized to exercise all the powers of the company to allot shares up to an aggregate nominal amount equal to the amount stated in the relevant ordinary resolution authorizing such allotment. The authorization referred to "—Preemptive Rights" above was included in the resolution passed by our shareholders on September 14, 2017 and remains in force at the date of this prospectus.

The provisions of section 561 of the Companies Act (which confer on shareholders rights of preemption in respect of the allotment of equity securities which are paid up in cash) apply to the company except to the extent disappplied by special resolution of the company. Such preemption rights have been disapplied pursuant to the special resolution passed on September 14, 2017.

### ***Capital***

The company may by ordinary resolution consolidate or divide all of its share capital into shares of larger nominal value than its existing shares, or cancel any shares which, at the date of the ordinary resolution, have not been taken or agreed to be taken by any person and diminish the amount of its share capital by the nominal amount of shares so cancelled or sub-divide its shares, or any of them, into shares of smaller nominal value.

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The company may, in accordance with the Companies Act, reduce or cancel its share capital or any capital redemption reserve or share premium account in any manner and with and subject to any conditions, authorities and consents required by law.

### **Board of Directors**

Unless otherwise determined by the company by ordinary resolution, the number of directors (other than any alternate directors) shall not be less than two, but there shall be no maximum number of directors.

Subject to the Articles and the Companies Act, the company may by ordinary resolution appoint a person who is willing to act as a director and the board of directors shall have power at any time to appoint any person who is willing to act as a director, in both cases either to fill a vacancy or as an addition to the existing board of directors.

At every subsequent annual general meeting any director who either (i) has been appointed by the board of directors since the last annual general meeting or (ii) was not appointed or reappointed at one of the preceding two annual general meetings, must retire from office and may offer themselves for reappointment by the shareholders by ordinary resolution.

Subject to the provisions of the Articles, the board of directors may regulate their proceedings as they deem appropriate. A director may, and the secretary at the request of a director shall, call a meeting of the directors.

The quorum for a meeting of the board of directors shall be fixed from time to time by a decision of the board of directors, but it must never be less than two and unless otherwise fixed, it is two.

Questions and matters requiring resolution arising at a meeting shall be decided by a majority of votes of the participating directors, with each director having one vote. In the case of an equality of votes, the chairman will only have a casting vote or second vote when an acquisition has been completed.

Directors shall be entitled to receive such remuneration as the board shall determine for their services to the company as directors, and for any other service which they undertake for the company provided that the aggregate fees payable to the directors must not exceed £250,000 per annum or such higher amount as may from time to time be decided by ordinary resolution of the company. The directors shall also be entitled to be paid all reasonable expenses properly incurred by them in connection with their attendance at meetings of shareholders or class meetings, board of director or committee meetings or otherwise in connection with the exercise of their powers and the discharge of their responsibilities in relation to the company.

The board of directors may, in accordance with the requirements in the Articles, authorize any matter proposed to them by any director which would, if not authorized, involve a director breaching his duty under the Companies Act, to avoid conflicts of interests.

A director seeking authorization in respect of such conflict shall declare to the board of directors the nature and extent of his interest in a conflict as soon as is reasonably practicable. The director shall provide the board with such details of the matter as are necessary for the board to decide how to address the conflict together with such additional information as may be requested by the board.

Any authorization by the board of directors will be effective only if:

- (i) to the extent permitted by the Companies Act, the matter in question shall have been proposed by any director for consideration in the same way that any other matter may be proposed to the directors under the provisions of the Articles;
- (ii) any requirement as to the quorum for consideration of the relevant matter is met without counting the conflicted director and any other conflicted director; and
- (iii) the matter is agreed to without the conflicted director voting or would be agreed to if the conflicted director's and any other interested director's vote is not counted.

Subject to the provisions of the Companies Act, every director, secretary or other officer of the company (other than an auditor) is entitled to be indemnified against all costs, charges, losses, damages and liabilities incurred by him in the actual purported exercise or discharge of his duties or exercise of his powers or otherwise in relation to them.

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### **General Meetings**

The company must convene and hold annual general meetings in accordance with the Companies Act. Under the Companies Act, an annual general meeting must be called by notice of at least 21 days.

No business shall be transacted at any general meeting unless a quorum is present when the meeting proceeds to business, but the absence of a quorum shall not preclude the choice or appointment of a chairman of the meeting which shall not be treated as part of the business of the meeting. Save as otherwise provided by the Articles, two shareholders present in person or by proxy and entitled to vote shall be a quorum for all purposes.

#### (i) Borrowing Powers

Subject to the Articles and the Companies Act, the board of directors may exercise all of the powers of the company to:

- (a) borrow money;
- (b) indemnify and guarantee;
- (c) mortgage or charge;
- (d) create and issue debentures and other securities; and
- (e) give security either outright or as collateral security for any debt, liability or obligation of the company or of any third party.

#### (ii) Capitalization of profits

The directors may, if they are so authorized by an ordinary resolution of the shareholders, decide to capitalize any undivided profits of the company (whether or not they are available for distribution), or any sum standing to the credit of the company's share premium account or capital redemption reserve. The directors may also, subject to the aforementioned ordinary resolution, appropriate any sum which they so decide to capitalize to the persons who would have been entitled to it if it were distributed by way of dividend and in the same proportions.

#### (iii) Uncertificated Shares

Subject to the Companies Act, the board of directors may permit title to shares of any class to be issued or held otherwise than by a certificate and to be transferred by means of a "relevant system" (i.e., the CREST System) without a certificate.

The board of directors may take such steps as it sees fit in relation to the evidencing of and transfer of title to uncertificated shares, any records relating to the holding of uncertificated shares and the conversion of uncertificated shares to certificated shares, or vice-versa.

The company may by notice to the holder of an uncertificated share, require that share to be converted into certificated form.

The board of directors may take such other action that the board considers appropriate to achieve the sale, transfer, disposal, forfeiture, re-allotment or surrender of an uncertificated share or otherwise to enforce a lien in respect of it.

### **Other Relevant Laws and Regulations**

#### ***The City Code on Takeovers and Mergers***

In March 2018, the UK Takeover Panel confirmed that we are not considered to be subject to The City Code on Takeovers and Mergers, or the Takeover Code. There are no provisions in the Articles which replicate the provisions of the Takeover Code.

We believe that this position is unlikely to change at any time in the near future, but in accordance with good practice, we will review the situation on a regular basis and co-operate and consult with the UK Takeover Panel if there is any material change in our circumstances with respect to matters which the UK Takeover Panel might consider relevant in their determination of jurisdiction over us.

#### ***Squeeze-out***

- (i) Under sections 979 to 982 of the Companies Act, if an offeror were to acquire, or unconditionally contract to acquire, not less than 90% of the ordinary shares of the company, it could then compulsorily acquire the remaining 10%. It would do so by sending a notice to outstanding shareholders telling them that it will compulsorily acquire their shares, provided that no such notice may be served after the end of: (a) the period of three months beginning with the day after the last day on which the offer can be accepted; or (b) if earlier, and

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the offer is not one to which section 943(1) of the Companies Act applies, the period of six months beginning with the date of the offer.

- (ii) Six weeks following service of the notice, the offeror must send a copy of it to the company together with the consideration for the ordinary shares to which the notice relates, and an instrument of transfer executed on behalf of the outstanding shareholder(s) by a person appointed by the offeror.
- (iii) The company will hold the consideration on trust for the outstanding shareholders.

### **Sell-out**

- (i) Sections 983 to 985 of the Companies Act also give minority shareholders in the company a right to be bought out in certain circumstances by an offeror who has made a takeover offer. If a takeover offer relating to all the ordinary shares of the company is made at any time before the end of the period within which the offer could be accepted and the offeror held or had agreed to acquire not less than 90% of the ordinary shares, any holder of shares to which the offer related who had not accepted the offer could by a written communication to the offeror require it to acquire those shares. The offeror is required to give any shareholder notice of his right to be bought out within one month of that right arising. The offeror may impose a time limit on the rights of minority shareholders to be bought out, but that period cannot end less than three months after the end of the acceptance period, or, if longer a period of three months from the date of the notice.
- (ii) If a shareholder exercises his rights, the offeror is bound to acquire those shares on the terms of the offer or on such other terms as may be agreed.

### **Differences in Corporate Law**

The applicable provisions of the Companies Act differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of the Companies Act applicable to us and the General Corporation Law of the State of Delaware relating to shareholders' rights and protections.

	<b>ENGLAND AND WALES</b>	<b>DELAWARE</b>
Number of Directors	Under the Companies Act, a public limited company must have at least two directors and the number of directors may be fixed by or in the manner provided in a company's articles of association.	Under Delaware law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws.
Removal of Directors	Under the Companies Act, shareholders may remove a director without cause by an ordinary resolution (which is passed by a simple majority of those voting in person or by proxy at a general meeting) irrespective of any provisions of any service contract the director has with the company, provided 28 clear days' notice of the resolution has been given to the company and its shareholders. On receipt of notice of an intended resolution to remove a director, the company must forthwith send a copy of the notice to the director concerned. Certain other procedural requirements under the Companies Act must also be followed, such as allowing the director to make representations against his or her removal either at the meeting or in writing.	Under Delaware law, any director or the entire board of directors may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except (i) unless the certificate of incorporation provides otherwise, in the case of a corporation whose board of directors is classified, stockholders may effect such removal only for cause, or (ii) in the case of a corporation having cumulative voting, if less than the entire board of directors is to be removed, no director may be removed without cause if the votes cast against his removal would be sufficient to elect him if then cumulatively voted at an election of the entire board of directors, or, if there are classes of directors, at an election of the class of directors of which he is a part.

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	<b>ENGLAND AND WALES</b>	<b>DELAWARE</b>
Vacancies on the Board of Directors	Under English law, the procedure by which directors, other than a company's initial directors, are appointed is generally set out in a company's articles of association, provided that where two or more persons are appointed as directors of a public limited company by resolution of the shareholders, resolutions appointing each director must be voted on individually.	Under Delaware law, vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) or by a sole remaining director unless (i) otherwise provided in the certificate of incorporation or bylaws of the corporation or (ii) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case a majority of the other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.
Annual General Meeting	Under the Companies Act, a public limited company must hold an annual general meeting in each six-month period following the company's annual accounting reference date.	Under Delaware law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws.
General Meeting	Under the Companies Act, a general meeting of the shareholders of a public limited company may be called by the directors.  Shareholders holding at least 5% of the paid-up capital of the company carrying voting rights at general meetings (excluding any paid up capital held as treasury shares) can require the directors to call a general meeting and, if the directors fail to do so within a certain period, may themselves convene a general meeting.	Under Delaware law, special meetings of the stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.
Notice of General Meetings	Under the Companies Act, at least 21 days' notice must be given for an annual general meeting and any resolutions to be proposed at the meeting. Subject to a company's articles of association providing for a longer period, at least 14 days' notice is required for any other general meeting of a public limited company. In addition, certain matters, such as the removal of directors or auditors, require special notice, which is 28 days' notice. The shareholders of a company may consent to a shorter notice period, the proportion of shareholders' consent required being 100% of those entitled to attend and vote in the case of an annual general meeting and, in the case of any other general meeting, a majority in number of the members having a right to	Under Delaware law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, and hour of the meeting.

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	attend and vote at the meeting, being a majority who together hold not less than 95% in nominal value of the shares giving a right to attend and vote at the meeting.	
Proxy	Under the Companies Act, at any meeting of shareholders, a shareholder may designate another person to attend, speak and vote at the meeting on their behalf by proxy.	Under Delaware law, at any meeting of stockholders, a stockholder may designate another person to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.
Preemptive Rights	Under the Companies Act, "equity securities," being (i) shares in the company other than shares that, with respect to dividends and capital, carry a right to participate only up to a specified amount in a distribution, referred to as "ordinary shares," or (ii) rights to subscribe for, or to convert securities into, ordinary shares, proposed to be allotted for cash must be offered first to the existing equity shareholders in the company in proportion to the respective nominal value of their holdings, unless an exception applies or a special resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise in each case in accordance with the provisions of the Companies Act.	Under Delaware law, shareholders have no preemptive rights to subscribe to additional issues of stock or to any security convertible into such stock unless, and except to the extent that, such rights are expressly provided for in the certificate of incorporation.
Authority to Allot	Under the Companies Act, the directors of a company must not allot shares or grant rights to subscribe for or convert any security into shares unless an exception applies or an ordinary resolution to the contrary has been passed by shareholders in a general meeting or the articles of association provide otherwise, in each case in accordance with the provisions of the Companies Act.	Under Delaware law, if the corporation's charter or certificate of incorporation so provides, the board of directors has the power to authorize the issuance of stock. The board may authorize capital stock to be issued for consideration consisting of cash, any tangible or intangible property or any benefit to the corporation or any combination thereof. It may determine the amount of such consideration by approving a formula. In the absence of actual fraud in the transaction, the judgment of the directors as to the value of such consideration is conclusive.

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	ENGLAND AND WALES	DELAWARE
Liability of Directors and Officers	<p>Under the Companies Act, any provision, whether contained in a company's articles of association or any contract or otherwise, that purports to exempt a director of a company, to any extent, from any liability that would otherwise attach to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company, is void. Any provision by which a company directly or indirectly provides an indemnity, to any extent, for a director of the company or of an associated company against any liability attaching to him in connection with any negligence, default, breach of duty or breach of trust in relation to the company of which he is a director is also void except as permitted by the Companies Act, which provides exceptions for the company to (i) purchase and maintain insurance against such liability; (ii) provide a "qualifying third party indemnity," or an indemnity against liability incurred by the director to a person other than the company or an associated company or criminal proceedings in which he is convicted; and (iii) provide a "qualifying pension scheme indemnity," or an indemnity against liability incurred in connection with the company's activities as trustee of an occupational pension plan.</p>	<p>Under Delaware law, a corporation's certificate of incorporation may include a provision eliminating or limiting the personal liability of a director to the corporation and its stockholders for damages arising from a breach of fiduciary duty as a director. However, no provision can limit the liability of a director for:</p> <ul style="list-style-type: none"><li>▪ any breach of the director's duty of loyalty to the corporation or its stockholders;</li><li>▪ acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;</li><li>▪ intentional or negligent payment of unlawful dividends or stock purchases or redemptions; or</li><li>▪ any transaction from which the director derives an improper personal benefit.</li></ul>
Voting Rights	<p>Under English law, unless a poll is demanded by the shareholders of a company or is required by the chairman of the meeting or the company's articles of association, shareholders shall vote on all resolutions on a show of hands. Under the Companies Act, a poll may be demanded by (i) not fewer than five shareholders having the right to vote on the resolution; (ii) any shareholder(s) representing not less than 10% of the total voting rights of all the shareholders having the right to vote on the resolution (excluding any voting rights attaching to treasury shares); or (iii) any shareholder(s) holding shares in the company conferring a right to vote on the resolution (excluding any voting rights attaching to treasury shares) being shares on which an aggregate sum has been paid up equal to not less than 10% of the total sum paid up on all the shares conferring</p>	<p>Delaware law provides that, unless otherwise provided in the certificate of incorporation, each stockholder is entitled to one vote for each share of capital stock held by such stockholder.</p>

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	<p>that right. A company's articles of association may provide more extensive rights for shareholders to call a poll.</p> <p>Under English law, an ordinary resolution is passed on a show of hands if it is approved by a simple majority (more than 50%) of the votes cast by shareholders present (in person or by proxy) and entitled to vote. If a poll is demanded, an ordinary resolution is passed if it is approved by holders representing a simple majority of the total voting rights of shareholders present, in person or by proxy, who, being entitled to vote, vote on the resolution. Special resolutions require the affirmative vote of not less than 75% of the votes cast by shareholders present, in person or by proxy, at the meeting.</p>	
Shareholder Vote on Certain Transactions	<p>The Companies Act provides for schemes of arrangement, which are arrangements or compromises between a company and any class of shareholders or creditors and used in certain types of reconstructions, amalgamations, capital reorganizations or takeovers. These arrangements require:</p> <ul style="list-style-type: none"><li>▪ the approval at a shareholders' or creditors' meeting convened by order of the court, of a majority in number of shareholders or creditors representing 75% in value of the capital held by, or debt owed to, the class of shareholders or creditors, or class thereof present and voting, either in person or by proxy; and</li><li>▪ the approval of the court.</li></ul>	<p>Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires:</p> <ul style="list-style-type: none"><li>▪ the approval of the board of directors; and</li><li>▪ the approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of the corporation entitled to vote on the matter.</li></ul>
Standard of Conduct for Directors	<p>Under English law, a director owes various statutory and fiduciary duties to the company, including:</p> <ul style="list-style-type: none"><li>▪ to act in the way he considers, in good faith, would be most likely to promote the success of the company for the benefit of its members as a whole;</li><li>▪ to avoid a situation in which he has, or can have, a direct or indirect interest that conflicts, or</li></ul>	<p>Delaware law does not contain specific provisions setting forth the standard of conduct of a director. The scope of the fiduciary duties of directors is generally determined by the courts of the State of Delaware. In general, directors have a duty to act without self-interest, on a well-informed basis and in a manner they reasonably believe to be in the best interest of the stockholders.</p> <p>Directors of a Delaware corporation owe fiduciary duties of care and loyalty to the</p>



	<u>ENGLAND AND WALES</u>	<u>DELAWARE</u>
	<p>possibly conflicts, with the interests of the company;</p> <ul style="list-style-type: none"> <li>▪ to act in accordance with the company's constitution and only exercise his powers for the purposes for which they are conferred;</li> <li>▪ to exercise independent judgment;</li> <li>▪ to exercise reasonable care, skill and diligence;</li> <li>▪ not to accept benefits from a third party conferred by reason of his being a director or doing, or not doing, anything as a director; and</li> <li>▪ to declare any interest that he has, whether directly or indirectly, in a proposed or existing transaction or arrangement with the company.</li> </ul>	<p>corporation and to its shareholders. The duty of care generally requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. In general, but subject to certain exceptions, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation.</p> <p>However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation.</p> <p>In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the shareholders.</p>
Stockholder Suits	<p>Under English law, generally, the company, rather than its shareholders, is the proper claimant in an action in respect of a wrong done to the company or where there is an irregularity in the company's internal management. Notwithstanding this general position, the Companies Act provides that (i) a court may allow a shareholder to bring a derivative claim (that is, an action in respect of and on behalf of the company) in respect of a cause of action arising from a director's negligence, default, breach of duty or breach of trust and (ii) a shareholder may bring a claim for a court order where the company's affairs have been or are being conducted in a manner</p>	<p>Under Delaware law, a stockholder may initiate a derivative action to enforce a right of a corporation if the corporation fails to enforce the right itself. The complaint must:</p> <ul style="list-style-type: none"> <li>▪ state that the plaintiff was a stockholder at the time of the transaction of which the plaintiff complains or that the plaintiff's shares thereafter devolved on the plaintiff by operation of law; and</li> <li>▪ allege with particularity the efforts made by the plaintiff to obtain the action the plaintiff desires from the directors and the</li> </ul>

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that is unfairly prejudicial to some of its shareholders.	reasons for the plaintiff's failure to obtain the action; or <ul style="list-style-type: none"><li>state the reasons for not making the effort.</li></ul> Additionally, the plaintiff must remain a stockholder through the duration of the derivative suit. The action will not be dismissed or compromised without the approval of the Delaware Court of Chancery.

**Stock Exchange Listing**

The ADSs have been listed on the Nasdaq Global Select Market under the symbol "NITE" since September 28, 2017.

**Transfer Agent and Registrar of Shares**

Our share register is maintained by Computershare Investor Services plc. The share register reflects only record owners of our ordinary shares. Holders of our ADSs will not be treated as one of our shareholders and their names will therefore not be entered in our share register. The depositary, the custodian or their nominees will be the holder of the shares underlying our ADSs. Holders of our ADSs have a right to receive the ordinary shares underlying their ADSs. For discussion on our ADSs and ADS holder rights, see "Description of American Depositary Shares" in this prospectus.

## DESCRIPTION OF AMERICAN DEPOSITARY SHARES

### American Depositary Shares

Citibank, N.A., or Citibank, has agreed to act as the depositary for the ADSs. Citibank's depositary offices are located at 388 Greenwich Street, New York, New York 10013. ADSs represent ownership interests in securities that are on deposit with the depositary. ADSs may be represented by certificates that are commonly known as American Depositary Receipts, or ADRs. The depositary typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank, N.A. (London) located at Citigroup Centre, Canary Wharf, London, E14 5LB, United Kingdom.

We have appointed Citibank as depositary pursuant to a deposit agreement. A copy of the deposit agreement is on file with the SEC under cover of a registration statement on Form F-6. You may obtain a copy of the deposit agreement from the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and from the SEC's website ([www.sec.gov](http://www.sec.gov)). Please refer to registration number 333-220343 when retrieving such copy.

We are providing you with a summary description of the material terms of the ADSs and of your material rights as an owner of ADSs. Summaries by their nature lack the precision of the information summarized and the rights and obligations of an owner of ADSs will be determined by reference to the terms of the deposit agreement and not by this summary. We urge you to review the deposit agreement in its entirety. The portions of this summary that are italicized describe matters that may be relevant to ownership of ADSs but may not be contained in the deposit agreement.

Each ADS represents the right to receive, and to exercise the beneficial ownership interests in, one ordinary share that is on deposit with the depositary and/or custodian. An ADS also represents the right to receive, and to exercise the beneficial interests in, any other property received by the depositary or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. We and the depositary may agree to change the ADS-to-ordinary share ratio by amending the deposit agreement. This amendment may give rise to, or change, the depositary fees payable by ADS owners. The custodian, the depositary and their respective nominees will hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depositary, the custodian or their nominees. Beneficial ownership in the deposited property will under the terms of the deposit agreement be vested in the beneficial owners of the ADSs. The depositary, the custodian and their respective nominees will be the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. A beneficial owner of ADSs may or may not be the holder of ADSs. Beneficial owners of ADSs will be able to receive, and to exercise beneficial ownership interests in, the deposited property only through the registered holders of the ADSs, the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depositary, and the depositary (on behalf of the owners of the corresponding ADSs) directly, or indirectly, through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.

If you become an owner of ADSs, you will become a party to the deposit agreement and therefore will be bound to its terms and to the terms of any ADR that represents your ADSs. The deposit agreement and the ADR specify our rights and obligations as well as your rights and obligations as owner of ADSs and those of the depositary. As an ADS holder you appoint the depositary to act on your behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of ordinary shares will continue to be governed by the laws of England and Wales, which may be different from the laws of the United States.

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with such reporting requirements and obtaining such approvals. Neither the depositary, the custodian, us or any of their or our respective agents or affiliates shall be required to take any actions whatsoever on your behalf to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

*The manner in which you own ADSs (e.g., in brokerage account vs. as registered holder, or as holder of certificated vs. uncertificated) may affect your rights and obligations, and the manner in which the depositary's services are*

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*made available to you. As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depository will hold on your behalf the shareholder rights attached to the ordinary shares underlying your ADSs. As an owner of ADSs you will be able to exercise the shareholders rights for the ordinary shares represented by your ADSs through the depository only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.*

As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depository in your name reflecting the registration of uncertificated ADSs directly on the books of the depository (commonly referred to as the direct registration system or DRS). The direct registration system reflects the uncertificated (book-entry) registration of ownership of ADSs by the depository. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depository to the holders of the ADSs. The direct registration system includes automated transfers between the depository and The Depository Trust Company, or DTC, the central book-entry clearing and settlement system for equity securities in the United States. If you decide to hold your ADSs through your brokerage or safekeeping account, you must rely on the procedures of your broker or bank to assert your rights as ADS owner. Banks and brokers typically hold securities such as the ADSs through clearing and settlement systems such as DTC. The procedures of such clearing and settlement systems may limit your ability to exercise your rights as an owner of ADSs. Please consult with your broker or bank if you have any questions concerning these limitations and procedures. All ADSs held through DTC will be registered in the name of a nominee of DTC. This summary description assumes you have opted to own the ADSs directly by means of an ADS registered in your name and, as such, we will refer to you as the "holder." When we refer to "you," we assume the reader owns ADSs and will own ADSs at the relevant time.

The registration of the ordinary shares in the name of the depository or the custodian shall, to the maximum extent permitted by applicable law, vest in the depository or the custodian the record ownership in the applicable ordinary shares with the beneficial ownership rights and interests in such ordinary shares being at all times vested with the beneficial owners of the ADSs representing the ordinary shares. The depository or the custodian shall at all times be entitled to exercise the beneficial ownership rights in all deposited property, in each case only on behalf of the holders and beneficial owners of the ADSs representing the deposited property.

### **Dividends and Other Distributions**

As a holder of ADSs, you generally have the right to receive the distributions we make on the securities deposited with the custodian. Your receipt of these distributions may be limited, however, by practical considerations and legal limitations. Holders of ADSs will receive such distributions under the terms of the deposit agreement in proportion to the number of ADSs held as of the specified record date, after deduction the applicable fees, taxes and expenses.

#### ***Distributions of Cash***

Whenever we make a cash distribution for the securities on deposit with the custodian, we will deposit the funds with the custodian. Upon receipt of confirmation of the deposit of the requisite funds, the depository will arrange for the funds to be converted into U.S. dollars and for the distribution of the U.S. dollars to the holders, subject to the laws and regulations of England and Wales.

The conversion into U.S. dollars will take place only if practicable and if the U.S. dollars are transferable to the United States. The depository will apply the same method for distributing the proceeds of the sale of any property (such as undistributed rights) held by the custodian in respect of securities on deposit.

The distribution of cash will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. The depository will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable holders and beneficial owners of ADSs until the distribution can be effected or the funds that the depository holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States.

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***Distributions of Shares***

Whenever we make a free distribution of ordinary shares for the securities on deposit with the custodian, we will deposit the applicable number of ordinary shares with the custodian. Upon receipt of confirmation of such deposit, the depositary will either distribute to holders new ADSs representing the ordinary shares deposited or modify the ADS-to-ordinary shares ratio, in which case each ADS you hold will represent rights and interests in the additional ordinary shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-ordinary share ratio upon a distribution of ordinary shares will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depositary may sell all or a portion of the new ordinary shares so distributed.

No such distribution of new ADSs will be made if it would violate a law (e.g., the U.S. securities laws) or if it is not operationally practicable. If the depositary does not distribute new ADSs as described above, it may sell the ordinary shares received upon the terms described in the deposit agreement and will distribute the proceeds of the sale as in the case of a distribution of cash.

***Distributions of Rights***

Whenever we intend to distribute rights to purchase additional ordinary shares, we will give prior notice to the depositary and we will assist the depositary in determining whether it is lawful and reasonably practicable to distribute rights to purchase additional ADSs to holders.

The depositary will establish procedures to distribute rights to purchase additional ADSs to holders and to enable such holders to exercise such rights if it is lawful and reasonably practicable to make the rights available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement (such as opinions to address the lawfulness of the transaction). You may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs upon the exercise of your rights. The depositary is not obligated to establish procedures to facilitate the distribution and exercise by holders of rights to purchase new ordinary shares other than in the form of ADSs.

The depositary will not distribute the rights to you if:

- we do not timely request that the rights be distributed to you or we request that the rights not be distributed to you; or
- we fail to deliver satisfactory documents to the depositary; or
- it is not reasonably practicable to distribute the rights.

The depositary will sell the rights that are not exercised or not distributed if such sale is lawful and reasonably practicable. The proceeds of such sale will be distributed to holders as in the case of a cash distribution. If the depositary is unable to sell the rights, it will allow the rights to lapse.

***Elective Distributions***

Whenever we intend to distribute a dividend payable at the election of shareholders either in cash or in additional shares, we will give prior notice thereof to the depositary and will indicate whether we wish the elective distribution to be made available to you. In such case, we will assist the depositary in determining whether such distribution is lawful and reasonably practicable.

The depositary will make the election available to you only if it is reasonably practicable and if we have provided all of the documentation contemplated in the deposit agreement. In such case, the depositary will establish procedures to enable you to elect to receive either cash or additional ADSs, in each case as described in the deposit agreement.

If the election is not made available to you, you will receive either cash or additional ADSs, depending on what a shareholder in England and Wales would receive upon failing to make an election, as more fully described in the deposit agreement.

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### ***Other Distributions***

Whenever we intend to distribute property other than cash, ordinary shares or rights to purchase additional ordinary shares, we will notify the depositary in advance and will indicate whether we wish such distribution to be made to you. If so, we will assist the depositary in determining whether such distribution to holders is lawful and reasonably practicable.

If it is reasonably practicable to distribute such property to you and if we provide all of the documentation contemplated in the deposit agreement, the depositary will distribute the property to the holders in a manner it deems practicable.

The distribution will be made net of fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes and governmental charges, the depositary may sell all or a portion of the property received.

The depositary will *not* distribute the property to you and will sell the property if:

- we do not request that the property be distributed to you or if we ask that the property not be distributed to you; or
- we do not deliver satisfactory documents to the depositary; or
- the depositary determines that all or a portion of the distribution to you is not reasonably practicable.

The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

### ***Redemption***

Whenever we decide to redeem any of the securities on deposit with the custodian, we will notify the depositary in advance. If it is practicable and if we provide all of the documentation contemplated in the deposit agreement, the depositary will provide notice of the redemption to the holders.

The custodian will be instructed to surrender the shares being redeemed against payment of the applicable redemption price. The depositary will convert the redemption funds received into U.S. dollars upon the terms of the deposit agreement and will establish procedures to enable holders to receive the net proceeds from the redemption upon surrender of their ADSs to the depositary. You may have to pay fees, expenses, taxes and other governmental charges upon the redemption of your ADSs. If less than all ADSs are being redeemed, the ADSs to be retired will be selected by lot or on a pro rata basis, as the depositary may determine.

### **Changes Affecting Ordinary Shares**

The ordinary shares held on deposit for your ADSs may change from time to time. For example, there may be a change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of such ordinary shares or a recapitalization, reorganization, merger, consolidation or sale of assets of the company.

If any such change were to occur, your ADSs would, to the extent permitted by law, represent the right to receive the property received or exchanged in respect of the ordinary shares held on deposit. The depositary may in such circumstances deliver new ADSs to you, amend the deposit agreement, the ADRs and the applicable Registration Statement(s) on Form F-6, call for the exchange of your existing ADSs for new ADSs and take any other actions that are appropriate to reflect as to the ADSs the change affecting the ordinary shares. If the depositary may not lawfully distribute such property to you, the depositary may sell such property and distribute the net proceeds to you as in the case of a cash distribution.

### **Issuance of ADSs upon Deposit of Ordinary Shares**

Upon completion of this offering, the ordinary shares being offered pursuant to this prospectus will be deposited by us with the custodian. Upon receipt of confirmation of such deposit, the depositary will issue ADSs to the underwriters named in this prospectus.

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After the closing of this offering, the depositary may create ADSs on your behalf if you or your broker deposit ordinary shares with the custodian. The depositary will deliver these ADSs to the person you indicate only after you pay any applicable issuance fees and any charges and taxes payable for the transfer of the ordinary shares to the custodian. Your ability to deposit ordinary shares and receive ADSs may be limited by United States and England and Wales legal considerations applicable at the time of deposit.

The issuance of ADSs may be delayed until the depositary or the custodian receives confirmation that all required approvals have been given and that the ordinary shares have been duly transferred to the custodian. The depositary will only issue ADSs in whole numbers.

When you make a deposit of ordinary shares, you will be responsible for transferring good and valid title to the depositary. As such, you will be deemed to represent and warrant that:

- the ordinary shares are duly authorized, validly issued, fully paid, non-assessable and legally obtained;
- all preemptive (and similar) rights, if any, with respect to such ordinary shares have been validly waived or exercised;
- you are duly authorized to deposit the ordinary shares;
- the ordinary shares presented for deposit are free and clear of any lien, encumbrance, security interest, charge, mortgage or adverse claim, and are not, and the ADSs issuable upon such deposit will not be, "restricted securities" (as defined in the deposit agreement);
- the ordinary shares presented for deposit have not been stripped of any rights or entitlements; and
- the deposit of shares does not violate any applicable provision of English law.

If any of the representations or warranties are incorrect in any way, we and the depositary may, at your cost and expense, take any and all actions necessary to correct the consequences of the misrepresentations.

### **Transfer, Combination and Split Up of ADRs**

As an ADR holder, you will be entitled to transfer, combine or split up your ADRs and the ADSs evidenced thereby. For transfers of ADRs, you will have to surrender the ADRs to be transferred to the depositary and also must:

- ensure that the surrendered ADR is properly endorsed or otherwise in proper form for transfer;
- provide such proof of identity and genuineness of signatures as the depositary deems appropriate;
- provide any transfer stamps required by the State of New York or the United States; and
- pay all applicable fees, charges, expenses, taxes and other government charges payable by ADR holders pursuant to the terms of the deposit agreement, upon the transfer of ADRs.

To have your ADRs either combined or split up, you must surrender the ADRs in question to the depositary with your request to have them combined or split up, and you must pay all applicable fees, charges and expenses payable by ADR holders, pursuant to the terms of the deposit agreement, upon a combination or split up of ADRs.

### **Withdrawal of Ordinary Shares Upon Cancellation of ADSs**

As a holder, you will be entitled to present your ADSs to the depositary for cancellation and then receive the corresponding number of underlying ordinary shares at the custodian's offices. Your ability to withdraw the ordinary shares held in respect of the ADSs may be limited by United States and England and Wales considerations applicable at the time of withdrawal. In order to withdraw the ordinary shares represented by your ADSs, you will be required to pay to the depositary the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the ordinary shares. You assume the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

If you hold ADSs registered in your name, the depositary may ask you to provide proof of identity and genuineness of any signature and such other documents as the depositary may deem appropriate before it will cancel your ADSs. The withdrawal of the ordinary shares represented by your ADSs may be delayed until the depositary receives satisfactory evidence of compliance with all applicable laws and regulations. Please keep in mind that the depositary will only accept ADSs for cancellation that represent a whole number of securities on deposit.

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You will have the right to withdraw the securities represented by your ADSs at any time except as a result of:

- temporary delays that may arise because (i) the transfer books for the ordinary shares or ADSs are closed, or (ii) ordinary shares are immobilized on account of a shareholders' meeting or a payment of dividends;
- obligations to pay fees, taxes and similar charges;
- restrictions imposed because of laws or regulations applicable to ADSs or the withdrawal of securities on deposit; and/or
- other circumstances specifically contemplated by Section I.A.(l) of the General Instructions to Form F-6 (as such General Instructions may be amended from time to time).

The deposit agreement may not be modified to impair your right to withdraw the securities represented by your ADSs except to comply with mandatory provisions of law.

### **Voting Rights**

As a holder, you generally have the right under the deposit agreement to instruct the depositary to exercise the voting rights for the ordinary shares represented by your ADSs. The voting rights of holders of ordinary shares are described in "Description of Share Capital and Articles of Association—Articles of Association" in this prospectus.

At our request, the depositary will distribute to you any notice of shareholders' meeting received from us together with information explaining how to instruct the depositary to exercise the voting rights of the securities represented by ADSs. In lieu of distributing such materials, the depositary may distribute to holders of ADSs instructions on how to receive such materials upon request.

If the depositary timely receives voting instructions from a holder of ADSs, it will endeavor to vote (or cause the custodian to vote) the securities (in person or by proxy) represented by the holder's ADSs as follows:

- **If voting at the shareholders' meeting is by show of hands:** The depositary will vote (or cause the custodian to vote) all the securities represented by ADSs in accordance with the voting instructions received from a majority of the ADS holders who provided voting instructions; and
- **If voting at the shareholders' meeting is by poll:** The depositary will vote (or cause the custodian to vote) the securities represented by ADSs in accordance with the voting instructions received from the holders of ADSs.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated in the deposit agreement). Please note that the ability of the depositary to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities on deposit. We cannot assure you that you will receive voting materials in time to enable you to return voting instructions to the depositary in a timely manner.



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**Fees and Charges**

As an ADS holder, you will be required to pay the following fees under the terms of the deposit agreement:

<u>SERVICE</u>	<u>FEE</u>
Issuance of ADSs (e.g., an issuance of ADS upon a deposit of ordinary shares or upon a change in the ADS(s)-to-ordinary shares ratio), excluding ADS issuances as a result of distributions of ordinary shares	Up to \$0.05 per ADS issued
Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property or upon a change in the ADS(s)-to-ordinary shares ratio, or for any other reason)	Up to \$0.05 per ADS cancelled
Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to \$0.05 per ADS held
Distribution of ADSs pursuant to (i) share dividends or other free share distributions, or (ii) exercise of rights to purchase additional ADSs	Up to \$0.05 per ADS held
Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to \$0.05 per ADS held
ADS Services	Up to \$0.05 per ADS held on the applicable record date(s) established by the depository

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As an ADS holder you will also be responsible to pay certain charges such as:

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of ordinary shares on the share register and applicable to transfers of ordinary shares to or from the name of the custodian, the depository or any nominees upon the making of deposits and withdrawals, respectively;
- certain cable, telex and facsimile transmission and delivery expenses;
- the expenses and charges incurred by the depository in the conversion of foreign currency;
- the fees and expenses incurred by the depository in connection with compliance with exchange control regulations and other regulatory requirements applicable to ordinary shares, ADSs and ADRs; and
- the fees and expenses incurred by the depository, the custodian or any nominee in connection with the servicing or delivery of deposited property.

ADS fees and charges payable upon (i) the issuance of ADSs, and (ii) the cancellation of ADSs are charged to the person to whom the ADSs are issued (in the case of ADS issuances) and to the person whose ADSs are cancelled (in the case of ADS cancellations). In the case of ADSs issued by the depository into DTC, the ADS issuance and cancellation fees and charges may be deducted from distributions made through DTC, and may be charged to the DTC participant(s) receiving the ADSs being issued or the DTC participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the beneficial owner(s) and will be charged by the DTC participant(s) to the account of the applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participants as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are charged to the holders as of the applicable ADS record date. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs.

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In the event of refusal to pay the depositary fees, the depositary may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary fees from any distribution to be made to the ADS holder. Certain of the depositary fees and charges (such as the ADS services fee) may become payable shortly after the closing of the ADS offering. Note that the fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary. You will receive prior notice of such changes. The depositary may reimburse us for certain expenses incurred by us in respect of the ADR program, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary agree from time to time.

### **Amendments and Termination**

We may agree with the depositary to modify the deposit agreement at any time without your consent. We undertake to give holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to your substantial rights any modifications or supplements that are reasonably necessary for the ADSs to be registered under the Securities Act of 1933, as amended, or the Securities Act, or to be eligible for book-entry settlement, in each case without imposing or increasing the fees and charges you are required to pay. In addition, we may not be able to provide you with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

You will be bound by the modifications to the deposit agreement if you continue to hold your ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent you from withdrawing the ordinary shares represented by your ADSs (except as permitted by law).

We have the right to direct the depositary to terminate the deposit agreement. Similarly, the depositary may in certain circumstances on its own initiative terminate the deposit agreement. In either case, the depositary must give notice to the holders at least 30 days before termination. Until termination, your rights under the deposit agreement will be unaffected.

### **Termination**

After termination, the depositary will continue to collect distributions received (but will not distribute any such property until you request the cancellation of your ADSs) and may sell the securities held on deposit. After the sale, the depositary will hold the proceeds from such sale and any other funds then held for the holders of ADSs in a non-interest bearing account. At that point, the depositary will have no further obligations to holders other than to account for the funds then held for the holders of ADSs still outstanding (after deduction of applicable fees, taxes and expenses).

### **Books of Depositary**

The depositary will maintain ADS holder records at its depositary office. You may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

The depositary will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up and transfer of ADSs. These facilities may be closed from time to time, to the extent not prohibited by law.

### **Transmission of Notices, Reports and Proxy Soliciting Material**

The depositary will make available for your inspection at its office all communications that it receives from us as a holder of deposited securities that we make generally available to holders of deposited securities. Subject to the terms of the deposit agreement, the depositary will send you copies of those communications or otherwise make those communications available to you if we ask it to.

### **Limitations on Obligations and Liabilities**

The deposit agreement limits our obligations and the depositary's obligations to you. Please note the following:

- We and the depositary are obligated only to take the actions specifically stated in the deposit agreement without negligence or bad faith.
- The depositary disclaims any liability for any failure to carry out voting instructions, for any manner in which a vote is cast or for the effect of any vote, provided it acts in good faith and without negligence and in accordance with the terms of the deposit agreement.
- The depositary disclaims any liability for any failure to determine the lawfulness or practicality of any action, for the content of any document forwarded to you on our behalf or for the accuracy of any translation of such a document, for the investment risks associated with investing in ordinary shares, for the validity or worth of the ordinary shares, for any tax consequences that result from the ownership of ADSs, for the credit-worthiness of any third party, for allowing any rights to lapse under the terms of the deposit agreement, for the timeliness of any of our notices or for our failure to give notice.
- We and the depositary will not be obligated to perform any act that is inconsistent with the terms of the deposit agreement.
- We and the depositary disclaim any liability if we or the depositary are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or future of any law or regulation, or by reason of present or future provision of any provision of our Articles of Association, or any provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our control.
- We and the depositary disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our Articles of Association or in any provisions of or governing the securities on deposit.
- We and the depositary further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting ordinary shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information.
- We and the depositary also disclaim liability for the inability by a holder to benefit from any distribution, offering, right or other benefit that is made available to holders of ordinary shares but is not, under the terms of the deposit agreement, made available to you.
- We and the depositary may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties.
- We and the depositary also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement.
- No disclaimer of any Securities Act liability is intended by any provision of the deposit agreement.

Nothing in the deposit agreement gives rise to a partnership or joint venture, or establishes a fiduciary relationship, among us, the depositary bank and you as ADS holder.

Nothing in the deposit agreement precludes Citibank (or its affiliates) from engaging in transactions in which parties adverse to us or the ADS owners have interests, and nothing in the deposit agreement obligates Citibank to disclose those transactions, or any information obtained in the course of those transactions, to us or to the ADS owners, or to account for any payment received as part of those transactions.

### **Pre-Release Transactions**

Subject to the terms and conditions of the deposit agreement, the depositary may issue to broker/dealers ADSs before receiving a deposit of ordinary shares or release ordinary shares to broker/dealers before receiving ADSs for cancellation. These transactions are commonly referred to as "pre-release transactions," and are entered into between the depositary and the applicable broker/dealer. The deposit agreement limits the aggregate size of pre-release transactions (not to exceed 30% of the ordinary shares on deposit in the aggregate) and imposes a

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number of conditions on such transactions (e.g., the need to receive collateral, the type of collateral required, the representations required from brokers, etc.). The depository may retain the compensation received from the pre-release transactions.

### **Taxes**

You will be responsible for the taxes and other governmental charges payable on the ADSs and the securities represented by the ADSs. We, the depository and the custodian may deduct from any distribution the taxes and governmental charges payable by holders and may sell any and all property on deposit to pay the taxes and governmental charges payable by holders. You will be liable for any deficiency if the sale proceeds do not cover the taxes that are due.

The depository may refuse to issue ADSs, to deliver, transfer, split and combine ADRs or to release securities on deposit until all taxes and charges are paid by the applicable holder. The depository and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depository and to the custodian proof of taxpayer status and residence and such other information as the depository and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depository and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

### **Foreign Currency Conversion**

The depository will arrange for the conversion of all foreign currency received into U.S. dollars if such conversion is practical, and it will distribute the U.S. dollars in accordance with the terms of the deposit agreement. You may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

If the conversion of foreign currency is not practical or lawful, or if any required approvals are denied or not obtainable at a reasonable cost or within a reasonable period, the depository may take the following actions in its discretion:

- Convert the foreign currency to the extent practical and lawful and distribute the U.S. dollars to the holders for whom the conversion and distribution is lawful and practical.
- Distribute the foreign currency to holders for whom the distribution is lawful and practical.
- Hold the foreign currency (without liability for interest) for the applicable holders.

### **Governing Law/Waiver of Jury Trial**

The deposit agreement and the ADRs will be interpreted in accordance with the laws of the State of New York. The rights of holders of ordinary shares (including ordinary shares represented by ADSs) is governed by the laws of England and Wales.

AS A PARTY TO THE DEPOSIT AGREEMENT, YOU IRREVOCABLY WAIVE YOUR RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF THE DEPOSIT AGREEMENT OR THE ADRs AGAINST US AND/OR THE DEPOSITARY.

## SHARES AND ADSs ELIGIBLE FOR FUTURE SALE

Upon completion of this offering, we will have 32,884,103 ordinary shares outstanding, which includes the issuance of 4,000,000 ADSs representing 4,000,000 ordinary shares. Future sales of ADSs in the public market immediately after this offering, and the availability of ADSs for future sale, could adversely affect the market price of the ADSs prevailing from time to time. Some of our ordinary shares are subject to contractual and legal restrictions on resale as described below. There may be sales of substantial amounts of our ADSs or ordinary shares in the public market after such restrictions lapse, which could adversely affect prevailing market prices of our ADSs.

We expect \_\_\_\_\_ ordinary shares represented by ADSs, or \_\_\_\_\_ ordinary shares represented by ADSs if the underwriters exercise in full their option to purchase additional ADSs, sold in this offering will be freely transferable without restriction, except for any shares purchased by one or more of our existing "affiliates," as that term is defined in Rule 144 under the Securities Act.

### **Rule 144**

In general, persons who have beneficially owned restricted ordinary shares for at least six months, and any affiliate of the company who owns either restricted or unrestricted securities, are entitled to sell their securities without registration with the SEC under an exemption from registration provided by Rule 144 under the Securities Act.

#### ***Non-Affiliates***

Any person who is not deemed to have been one of our affiliates at the time of, or at any time during the three months preceding, a sale may sell an unlimited number of restricted securities under Rule 144 if:

- the restricted securities have been held for at least six months, including the holding period of any prior owner other than one of our affiliates;
- we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale; and
- we are current in our Exchange Act reporting at the time of sale.

Any person who is not deemed to have been an affiliate of ours at the time of, or at any time during the three months preceding, a sale and has held the restricted securities for at least one year, including the holding period of any prior owner other than one of our affiliates, will be entitled to sell an unlimited number of restricted securities without regard to the length of time we have been subject to Exchange Act periodic reporting or whether we are current in our Exchange Act reporting.

#### ***Affiliates***

Persons seeking to sell restricted securities who are our affiliates at the time of, or any time during the three months preceding, a sale, would be subject to the restrictions described above. They are also subject to additional restrictions, by which such person would be required to comply with the manner of sale and notice provisions of Rule 144 and would be entitled to sell within any three-month period only that number of securities that does not exceed the greater of either of the following:

- 1% of the number of ordinary shares then outstanding, which will equal approximately 328,841 shares immediately after the closing of this offering; or
- the average weekly trading volume of our ordinary shares in the form of ADSs on the Nasdaq Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Additionally, persons who are our affiliates at the time of, or any time during the three months preceding, a sale may sell unrestricted securities under the requirements of Rule 144 described above, without regard to the six-month holding period of Rule 144, which does not apply to sales of unrestricted securities.

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**Rule 701**

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares from us under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701. Several holders of Rule 701 shares are subject to lock-up agreements as described below and in the section of this prospectus titled "Underwriting" and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

**Regulation S**

Regulation S provides generally that sales made in offshore transactions are not subject to the registration or prospectus delivery requirements of the Securities Act.

**Lock-up Agreements**

All of our directors and executive officers and certain beneficial owners of 5% of our ordinary shares have agreed, subject to limited exceptions, not to offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our ADSs, ordinary shares or such other securities for a period of 90 days after the date of this prospectus, without the prior written consent of Jefferies LLC and Barclays Capital Inc. See "Underwriting."

## MATERIAL INCOME TAX CONSIDERATIONS

*The following summary contains a description of material U.K. and U.S. federal income tax consequences of the acquisition, ownership and disposition of our ordinary shares or ADSs. This summary should not be considered a comprehensive description of all the tax considerations that may be relevant to the decision to acquire ADSs in this offering.*

### **Material U.S. Federal Income Tax Considerations for U.S. Holders**

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders (as defined below) described below of owning and disposing of the ordinary shares or ADSs. It is not a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire securities. This discussion applies only to such a U.S. Holder that holds the ordinary shares or ADSs as a capital asset for tax purposes (generally, property held for investment). In addition, it does not describe all of the tax consequences that may be relevant in light of such a U.S. Holder's particular circumstances, including state and local tax consequences, estate tax consequences, alternative minimum tax consequences, the potential application of the Medicare contribution tax, and tax consequences applicable to persons subject to certain special rules, such as:

- banks, insurance companies, and certain other financial institutions;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons holding ordinary shares or ADSs as part of a hedging transaction, "straddle," wash sale, conversion transaction or integrated transaction or persons entering into a constructive sale with respect to ordinary shares or ADSs;
- persons whose "functional currency" for U.S. federal income tax purposes is not the U.S. dollar;
- brokers, dealers or traders in securities, commodities or currencies;
- tax-exempt entities or government organizations;
- S corporations, partnerships, or other entities or arrangements classified as partnerships for U.S. federal income tax purposes;
- regulated investment companies or real estate investment trusts;
- persons who acquired the ordinary shares or ADSs pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons that own or are deemed to own ten percent or more of our outstanding shares (measured by either voting power or value);
- persons holding the ordinary shares or ADSs in connection with a trade or business, permanent establishment, or fixed base outside the United States; and
- persons holding the ordinary shares or ADSs who are required to accelerate the recognition of any item of gross income for U.S. federal income tax purposes with respect to the ordinary shares or ADSs as a result of such items being taken into account in an applicable financial statement.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds ordinary shares or ADSs, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership.

The discussion is based on the Code administrative pronouncements, judicial decisions, final, temporary and proposed Treasury Regulations, and the income tax treaty between the United Kingdom and the United States, or the Treaty, all as of the date hereof, changes to any of which may affect the tax consequences described herein—possibly with retroactive effect. U.S. Holders are encouraged to consult their tax advisers concerning the U.S. federal, state, local and foreign tax consequences of acquiring, owning and disposing of ordinary shares or ADSs in light of their particular circumstances.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of ordinary shares or ADSs who is eligible for all relevant benefits of the Treaty and is:

- (i) a citizen or individual resident of the United States;
- (ii) a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;

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- (iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- (iv) a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

The discussion below assumes that the representations contained in the deposit agreement are true and that the obligations in the deposit agreement and any related agreement will be complied with in accordance with their terms. Generally, a holder of an ADS should be treated for U.S. federal income tax purposes as holding the ordinary shares represented by the ADS. Accordingly, no gain or loss should be recognized upon an exchange of ADSs for ordinary shares. The U.S. Treasury has expressed concerns that intermediaries in the chain of ownership between the holder of an ADS and the issuer of the security underlying the ADS may be taking actions that are inconsistent with the beneficial ownership of the underlying security. The creditability of foreign taxes, if any, as described below, could be affected by actions taken by intermediaries in the chain of ownership between the holders of ADSs and our company if as a result of such actions the holders of ADSs are not properly treated as beneficial owners of the underlying ordinary shares.

### ***Taxation of Distributions***

Subject to the discussion below under “Passive Foreign Investment Company Rules,” distributions paid on ordinary shares or ADSs, other than certain pro rata distributions of ordinary shares or ADSs, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we may not calculate our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. Subject to applicable limitations, dividends paid to certain non-corporate U.S. Holders may be taxable at preferential rates applicable to “qualified dividend income.” The amount of the dividend will be treated as foreign-source dividend income to U.S. Holders and will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will generally be included in a U.S. Holder’s income on the date of the U.S. Holder’s receipt of the dividend. The amount of any dividend income paid in foreign currency will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt. Such gain or loss would generally be treated as U.S.-source ordinary income or loss. The amount of any distribution of property other than cash (and other than certain pro rata distributions of ordinary shares or ADSs or rights to acquire ordinary shares or ADSs) will be the fair market value of such property on the date of distribution.

For foreign tax credit limitation purposes, our dividends will generally be treated as passive category income. Because no U.K. income taxes will be withheld from dividends on ordinary shares or ADSs, there will be no creditable foreign taxes associated with any dividends that a U.S. Holder will receive.

### ***Sale or Other Taxable Disposition of Ordinary Shares and ADSs***

Subject to the discussion below under “Passive Foreign Investment Company Rules,” gain or loss realized on the sale or other taxable disposition of ordinary shares or ADSs will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder held the ordinary shares or ADSs for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder’s tax basis in the ordinary shares or ADSs disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

If the consideration received by a U.S. Holder is not paid in U.S. dollars, the amount realized will be the U.S. dollar value of the payment received determined by reference to the spot rate of exchange on the date of the sale or other disposition. However, if the ordinary shares or ADSs are treated as traded on an “established securities market” and you are either a cash basis taxpayer or an accrual basis taxpayer that has made a special election (which must be applied consistently from year to year and cannot be changed without the consent of the IRS), you will determine the U.S. dollar value of the amount realized in a non-U.S. dollar currency by translating the amount received at the spot rate of exchange on the settlement date of the sale. If you are an accrual basis taxpayer that is not eligible to or does not elect to determine the amount realized using the spot rate on the settlement date, you will recognize foreign



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currency gain or loss to the extent of any difference between the U.S. dollar amount realized on the date of sale or disposition and the U.S. dollar value of the currency received at the spot rate on the settlement date.

***Passive Foreign Investment Company Rules***

If we were classified as a PFIC in any taxable year, the treatment of distributions, and of sale or disposition gains, described above would not apply for that year and, potentially, future years. Instead, a U.S. Holder would be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. Holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

A non-U.S. corporation will be classified as a PFIC for any taxable year in which, after applying certain look-through rules, either:

- at least 75% of its gross income is passive income (such as interest income); or
- at least 50% of its gross assets (determined on the basis of a quarterly average) is attributable to assets that produce passive income or are held for the production of passive income.

We will be treated as owning our proportionate share of the assets and earning our proportionate share of the income of any other corporation, the equity of which we own, directly or indirectly, 25% or more (by value).

Based on our estimates of expected gross assets and income for the current taxable year, we believe that we were not a PFIC for our taxable year ended December 31, 2017 or any prior taxable year, and we believe that we will not be classified as a PFIC for the taxable year ending December 31, 2018. However, there can be no assurance that we will not be classified as a PFIC for the current taxable year or any prior or future taxable year. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis and the applicable law is subject to varying interpretation.

A separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. As a result, our PFIC status may change from year to year. The total value of our assets for purposes of the asset test generally will be calculated using the market price of the ordinary shares or ADSs, which may fluctuate considerably. Fluctuations in the market price of the ordinary shares or ADSs may result in our being a PFIC for any taxable year. Because of the uncertainties involved in establishing our PFIC status, our U.S. tax counsel expresses no opinion with respect to our PFIC status.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns the ordinary shares or ADSs, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns the ordinary shares or ADSs, regardless of whether we continue to meet the tests described above unless (i) we cease to be a PFIC and the U.S. Holder has made a "deemed sale" election under the PFIC rules, or (ii) the U.S. Holder makes a "QEF Election" (defined below), with respect to all taxable years during such U.S. Holder's holding period in which we are a PFIC. If the "deemed sale" election is made, a U.S. Holder will be deemed to have sold the ordinary shares or ADSs the U.S. Holder holds at their fair market value and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. Holder's ordinary shares or ADSs with respect to which such election was made will not be treated as shares in a PFIC and the U.S. Holder will not be subject to the rules described below with respect to any "excess distribution" the U.S. Holder receives from us or any gain from an actual sale or other disposition of the ordinary shares or ADSs.

For each taxable year we are treated as a PFIC with respect to any U.S. Holders, each such U.S. Holder will be subject to special tax rules with respect to any "excess distribution" such U.S. Holder receives and any gain such U.S. Holder recognizes from a sale or other disposition (including a pledge) of ordinary shares or ADSs, unless (i) such U.S. Holder makes a QEF Election or (ii) the ordinary shares or ADSs constitute "marketable" securities, and such U.S. Holder makes a mark-to-market election as discussed below. Distributions a U.S. Holder receives in a taxable year that are greater than 125% of the average annual distributions a U.S. Holder received during the shorter

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of the three preceding taxable years or the U.S. Holder's holding period for the ordinary shares or ADSs will generally be treated as excess distributions. Under these special tax rules:

- the excess distribution or gain will be allocated ratably over a U.S. Holder's holding period for the ordinary shares or ADSs;
- the amount allocated to the current taxable year, and any taxable year prior to the first taxable year in which we became a PFIC, will be treated as ordinary income; and
- the amount allocated to each other year will be subject to the highest tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years prior to the year of disposition or "excess distribution" cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of the ordinary shares or ADSs cannot be treated as capital, even if a U.S. Holder holds the ordinary shares or ADSs as capital assets. Distributions received from us in a year in which we are a PFIC (or in the next succeeding year) will not constitute qualified dividend income in the hands of non-corporate U.S. Holders.

If we are a PFIC for a given year, an affected U.S. Holder will generally be subject to similar rules with respect to distributions we receive from, and our dispositions of the stock of, any of our direct or indirect subsidiaries that also are PFICs, as if such distributions were indirectly received by, and/or dispositions were indirectly carried out by, such U.S. Holder.

U.S. Holders can avoid the interest charge on excess distributions or gain relating to the ordinary shares or ADSs by making a mark-to-market election with respect to the ordinary shares or ADSs, provided that the ordinary shares or ADSs are "marketable." Ordinary shares or ADSs will be marketable if they are "regularly traded" on one of several U.S. stock exchanges or on a foreign stock exchange that meets certain conditions. For these purposes, the ordinary shares or ADSs will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. Any trades that have as their principal purpose meeting this requirement will be disregarded. Our ADSs will be listed on Nasdaq, which is a qualified exchange for these purposes. Consequently, if our ADSs remain listed on Nasdaq and are regularly traded, we expect the mark-to-market election would be available to U.S. Holders if we are a PFIC.

A U.S. Holder that makes a mark-to-market election must include in ordinary income for each year an amount equal to the excess, if any, of the fair market value of the ordinary shares or ADSs held by that U.S. Holder at the close of the taxable year over that U.S. Holder's adjusted tax basis in those ordinary shares or ADSs. An electing U.S. Holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted basis in the ordinary shares or ADSs held by that U.S. Holder over the fair market value of those ordinary shares or ADSs at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains for prior years. Gains from an actual sale or other disposition of the ordinary shares or ADSs will be treated as ordinary income, and any losses incurred on a sale or other disposition of the shares will be treated as an ordinary loss to the extent of any net mark-to-market gains for prior years. Once made, the election cannot be revoked without the consent of the Internal Revenue Service, or the IRS, unless the ordinary shares or ADSs cease to be marketable.

A mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves "marketable." As a result, even if a U.S. Holder validly makes a mark-to-market election with respect to the ordinary shares or ADSs, the U.S. Holder may continue to be subject to the PFIC rules (described above) with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes.

Alternatively, a U.S. Holder can make an election, if we provide the necessary information, to treat us and each lower-tier PFIC as a qualified electing fund, or a QEF Election, in the first taxable year we (and our relevant subsidiaries) are treated as a PFIC with respect to the U.S. Holder. If such election remains in place while we and any lower-tier PFIC subsidiaries are PFICs, we and our subsidiaries will not be treated as PFICs with respect to such U.S. Holder. A U.S. Holder must make the QEF Election for us and for each of our subsidiaries that is a PFIC by attaching a separate properly completed IRS Form 8621 for each such PFIC to the U.S. Holder's timely filed

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U.S. federal income tax return. We currently intend to make the company's annual PFIC determination available on our website. Should we determine that we are a PFIC, we currently intend to provide the information necessary for a U.S. Holder to make a QEF Election with respect to us and to cause each lower-tier PFIC which we control to provide such information with respect to such lower-tier PFIC. However, we cannot guarantee that we will continue to provide such determination or information in future years.

If a U.S. Holder makes a QEF Election with respect to a PFIC, the U.S. Holder will be currently taxable on its pro rata share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is classified as a PFIC. If a U.S. Holder makes a QEF Election with respect to us, any distributions paid by us out of our earnings and profits that were previously included in the U.S. Holder's income under the QEF Election would not be taxable to that U.S. Holder. A U.S. Holder will increase its tax basis in its ordinary shares or ADSs by an amount equal to any income included under the QEF Election and will decrease its tax basis by any amount distributed on the ordinary shares or ADSs that is not included in the holder's income. In addition, a U.S. Holder will recognize capital gain or loss on the disposition of ordinary shares or ADSs in an amount equal to the difference between the amount realized and the holder's adjusted tax basis in the ordinary shares or ADSs. U.S. Holders should note that if they make QEF Elections with respect to us and lower-tier PFICs, they may be required to pay U.S. federal income tax with respect to their ordinary shares or ADSs for any taxable year significantly in excess of any cash distributions (which may be zero) received on the ordinary shares or ADSs for such taxable year.

Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to file an annual report containing such information as the U.S. Treasury may require. A U.S. Holder's failure to file the annual report will cause the statute of limitations for such U.S. Holder's U.S. federal income tax return to remain open with regard to the items required to be included in such report until three years after the U.S. Holder files the annual report, and, unless such failure is due to reasonable cause and not willful neglect, the statute of limitations for the U.S. Holder's entire U.S. federal income tax return will remain open during such period.

### ***Information Reporting and Backup Withholding***

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) the U.S. Holder is a corporation or other exempt recipient or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding.

Backup withholding is not an additional tax. The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the holder's U.S. federal income tax liability and may entitle it to a refund, provided that the required information is timely furnished to the IRS.

### ***Information with Respect to Foreign Financial Assets***

Certain U.S. Holders who are individuals (and, under regulations, certain entities) may be required to report information relating to the ordinary shares or ADSs, subject to certain exceptions (including an exception for ordinary shares or ADSs held in accounts maintained by certain U.S. financial institutions). Such U.S. Holders who fail to timely furnish the required information may be subject to a penalty. Additionally, if a U.S. Holder does not file the required information, the statute of limitations with respect to tax returns of the U.S. Holder to which the information relates may not close until three years after such information is filed.

**WE STRONGLY URGE YOU TO CONSULT YOUR TAX ADVISOR REGARDING THE U.S. FEDERAL, STATE, LOCAL AND FOREIGN TAX CONSEQUENCES OF ACQUIRING, OWNING AND DISPOSING OF THE ORDINARY SHARES OR ADSs IN LIGHT OF YOUR PARTICULAR CIRCUMSTANCES, INCLUDING (BUT NOT LIMITED TO) THE POTENTIAL IMPACT OF THE PFIC, FOREIGN TAX CREDIT AND TAX INFORMATION REPORTING RULES TO YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs.**

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### **U.K. Taxation**

The following is intended as a general guide to current U.K. tax law and HM Revenue & Customs, or HMRC, published practice applying as at the date of this prospectus (both of which are subject to change at any time, possibly with retrospective effect) relating to the holding of ADSs. It does not constitute legal or tax advice and does not purport to be a complete analysis of all U.K. tax considerations relating to the holding of ADSs, or all of the circumstances in which holders of ADSs may benefit from an exemption or relief from U.K. taxation. It is written on the basis that the company is and remains solely resident in the U.K. for tax purposes and will therefore be subject to the U.K. tax regime and not the U.S. tax regime save as set out above under “Material U.S. Federal Income Tax Considerations for U.S. Holders.”

Except to the extent that the position of non-U.K. resident persons is expressly referred to, this guide relates only to persons who are resident and, in the case of individuals, domiciled for tax purposes solely in the U.K. and do not carry on a trade in the U.K. or, in the case of a company, do not have a permanent establishment or fixed base in any other jurisdiction with which the holding of the ADSs is connected, and U.K. Holders, who are absolute beneficial owners of the ADSs (and do not hold the ADSs through an Individual Savings Account or a Self-Invested Personal Pension) and any dividends paid in respect of the ADSs or underlying ordinary shares (where the dividends are regarded for U.K. tax purposes as that person’s own income). It is assumed that for the purposes of this guide that a holder of an ADS is the beneficial owner of the underlying ordinary share for U.K. direct tax purposes.

This guide may not relate to certain classes of U.K. Holders, such as (but not limited to):

- persons who are connected with the company;
- financial institutions;
- insurance companies;
- charities or tax-exempt organizations;
- collective investment schemes;
- pension schemes;
- brokers or dealers in securities or persons who hold ADSs otherwise than as an investment;
- persons who have (or are deemed to have) acquired their ADSs by virtue of an office or employment or who are or have been officers or employees of the company or any of its affiliates; and
- individuals who are subject to U.K. taxation on a remittance basis.

THESE PARAGRAPHS ARE A SUMMARY OF CERTAIN U.K. TAX CONSIDERATIONS AND ARE INTENDED AS A GENERAL GUIDE ONLY. IT IS RECOMMENDED THAT ALL HOLDERS OF ADSs OBTAIN ADVICE AS TO THE CONSEQUENCES OF THE ACQUISITION, OWNERSHIP AND DISPOSAL OF THE ADSs IN THEIR OWN PARTICULAR CIRCUMSTANCES FROM THEIR OWN TAX ADVISORS. IN PARTICULAR, NON-U.K. RESIDENT OR DOMICILED PERSONS ARE ADVISED TO CONSIDER THE POTENTIAL IMPACT OF ANY RELEVANT DOUBLE TAXATION AGREEMENTS.

#### **Dividends**

##### *Withholding Tax*

Dividends paid by the company will not be subject to any withholding or deduction for or on account of U.K. tax.

##### *Income Tax*

An individual U.K. Holder may, depending on his or her particular circumstances, be subject to U.K. tax on dividends received from the company. An individual holder of ADSs who is not resident for tax purposes in the United Kingdom should not be chargeable to U.K. income tax on dividends received from the company unless he or she carries on (whether solely or in partnership) a trade, profession or vocation in the U.K. through a permanent establishment to which the ADSs are attributable.

Dividend income is treated as the top slice of the total income chargeable to U.K. income tax. An individual U.K. Holder who receives a dividend in the 2018/19 tax year will be charged at a nil rate on the first £2,000 of taxable dividend income. Dividend income in excess of amount will be charged at 7.5% to the extent that the excess falls within the basic rate tax band, 32.5% to the extent that the excess amount falls within the higher rate tax band, and 38.1% to the extent that the excess amount falls within the additional rate tax band.

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### *Corporation Tax*

A corporate holder of ADSs who is not resident for tax purposes in the United Kingdom should not be chargeable to U.K. corporation tax on dividends received from the company unless it carries on (whether solely or in partnership) a trade in the United Kingdom through a permanent establishment to which the ADSs are effectively connected.

Corporate U.K. Holders should not be subject to U.K. corporation tax on any dividend received from the company so long as the dividends qualify for exemption (as is likely), although certain conditions must be met (including anti-avoidance conditions). If the conditions for the exemption are not satisfied, or such U.K. Holder elects for an otherwise exempt dividend to be taxable, U.K. corporation tax will be chargeable on the amount of any dividends (at the main rate of 19% in the 2018/19 financial year).

### **Chargeable Gains**

A disposal or deemed disposal of ADSs by a U.K. Holder may, depending on the U.K. Holder's circumstances and subject to any available exemptions or reliefs (such as the annual exemption), give rise to a chargeable gain or an allowable loss for the purposes of U.K. capital gains tax and corporation tax on chargeable gains.

Any chargeable gain (or allowable loss) will generally be calculated by reference to the consideration received for the disposal of ADSs less the allowable cost to the holder of acquiring such ADSs.

If an individual U.K. Holder who is subject to U.K. income tax at either the higher or the additional rate is liable to U.K. capital gains tax on the disposal of ADSs, the applicable rate would be broadly, 20% (for the 2018/19 tax year). For an individual U.K. Holder who is subject to U.K. income tax at the basic rate and liable to U.K. capital gains tax on such disposal, the applicable rate would be, broadly, 10% (for the 2018/19 tax year), save to the extent that any capital gains exceed the unused basic rate tax band. In that case, the rate applicable to the excess would be 20% (for the 2018/19 tax year).

If a corporate U.K. Holder becomes liable to U.K. corporation tax on the disposal of ADSs, the main rate of U.K. corporation tax (19% in the 2018/19 financial year) would apply. Indexation allowance may reduce the amount of chargeable gain that is subject to corporation tax but may not create or increase any allowable loss. However, irrespective of the date of disposal of an asset, indexation allowance is only available up to December 31, 2017.

A corporate holder of ADSs which is not resident for tax purposes in the U.K. and does not have a U.K. permanent establishment with which the ADSs are effectively connected should not normally be liable to U.K. capital gains tax or corporation tax on chargeable gains on a disposal of ADSs. However, an individual holder of ADSs who has ceased to be resident for tax purposes in the U.K. for a period of less than five years and who disposes of ADSs during that period may be liable on his or her return to the United Kingdom to U.K. tax on any capital gain realized (subject to any available exemption or relief).

### **Stamp Duty and Stamp Duty Reserve Tax ("SDRT")**

The discussion below relates to the holders of our ordinary shares or ADSs wherever resident.

#### *Issue of Ordinary Shares and ADSs*

No U.K. stamp duty or stamp duty reserve tax, or SDRT, is payable on the issue of the underlying ordinary shares in registered form in the company.

#### *Transfers of Ordinary Shares*

An unconditional agreement to transfer ordinary shares will normally give rise to a charge to SDRT at the rate of 0.5% of the amount or value of the consideration payable for the transfer. The purchaser of the shares is, in general, liable for the SDRT. Instruments transferring ordinary shares in certificated form are generally also subject to stamp duty at the rate of 0.5% of the amount or value of the consideration given for the transfer (rounded up to the next £5.00). Stamp duty is normally paid by the purchaser. The charge to SDRT will, in general, be cancelled or, if already paid, repaid (generally with interest), where a transfer instrument has been duly stamped within six years of the charge arising.

An unconditional agreement to transfer ordinary shares to, or to a nominee or agent for, a person whose business is or includes the issue of depositary receipts or the provision of clearance services will generally be subject to SDRT (and, where the transfer is effected by a written instrument, stamp duty) at a higher rate of 1.5% of the amount or, in certain circumstances, the value of the consideration given for the transfer unless the clearance service has made

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and maintained an election under section 97A of the U.K. Finance Act 1986. It is understood that HMRC regards the facilities of DTC as a clearance service for these purposes and we are not aware of any section 97A election having been made by the DTC.

Based on current published HMRC practice following recent case law, no SDRT is generally payable where the transfer of ordinary shares to a clearance service or depositary receipt system outside the European Union is an integral part of an issue of share capital.

*Transfers of ADSs*

No U.K. stamp duty will in practice be payable on a written instrument transferring an ADS provided that the instrument of transfer is executed and remains at all times outside the United Kingdom. Where these conditions are not met, the transfer of, or agreement to transfer, an ADS could, depending on the circumstances, attract a charge to U.K. stamp duty at the rate of 0.5% of the value of the consideration.

SDRT should not be payable in respect of an agreement to transfer an ADS.

**UNDERWRITING**

Subject to the terms and conditions set forth in the underwriting agreement, dated \_\_\_\_\_, 2018, among us and Jefferies LLC and Barclays Capital Inc., as the representatives of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of ADSs shown opposite its name below:

<u>UNDERWRITER</u>	<u>NUMBER OF ADSs</u>
Jefferies LLC	
Barclays Capital Inc.	
UBS Securities LLC	
<b>Total</b>	<b><u>4,000,000</u></b>

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the ADSs if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the ADSs as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the ADSs, that you will be able to sell any of the ADSs held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the ADSs subject to their acceptance of the ADSs from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

**Commission and Expenses**

The underwriters have advised us that they propose to offer the ADSs to the public at the public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ \_\_\_\_\_ per ADS. The underwriters may allow, and certain dealers may reallow, a discount from the concession not in excess of \$ \_\_\_\_\_ per ADS to certain brokers and dealers. After the offering, the public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

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The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional ADSs.

	PER ADS		TOTAL	
	WITHOUT OPTION TO PURCHASE ADDITIONAL ADSs	WITH OPTION TO PURCHASE ADDITIONAL ADSs	WITHOUT OPTION TO PURCHASE ADDITIONAL ADSs	WITH OPTION TO PURCHASE ADDITIONAL ADSs
Public offering price	\$	\$	\$	\$
Underwriting discounts and commissions	\$	\$	\$	\$
Proceeds to us, before expenses	\$	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$700,000. We have also agreed to reimburse the underwriters for an aggregate of up to \$10,000 for certain of their offering expenses, including counsel fees and expenses in connection with the clearance of this offering with the Financial Industry Regulatory Authority, or FINRA. In accordance with FINRA Rule 5110, these reimbursed expenses are deemed underwriting compensation for this offering.

### **Listing**

Our ADSs are listed on the Nasdaq Global Select Market under the trading symbol "NITE."

### **Stamp Taxes**

If you purchase ADSs offered in this prospectus, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus.

### **Option to Purchase Additional ADSs**

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of 600,000 ADSs from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional ADSs proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more ADSs than the total number set forth on the cover page of this prospectus.

### **No Sales of Similar Securities**

We, our officers, directors and certain holders of greater than five percent of our outstanding ADSs, ordinary shares and other securities have agreed, subject to specified exceptions, not to directly or indirectly:

- 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 Exchange Act; or
- otherwise dispose of any ADSs or ordinary shares, options or warrants to acquire ADSs or ordinary shares, or securities exchangeable or exercisable for or convertible into ADSs or ordinary shares currently or hereafter owned either of record or beneficially; or
- publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus without the prior written consent of the representatives.

This restriction terminates after the close of trading of our ADSs on and including the 90<sup>th</sup> day after the date of this prospectus.



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The representatives may, in their sole discretion and at any time or from time to time before the termination of the 90-day period, release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of ADSs or ordinary shares prior to the expiration of the lock-up period.

### **Stabilization**

The underwriters have advised us that, pursuant to Regulation M under the Exchange Act, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of our ADSs at a level above that which might otherwise prevail in the open market. Establishing short sale positions may involve either “covered” short sales or “naked” short sales.

“Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional ADSs in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional ADSs or purchasing our ADSs in the open market. In determining the source of ADSs to close out the covered short position, the underwriters will consider, among other things, the price of ADSs available for purchase in the open market as compared to the price at which they may purchase ADSs through the option to purchase additional ADSs.

“Naked” short sales are sales in excess of the option to purchase additional ADSs. The underwriters must close out any naked short position by purchasing ADSs in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our ADSs in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of ADSs on behalf of the underwriters for the purpose of fixing or maintaining the price of the ADSs. A syndicate covering transaction is the bid for or the purchase of ADSs on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our ADSs or preventing or retarding a decline in the market price of our ADSs. As a result, the price of our ADSs may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the ADSs originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our ADSs. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our ADSs on the Nasdaq Global Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of our ADSs in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker’s bid, that bid must then be lowered when specified purchase limits are exceeded.

### **Electronic Distribution**

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of ADSs for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters’ web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

## **Other Activities and Relationships**

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the ADSs offered hereby. Any such short positions could adversely affect future trading prices of the ADSs offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

## **Disclaimers About Non-U.S. Jurisdictions**

### ***Australia***

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

A. You confirm and warrant that you are either:

- a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
- a person associated with the company under Section 708(12) of the Corporations Act; or
- a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

B. You warrant and agree that you will not offer any of the securities issued to you pursuant to this prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

### ***European Economic Area***

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), an offer to the public of any securities which are the subject of the offering contemplated by this prospectus may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any ADSs may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- to any legal entity which is a "qualified investor" as defined in the Prospectus Directive;

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- to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives of the underwriters nominated by us for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of ADSs shall require us or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an “offer to the public” in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe to the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression “Prospectus Directive” means Directive 2003/71/EC (and amendments thereto), and includes any relevant implementing measure in the Relevant Member State.

### ***MiFID II Product Governance***

Any distributor subject to MiFID II that is offering, selling or recommending the securities is responsible for undertaking its own target market assessment in respect of the securities and determining its own distribution channels for the purposes of the MiFID product governance rules under Commission Delegated Directive (EU) 2017/593 (“Delegated Directive”). Neither the Issuer nor the underwriters make any representations or warranties as to a distributor’s compliance with the Delegated Directive.

### ***Hong Kong***

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong, or the SFO, and any rules made under that Ordinance; or in other circumstances which do not result in the document being a “prospectus” as defined in the Companies Ordinance (Cap. 32) of Hong Kong, or the CO, or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

### ***Japan***

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

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### **Singapore**

This prospectus has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person as defined under Section 275(1), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred for six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- where no consideration is given for the transfer;
- where the transfer is by operation of law;
- as specified in Section 276(7) of the SFA; or
- as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Solely for the purposes of its obligation pursuant to Section 309B of the SFA, the Company has determined, and hereby notifies all relevant persons (as defined in the CMP Regulations 2018), that the shares are "prescribed capital markets products" (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

### **Switzerland**

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

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### **United Kingdom**

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, referred to herein as the Order, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated. Each such person is referred to herein as a Relevant Person.

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a Relevant Person should not act or rely on this document or any of its contents. Any investment or investment activity to which this prospectus relates is available only to Relevant Persons and will be engaged in only with Relevant Persons.

### **Israel**

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus is being distributed only to, and is directed only at, and any offer of our ADSs is directed only at, (i) a limited number of persons in accordance with the Israeli Securities Law and (ii) investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and “qualified individuals”, each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

### **Canada**

#### **(A) Resale Restrictions**

The distribution of ADSs in Canada is being made only in the provinces of Ontario, Quebec, Alberta and British Columbia on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of these securities are made. Any resale of our ADSs in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the securities.

#### **(B) Representations of Canadian Purchasers**

By purchasing ADSs in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

- the purchaser is entitled under applicable provincial securities laws to purchase our ADSs without the benefit of a prospectus qualified under those securities laws as it is an “accredited investor” as defined under National Instrument 45-106 *Prospectus Exemptions*,
- the purchaser is a “permitted client” as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*,
- where required by law, the purchaser is purchasing as principal and not as agent, and
- the purchaser has reviewed the text above under Resale Restrictions.

#### **(C) Conflicts of Interest**

Canadian purchasers are hereby notified that each of the underwriters are relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105—Underwriting Conflicts from having to provide certain conflict of interest disclosure in this document.

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*(D) Statutory Rights of Action*

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the prospectus (including any amendment thereto) such as this document contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser of these securities in Canada should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

*(E) Enforcement of Legal Rights*

All of our directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets and the assets of those persons may be located outside of Canada and, as a result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

*(F) Taxation and Eligibility for Investment*

Canadian purchasers of ADSs should consult their own legal and tax advisors with respect to the tax consequences of an investment in our ADSs in their particular circumstances and about the eligibility of our ADSs for investment by the purchaser under relevant Canadian legislation.

### EXPENSES OF THIS OFFERING

Set forth below is an itemization of the total expenses, excluding the underwriting discounts and commissions, which are expected to be incurred in connection with the sale of ADSs in this offering. With the exception of the registration fee payable to the SEC, all amounts are estimates.

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<b>EXPENSE</b>	<b>AMOUNT</b>
SEC registration fee	\$ 12,450
FINRA filing fee	15,500
Blue Sky and FINRA qualification expenses	25,000
Printing expenses	60,000
Legal fees and expenses	450,000
Accounting fees and expenses	125,000
Miscellaneous	12,050
<b>Total</b>	<b><u>\$700,000</u></b>

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## LEGAL MATTERS

The validity of our ADSs and certain other matters of English law will be passed upon for us by Osborne Clarke LLP. U.S. federal law will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP. Legal counsel to the underwriters in connection with this offering are Covington & Burling LLP.

## EXPERTS

The consolidated financial statements of Nightstar Therapeutics plc appearing in Nightstar Therapeutics plc's Annual Report (Form 20-F) for the year ended December 31, 2017, have been audited by Ernst & Young LLP (registered in the United Kingdom), our independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

## CHANGES IN REGISTRANT'S CERTIFYING ACCOUNTANT

On June 5, 2018, our board of directors, upon the recommendation of the audit committee, accepted the resignation of Ernst & Young LLP (registered in the United Kingdom), or EY UK, as our independent registered public accounting firm, effective immediately. We felt it appropriate to request the resignation and change from EY UK, the United Kingdom member firm of Ernst & Young Global Limited that has traditionally serviced our company, to Ernst & Young Global Limited's U.S. member firm, Ernst & Young LLP (registered in the United States), or EY US, to facilitate the logistics of our quarterly reviews and annual audits. We will continue to use EY UK as our statutory auditor for filings with Companies House in the United Kingdom.

The reports of EY UK on our consolidated financial statements for the fiscal years ended December 31, 2017 and 2016 did not contain an adverse opinion or disclaimer of opinion, and were not qualified or modified as to uncertainty, audit scope or accounting principles.

In connection with the audits of our financial statements for each of the two fiscal years in the period ended December 31, 2017, and the subsequent period through June 5, 2018, there were (i) no disagreements with EY UK on any matter of accounting principles or practices, financial statement disclosure or auditing scope or procedure which, if not resolved to the satisfaction of EY UK, would have caused EY UK to make reference to the matter in their reports on our consolidated financial statements for such periods, and (ii) no reportable events as set forth in Item 16F(a)(1)(v) of Form 20-F except a material weakness in our internal control over financial reporting attributable to our lack of sufficient financial reporting and accounting personnel for the period ended December 31, 2016, which we believe to have been remediated as of December 31, 2017, as disclosed in our Annual Report on Form 20-F for the year ended December 31, 2017 filed with the SEC on April 3, 2018 incorporated by reference herein.

We provided EY UK with a copy of this prospectus and the registration statement of which this prospectus forms a part and requested from EY UK a letter addressed to the SEC indicating whether or not it agrees with the above disclosures. A copy of the EY UK letter dated September 25, 2018 is filed as Exhibit 16.1 to the registration statement of which this prospectus forms a part.

Also, on June 5, 2018, our board of directors, upon the recommendation of the audit committee, approved the engagement of EY US as our independent registered public accounting firm for the fiscal year ending December 31, 2018, effective immediately.

During our two most recent fiscal years and through the date of our engagement of EY US, neither we nor anyone on our behalf consulted with EY US, other than consultations conducted in the ordinary course of the audit, regarding either (i) the application of accounting principles to a specified transaction, either completed or proposed, or the type of audit opinion that might be rendered with respect to our financial statements, and no written report or oral advice was provided to us by EY US that was an important factor considered by us in reaching a decision as to any accounting, auditing or financial reporting issue; or (ii) any matter that was the subject of a disagreement as defined in Item 16F(a)(1)(iv) of Form 20-F or a reportable event as defined in Item 16F(a)(1)(v) of Form 20-F.



## SERVICE OF PROCESS AND ENFORCEMENT OF LIABILITIES

We are incorporated and currently existing under the laws of England and Wales. In addition, certain of our directors and officers reside outside of the United States and most of the assets of our non-U.S. subsidiaries are located outside of the United States. As a result, it may be difficult for investors to effect service of process on us or those persons in the United States or to enforce in the United States judgments obtained in United States courts against us or those persons based on the civil liability or other provisions of the United States securities laws or other laws.

In addition, uncertainty exists as to whether the courts of England and Wales would:

- recognize or enforce judgments of United States courts obtained against us or our directors or officers predicated upon the civil liabilities provisions of the securities laws of the United States or any state in the United States; or
- entertain original actions brought in England and Wales against us or our directors or officers predicated upon the securities laws of the United States or any state in the United States.

We have been advised by Osborne Clarke LLP that there is currently no treaty between (i) the United States and (ii) England and Wales providing for reciprocal recognition and enforcement of judgments of United States courts in civil and commercial matters (although the United States and the United Kingdom are both parties to the New York Convention on the Recognition and Enforcement of Foreign Arbitral Awards) and that a final judgment for the payment of money rendered by any general or state court in the United States based on civil liability, whether predicated solely upon the United States securities laws, would not be automatically enforceable in England and Wales. We have also been advised by Osborne Clarke LLP that any final and conclusive monetary judgment for a definite sum obtained against us in United States courts would be treated by the courts of England and Wales as a cause of action in itself and sued upon as a debt at common law so that no retrial of the issues would be necessary, provided that:

- the relevant U.S. court had jurisdiction over the original proceedings according to English conflicts of laws principles at the time when proceedings were initiated;
- England and Wales courts had jurisdiction over the matter on enforcement and we either submitted to such jurisdiction or were resident or carrying on business within such jurisdiction and were duly served with process;
- the U.S. judgment was final and conclusive on the merits in the sense of being final and unalterable in the court that pronounced it and being for a definite sum of money;
- the judgment given by the courts was not in respect of penalties, taxes, fines or similar fiscal or revenue obligations (or otherwise based on a U.S. law that an English court considers to relate to a penal, revenue or other public law);
- the judgment was not procured by fraud;
- recognition or enforcement of the judgment in England and Wales would not be contrary to public policy or the Human Rights Act 1998;
- the proceedings pursuant to which judgment was obtained were not contrary to natural justice;
- the U.S. judgment was not arrived at by doubling, trebling or otherwise multiplying a sum assessed as compensation for the loss or damages sustained and not being otherwise in breach of Section 5 of the U.K. Protection of Trading Interests Act 1980, or is a judgment based on measures designated by the Secretary of State under Section 1 of that Act;
- there is not a prior decision of an English court or the court of another jurisdiction on the issues in question between the same parties; and
- the English enforcement proceedings were commenced within the limitation period.

Whether these requirements are met in respect of a judgment based upon the civil liability provisions of the United States securities laws, including whether the award of monetary damages under such laws would constitute a penalty, is an issue for the court making such decision.

Subject to the foregoing, investors may be able to enforce in England and Wales judgments in civil and commercial matters that have been obtained from U.S. federal or state courts. Nevertheless, we cannot assure you that those judgments will be recognized or enforceable in England and Wales.

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If an English court gives judgment for the sum payable under a U.S. judgment, the English judgment will be enforceable by methods generally available for this purpose. These methods generally permit the English court discretion to prescribe the manner of enforcement. In addition, it may not be possible to obtain an English judgment or to enforce that judgment if the judgment debtor is or becomes subject to any insolvency or similar proceedings, or if the judgment debtor has any set-off or counterclaim against the judgment creditor. Also note that, in any enforcement proceedings, the judgment debtor may raise any counterclaim that could have been brought if the action had been originally brought in England unless the subject of the counterclaim was in issue and denied in the U.S. proceedings.

### **WHERE YOU CAN FIND ADDITIONAL INFORMATION**

We have filed with the SEC a registration statement (including amendments and exhibits to the registration statement) on Form F-1 under the Securities Act. A related registration statement on Form F-6 has been filed with the SEC to register the ADSs. This prospectus, which forms a part of the registration statement, does not contain all of the information included in the registration statement and the exhibits and schedules to the registration statement. Certain information is omitted, and you should refer to the registration statement and its exhibits and schedules for that information. If a document has been filed as an exhibit to the registration statement, we refer you to the copy of the document that has been filed. Each statement in this prospectus relating to a document filed as an exhibit is qualified in all respects by the filed exhibit.

You may review a copy of the registration statement, including exhibits and any schedule filed therewith, and obtain copies of such materials at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet website (<http://www.sec.gov>) that contains reports, proxy and information statements and other information regarding issuers, like us, that file electronically with the SEC.

We are subject to the information reporting requirements of the Exchange Act applicable to foreign private issuers. Accordingly, we are required to file reports and other information with the SEC, including annual reports on Form 20-F and reports on Form 6-K. Those reports may be inspected without charge at the locations described above. As a foreign private issuer, we are exempt from the rules under the Exchange Act related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act.

We have determined that, as of June 30, 2018, we no longer qualify as a "foreign private issuer" under the rules and regulations of the SEC. We made the determination based on the fact that, as of June 30, 2018, more than 50 percent of our outstanding voting securities were directly or indirectly owned or record by residents of the United States and a majority of our executive officers were U.S. citizens or residents. As a result, beginning January 1, 2019, we anticipate that our future annual filings with the SEC will be made on Form 10-K (including our annual report for the year ending December 31, 2018) rather than on Form 20-F. In addition, commencing on January 1, 2019, we will be required to expand our reporting consistent with that of a domestic U.S. filer, including filing quarterly reports on Form 10-Q and current reports on Form 8-K. We will also be subject to SEC rules governing the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act; the provisions of Regulation Fair Disclosure, which regulate the selective disclosure of material information; and the sections of the Exchange Act requiring insiders to file public reports of their share ownership and trading activities and establishing insider liability for profits realized from any "short-swing" transactions in our equity securities. In addition, beginning January 1, 2019, we will also be subject to the Nasdaq Stock Market listing requirements applicable to domestic U.S. issuers.

We maintain a corporate website at [www.nightstartx.com](http://www.nightstartx.com). Information contained in, or that can be accessed through, our website is not a part of, and shall not be incorporated by reference into, this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

## INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus. We incorporate by reference into this prospectus the information or documents listed below that we have filed with the SEC:

- our Annual Report on Form 20-F for the year ended December 31, 2017, filed with the SEC on April 3, 2018;
- our Reports of Foreign Private Issuer on Form 6-K for the quarters ended March 31, 2018 and June 30, 2018, furnished to the SEC on June 13, 2018 and August 15, 2018, respectively; and
- our Reports of Foreign Private Issuer on Form 6-K furnished to the SEC on September 13, 2018, and September 25, 2018.

Notwithstanding the statements in the preceding paragraphs, no document, report or exhibit (or portion of any of the foregoing) or any other information that we have “furnished” to the SEC pursuant to the Exchange Act shall be incorporated by reference into this prospectus.

We will furnish without charge to you, or any beneficial owner, on written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus, including exhibits to these documents. You should direct any requests for documents to Investor Relations, Nightstar Therapeutics plc, 10 Midford Place, 2nd Floor, London W1T 5BJ United Kingdom, telephone number: +44 (0)20 7062 2777, email address: [investors@nightstartx.com](mailto:investors@nightstartx.com).

You also may access these filings on our website at [www.nightstartx.com](http://www.nightstartx.com). We do not incorporate the information on our website into this prospectus or any supplement to this prospectus and you should not consider any information on, or that can be accessed through, our website as part of this prospectus or any supplement to this prospectus (other than those filings with the SEC that we specifically incorporate by reference into this prospectus or any supplement to this prospectus).

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed modified, superseded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus modifies, supersedes or replaces such statement.

**4,000,000 American Depositary Shares**



**Representing 4,000,000 Ordinary Shares**

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**PRELIMINARY PROSPECTUS**

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, 2018

**Jefferies**

**Barclays**

**UBS Investment Bank**

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**PART II**  
**INFORMATION NOT REQUIRED IN PROSPECTUS**

**Item 6. Indemnification of Directors and Officers.**

Subject to the U.K. Companies Act 2006, members of the registrant's board of directors and its officers (excluding auditors) have the benefit of the following indemnification provisions in the registrant's Articles of Association:

Current and former members of the registrant's board of directors or officers shall be reimbursed for:

- (i) all costs, charges, losses, expenses and liabilities sustained or incurred in relation to his or her actual or purported execution of his or her duties in relation to the registrant, including any liability incurred in defending any criminal or civil proceedings; and
- (ii) expenses incurred or to be incurred in defending any criminal or civil proceedings, in an investigation by a regulatory authority or against a proposed action to be taken by a regulatory authority, or in connection with any application for relief under the statutes of the United Kingdom and any other statutes that concern and affect the registrant as a company, or collectively the Statutes, arising in relation to the registrant or an associated company, by virtue of the actual or purposed execution of the duties of his or her office or the exercise of his or her powers.

In the case of current or former members of the registrant's board of directors, there shall be no entitlement to reimbursement as referred to above for (i) any liability incurred to the registrant or any associated company, (ii) the payment of a fine imposed in any criminal proceeding or a penalty imposed by a regulatory authority for non-compliance with any requirement of a regulatory nature, (iii) the defense of any criminal proceeding if the member of the registrant's board of directors is convicted, (iv) the defense of any civil proceeding brought by the registrant or an associated company in which judgment is given against the director, and (v) any application for relief under the statutes of the United Kingdom and any other statutes that concern and affect the registrant as a company in which the court refuses to grant relief to the director.

In addition, members of the registrant's board of directors and its officers who have received payment from the registrant under these indemnification provisions must repay the amount they received in accordance with the Statutes or in any other circumstances that the registrant may prescribe or where the registrant has reserved the right to require repayment.

The underwriting agreement the registrant will enter into in connection with the offering of American Depositary Shares being registered hereby provides that the underwriters will indemnify, under certain conditions, the registrant's board of directors and its officers against certain liabilities arising in connection with this offering.

**Item 7. Recent Sales of Unregistered Securities.**

Set forth below is information regarding share capital issued by NightstaRx Limited since January 1, 2015. None of the below described transactions involved any underwriters, underwriting discounts or commissions, or any public offering. Some of the transactions described below involved directors, officers and 5% shareholders and are more fully described under the section titled "Related Party Transactions."

In July 2017, Nightstar Therapeutics Limited was incorporated in England and Wales with nominal assets and liabilities for the purposes of consummating a corporate reorganization by which it acquired the outstanding share capital of NightstaRx Limited, as more fully described in Note 7 to our audited financial statements included in our Annual Report on Form 20-F for the fiscal year ended December 31, 2017 incorporated herein by reference. Following the share exchange by which the outstanding shares of NightstaRx Limited were exchanged for the same number and class of newly issued ordinary shares of Nightstar Therapeutics Limited, the nominal value of the ordinary shares was £0.01 per share.

1. In May 2014, NightstaRx Limited issued an aggregate of 6,000,000 Class A ordinary shares to one investor at a price per share of \$1.68, for aggregate proceeds of \$10.1 million.

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2. In December 2014, NightstaRx Limited issued an aggregate of:
  - a. 20,790 Class B ordinary shares to three employees at the nominal value of £0.00001 per share;
  - b. 26,235 Class D ordinary shares to three employees at the nominal value of £0.00001 per share; and
  - c. 29,411 Class B ordinary shares, 252,142 Class C ordinary shares and 367,281 Class D ordinary shares to our Chief Executive Officer, in each case at the nominal value of £0.00001 per share.
3. In March 2015, NightstaRx Limited issued an aggregate of:
  - a. 29,105 Class C ordinary shares to one employee at the nominal value of £0.00001 per share; and
  - b. 353,419 Class D ordinary shares to four employees at the nominal value of £0.00001 per share, including 2,363 Class D ordinary shares to our co-founder and a member of our board of directors.
4. In June 2015, NightstaRx Limited issued an aggregate of 1,000,000 Class A ordinary shares to two investors at a price per share of \$1.57, for aggregate subscription proceeds of \$1.6 million.
5. In November 2015, NightstaRx Limited issued an aggregate of 5,225,139 Class A ordinary shares to four investors and one employee at an average price per share of \$2.40, for aggregate proceeds of \$12.5 million, including 37,500 Class A ordinary shares issued to our Chief Executive Officer.
6. In February 2016, NightstaRx Limited issued 100 Class E1 ordinary shares to our Chief Executive Officer at the nominal value of £0.00001 per share.
7. In July 2016, NightstaRx Limited issued (i) 459,420 Class E1 ordinary shares to 15 employees at the nominal value of £0.00001 per share, including 180,000 shares to our Chief Executive Officer and 95,397 shares to a member of our board of directors; (ii) 286,000 Class E2 ordinary shares to 13 employees at the nominal value of £0.00001 per share, including 180,000 shares to our Chief Executive Officer; (iii) 180,000 Class E3 ordinary shares to our Chief Executive Officer at the nominal value of £0.00001 per share; and (iv) 180,000 Class E4 ordinary shares to our Chief Executive Officer at the nominal value of £0.00001 per share.
8. In September 2016, NightstaRx Limited issued 6,605,103 Class A ordinary shares to three investors and one employee at an average price per share of \$1.71, for aggregate proceeds of \$11.3 million, including 26,854 Class A ordinary shares issued to our Chief Executive Officer.
9. In September 2016, NightstaRx Limited issued 20,000 Class E1 ordinary shares to an employee at the nominal value of £0.00001 per share.
10. In October 2016, NightstaRx Limited issued (i) 113,500 Class E1 ordinary shares to two employees at the nominal value of £0.00001 per share, including 108,500 shares to our Chief Scientific Officer; and (ii) 108,500 Class E2 ordinary shares, 108,500 Class E3 ordinary shares and 108,500 Class E4 ordinary shares, in each case at the nominal value of £0.00001 per share, to our Chief Scientific Officer.
11. In November 2016, NightstaRx Limited issued 86,000 Class E1 ordinary shares to a member of our board of directors at the nominal value of £0.00001 per share.
12. In March 2017, NightstaRx Limited issued 25,500 Class E1 ordinary shares to three employees at the nominal value of £0.00001 per share.
13. In April 2017, NightstaRx Limited issued (i) 277,000 Class E1 ordinary shares to three employees at the nominal value of £0.00001 per share, including 87,000 Class E1 ordinary shares to our Chief Financial Officer and 173,000 Class E1 ordinary shares to a member of our board of directors; and (ii) 87,000 Class E2 ordinary shares, 87,000 Class E3 ordinary shares and 87,000 Class E4 ordinary shares to our Chief Financial Officer, in each case at the nominal value of £0.00001 per share.
14. In May 2017, NightstaRx Limited issued 89,000 Class E3 ordinary shares to 14 employees at the nominal value of £0.00001 per share.
15. In June 2017, NightstaRx Limited issued an aggregate of 19,274,151 Class A ordinary shares to a total of nine investors and one employee at an average price per share of \$3.31, for aggregate proceeds of \$63.8 million, including 85,646 Class A ordinary shares issued to our Chief Executive Officer.
16. In July 2017, NightstaRx Limited issued 165,000 Class F ordinary shares to two employees at the nominal value of £0.00001 per share.
17. In August 2017, NightstaRx Limited issued 1,689,780 Class F ordinary shares consisting of (i) 1,414,787 Class F ordinary shares to five employees at the nominal value of £0.00001 per share, including 607,541 Class F ordinary shares to our Chief Executive Officer, 597,000 Class F ordinary shares to our Chief

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Development Officer, 99,994 Class F ordinary shares to our Chief Scientific Officer and 95,598 Class F ordinary shares to our Chief Financial Officer; and (ii) 274,993 Class F ordinary shares to three members of our board of directors at the nominal value of £0.00001 per share.

The offers, sales and issuances of the securities described above were exempt from registration either (i) under Section 4(a)(2) of the Securities Act of 1933, as amended, or the Securities Act, in that the transactions did not involve any public offering, (ii) under Rule 701 promulgated under the Securities Act in that the transactions were under compensatory benefit plans and contracts relating to compensation or (iii) under Regulation S promulgated under the Securities Act in that offers, sales and issuances were not made to persons in the United States and no directed selling efforts were made in the United States.

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**Item 8. Exhibits and Financial Statement Schedules**  
**Exhibits**

EXHIBIT NUMBER	DESCRIPTION OF EXHIBIT	INCORPORATED BY REFERENCE			
		SCHEDULE/ FORM	FILE NUMBER	EXHIBIT	FILE DATE
1.1*	Form of Underwriting Agreement.				
3.1	<a href="#">Articles of Association of Nightstar Therapeutics plc.</a>	Form 20-F	0001-38217	1.1	4/3/18
4.1	<a href="#">Deposit Agreement.</a>	Form 20-F	0001-38217	2.1	4/3/18
4.2	<a href="#">Form of American Depositary Receipt (included in exhibit 4.1).</a>	Form 20-F	0001-38217	2.1	4/3/18
5.1	<a href="#">Opinion of Osborne Clarke LLP.</a>				
8.1	<a href="#">Tax Opinion of Wilmer Cutler Pickering Hale and Dorr LLP.</a>				
8.2	<a href="#">Tax Opinion of Osborne Clarke LLP.</a>				
10.1#	<a href="#">Nightstar Therapeutics plc 2017 Equity Incentive Plan.</a>	Form F-1	333-220289	10.1	9/15/17
10.2#	<a href="#">Non-Employee Sub Plan to the Nightstar Therapeutics plc 2017 Equity Incentive Plan.</a>	Form F-1/A	333-220289	10.2	9/15/17
10.3†	<a href="#">License of Technology by and between NightstaRx Limited and Oxford University Innovation Limited (formerly Isis Innovation Limited), dated as of November 13, 2013, as amended, effective as of October 15, 2014.</a>	Form F-1	333-220289	10.3	8/31/17
10.4†	<a href="#">License of Technology by and between NightstaRx Limited and Oxford University Innovation Limited (formerly Isis Innovation Limited), dated November 5, 2015.</a>	Form F-1/A	333-220289	10.4	9/15/17
10.5†	<a href="#">Non-Exclusive Patent License Agreement by and between NightstaRx Limited and Oxford BioMedica (UK) Limited, dated as of December 5, 2013.</a>	Form F-1	333-220289	10.5	8/31/17
10.6†	<a href="#">License of Technology by and between NightstaRx Limited and Oxford University Innovation Limited (formerly Isis Innovation Limited), dated October 12, 2017.</a>	Form 20-F	0001-38217	4.4	4/3/18
10.7#	<a href="#">Amended and Restated Employment Agreement by and among Nightstar, Inc., Nightstar Therapeutics Limited and David Fellows, dated as of September 12, 2017.</a>	Form F-1/A	333-220289	10.6	9/15/17
10.8#	<a href="#">Form of Deed of Indemnity between the registrant and each of its officers and directors.</a>	Form F-1/A	333-220289	10.7	9/15/17
16.1	<a href="#">Securities and Exchange Commission response letter from Ernst &amp; Young LLP, United Kingdom.</a>				



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EXHIBIT NUMBER	DESCRIPTION OF EXHIBIT	INCORPORATED BY REFERENCE			
		SCHEDULE/ FORM	FILE NUMBER	EXHIBIT	FILE DATE
21.1	<a href="#">Subsidiaries of the registrant.</a>	Form 20-F	0001-38217	8.1	4/3/2018
23.1	<a href="#">Consent of independent registered public accounting firm.</a>				
23.2	<a href="#">Consent of Osborne Clarke LLP (included in exhibit 5.1).</a>				
23.3	<a href="#">Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in exhibit 8.1).</a>				
24.1	<a href="#">Power of Attorney (included on signature page to this registration statement).</a>				

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\* To be filed by amendment.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and have been filed separately with the U.S. Securities and Exchange Commission.

# Indicates a management contract or any compensatory plan, contract or arrangement.

**Financial Statement Schedules**

None. All schedules have been omitted because the information required to be set forth therein is not applicable or has been included in the consolidated financial statements and notes thereto incorporated herein by reference.

**Item 9. Undertakings.**

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the provisions described in Item 6 hereof, or otherwise, the registrant has been advised that in the opinion of the U.S. Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned registrant hereby undertakes that:

(i) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(ii) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form F-1 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of London, United Kingdom, on the 25th day of September, 2018.

**NIGHTSTAR THERAPEUTICS PLC**

By: /s/ David Fellows \_\_\_\_\_

David Fellows  
Chief Executive Officer

KNOW ALL BY THESE PRESENT, that each person whose signature appears below hereby constitutes and appoints David Fellows and Senthil Sundaram, and each of them, his or her true and lawful agent, proxy and attorney-in-fact, with full power of substitution and resubstitution, for and in his or her name, place and stead, in any and all capacities, to (i) act on, sign and file with the Securities and Exchange Commission any and all amendments (including post-effective amendments) to this Registration Statement together with all schedules and exhibits thereto and any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended, together with all schedules and exhibits thereto, (ii) act on, sign and file such certificates, instruments, agreements and other documents as may be necessary or appropriate in connection therewith, (iii) act on and file any supplement to any prospectus included in this Registration Statement or any such amendment or any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and (iv) take any and all actions which may be necessary or appropriate to be done, as fully for all intents and purposes as he or she might or could do in person, hereby approving, ratifying and confirming all that such agent, proxy and attorney-in-fact or any of his or her substitutes may lawfully do or cause to be done by virtue thereof.

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Pursuant to the requirements of the Securities Act, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

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<u>SIGNATURE</u>	<u>TITLE</u>	<u>DATE</u>
<u>/s/ David Fellows</u> David Fellows	Chief Executive Officer and Director ( <i>Principal Executive Officer</i> )	September 25, 2018
<u>/s/ Senthil Sundaram</u> Senthil Sundaram	Chief Financial Officer ( <i>Principal Financial Officer and Principal Accounting Officer</i> )	September 25, 2018
<u>/s/ Chris Hollowood</u> Chris Hollowood	Chairman of the Board of Directors	September 25, 2018
<u>/s/ Paula K. Cobb</u> Paula K. Cobb	Director	September 25, 2018
<u>/s/ David C. Lubner</u> David C. Lubner	Director	September 25, 2018
<u>/s/ James McArthur</u> James McArthur	Director	September 25, 2018
<u>/s/ David M. Mott</u> David M. Mott	Director	September 25, 2018
<u>/s/ Scott M. Whitcup</u> Scott M. Whitcup	Director	September 25, 2018
By: <u>/s/ Senthil Sundaram</u> Name: Senthil Sundaram Title: Chief Financial Officer	Authorized Representative in the United States	September 25, 2018

Nightstar Therapeutics plc  
10 Midford Place  
2nd Floor  
London  
W1T 5BJ  
United Kingdom

25 September 2018

Dear Sir/Madam,

**Nightstar Therapeutics plc — Form F-1 Registration Statement**

1. **Background**

1.1 *Our role*

We act as English Law (as defined in paragraph 5.1(a)) legal advisers to Nightstar Therapeutics plc, a public limited company incorporated under the laws of England and Wales (the “**Company**” or “**you**”), in connection with the offering and issue by the Company (the “**Offering**”) of up to 4,600,000 new ordinary shares (including 600,000 new ordinary shares issuable upon exercise of the underwriters’ option granted by the Company) each of nominal value one penny per share of the Company (the “**New Ordinary Shares**”), each represented by one American Depositary Share of the Company (the “**ADSs**” and, together with the New Ordinary Shares, the “**Securities**”), all pursuant to the underwriting agreement to be made between the underwriters and the Company (the “**Underwriting Agreement**”).

1.2 *English Law opinion*

We have been asked to provide you with this English Law opinion (this “**Opinion**”) in connection with a registration statement (as amended, the “**Registration Statement**”) on Form F-1 filed by the Company with the U.S. Securities and Exchange Commission (the “**SEC**”) pursuant to the U.S. Securities Act of 1933, as amended (the “**Securities Act**”) and the rules and regulations promulgated thereunder (the “**Rules**”).

1.3 *Interpretation*

In this Opinion, headings are for ease of reference only and shall not affect the interpretation of this Opinion and all references to paragraphs and schedules are to paragraphs and schedules of this Opinion unless the context provides otherwise.

This Opinion is limited to the matters stated herein and no opinion is implied or may be inferred beyond the matters expressly stated herein.

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Osborne Clarke LLP  
One London Wall, London, EC2Y 5EB or DX 466 London Chancery Lane WC2 T +44 207 105 7000 F +44 207 105 7005

Osborne Clarke LLP is a limited liability partnership registered in England and Wales with registered number OC397443 whose registered office is at One London Wall, London EC2Y 5EB. It is authorised and regulated in the UK by the Solicitors Regulation Authority (SRA) and is registered as a recognised body with SRA number 619990.

The term ‘partner’ refers to a member of Osborne Clarke LLP. A list of members of Osborne Clarke LLP and their professional qualifications is available for inspection at the registered office. Any advice given by any individual member, employee, or consultant is the responsibility of Osborne Clarke LLP and not the individual.

Osborne Clarke LLP is part of an international legal practice.

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## 2. Examinations and enquiries

### 2.1 Documents examined

For the purposes of giving this Opinion, we have examined the following documents (the “**Documents**”):

- (a) the Registration Statement;
- (b) a copy of the certificate of incorporation and the articles of association as in force at the date of this Opinion (the “**Articles of Association**”) of the Company (together, the “**Constitutional Documents**”);
- (c) a copy of the minutes of a meeting of the board of directors of the Company held on 12 September 2018 at which it was resolved, amongst other things, to proceed with the Offering of the Securities (the “**Corporate Authorities**”);
- (d) a copy of the written resolutions of the shareholders of the Company dated 14 September 2017 resolving, amongst other things, to give the directors of the Company authority to allot ordinary shares and dis-apply pre-emption rights on the offering and issuance of ordinary shares of the Company up to an aggregate nominal amount of £1,000,000 (the “**Shareholder Resolutions**”); and
- (e) the Searches (as defined in paragraph 2.2).

We have examined all documents and made such enquiries as we have deemed necessary for the purpose of giving this Opinion.

### 2.2 Enquiries made

For the purpose of giving this Opinion, we have:

- (a) on 24 September 2018 obtained searches of the online register kept by the Registrar of Companies in England and Wales in respect of the Company (the “**Company Searches**”); and
- (b) made online enquiries in respect of the Company of the Central Index of Winding Up Petitions at the Companies Court (High Court of Justice in England) at 10:37 a.m. (London time) on 24 September 2018 via the CourtCheX (Winding Up Search) provided by Legalinx 7Side (the “**Winding-up Inquiry**”),

the Company Searches and the Winding-up Inquiry, together the “**Searches**”.

### 2.3 No other examination or enquiry

For the purposes of giving this Opinion, we have only examined and relied on the Documents and made the Searches. We have not conducted any independent research or investigation into, nor examined any other contracts, instruments or other documents entered into by or affecting the Company nor any other corporate records of the Company. We have made no further enquiries concerning the Company or the Offering or any other matter in connection with the giving of this Opinion (including not making any searches or enquiries of any other public register or records to obtain information or to verify any information given to us).

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### 3. Assumptions

#### 3.1 *General statement regarding assumptions*

The opinions set out in paragraph 4 are given on the basis of the assumptions set out in the remainder of this paragraph 3.

#### 3.2 *Signatures and documents*

- (a) That all documents submitted to us as photocopies, portable document format (PDF) copies, facsimile copies or e-mail conformed copies (or any other means) are complete and conform to the original document.
- (b) That all documents referred to in paragraph 3.2(a) are authentic and complete copies of all such original documents.
- (c) That where a document has been examined by us in draft or specimen form, it will be or has been executed in the form of that draft or specimen.
- (d) That all representations and statements as to factual matters expressed in the documents referred to in paragraph 3.2(a) are true and accurate.
- (e) That all signatures, seals and stamps on such documents referred to in paragraph 3.2(a) are genuine.
- (f) That the Registration Statement has been or will have been filed with the SEC in the form referred to in this Opinion.

#### 3.3 *Foreign laws*

- (a) That the Company is not subject to any insolvency procedure in a country other than England and Wales and that no steps have been taken to subject it to such a procedure.
- (b) That the term “non-assessable” in relation to the New Ordinary Shares means under English Law that holders of such shares, in respect of which all amounts due on such shares as to the nominal amount and any premium thereon have been fully paid, will be under no obligation to contribute to the liabilities of the Company solely in their capacity as holders of such New Ordinary Shares.

#### 3.4 *Corporate Authorities*

- (a) That the meetings of the Company constituting the Corporate Authorities were properly convened, constituted and held in accordance with all applicable laws and regulations (including the Articles of Association), that a duly qualified quorum of directors was present in each case throughout the meeting and voted in favor of the resolutions and that the provisions contained in the U.K. Companies Act 2006 or the Articles of Association relating to the declaration of directors’ interests were duly observed.
- (b) That, in each case, the minutes of the Corporate Authorities are a true record of the proceedings of the relevant meeting, that the resolutions shown in those minutes were duly passed in accordance with the directors’ statutory duties and that the respective resolutions have not been amended or rescinded and remain in full force and effect.

#### 3.5 *Shareholder Resolutions*

That the Shareholder Resolutions were duly passed in accordance with all applicable laws and regulations by the shareholders of the Company and have not been amended or rescinded and remain in full force and effect.

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### 3.6 *Accuracy and completeness of information*

- (a) That the copies of the Constitutional Documents are complete and up-to-date and that no amendments have been made to such documents.
- (b) That there has been no change in the position since the date on which the Searches were made and that the information disclosed in the Searches was accurate, complete and up to date and there is no information which, for any reason, should have been disclosed by the Searches but was not so disclosed.
- (c) That all the information supplied to us by the Company (through any of its employees, officers or agents) remains true, accurate, complete and up-to-date and there has been no amendment to any such information subsequent to it being given to us.
- (d) That each of the individuals who claims to be an officer of the Company is the individual whom they claim to be and holds the office they claim to hold.

## 4. **Opinions**

### 4.1 *General statement regarding opinions*

- (a) The opinions set out in the remainder of this paragraph 4 are given on the basis of the examination and enquiries referred to in paragraph 2 and the assumptions made in paragraph 3 and subject to the qualifications set out in paragraph 5.
- (b) This Opinion is strictly limited to the matters expressly stated in the remainder of this paragraph 4 and subject to the provisions of paragraph 6 and is not to be construed as extending by implication to any other matter.

### 4.2 *Opinions*

Based on the foregoing and subject to the assumptions and qualifications set out in this Opinion, we are of the opinion that:

- (a) The Company is duly incorporated and validly existing as a public limited company under English Law and has full power, capacity and authority under the Articles of Association to own its assets and to conduct its business as described in the Registration Statement.
- (b) Once allotted and issued, delivered and paid for in accordance with and as contemplated by the provisions of the Underwriting Agreement, the Securities will be validly allotted and issued, fully paid and non-assessable.
- (c) Relying exclusively on the information disclosed to us in the Searches, no resolution for the winding up of the Company has been passed, no order for the winding-up of the Company has been made, no petition for the winding-up of the Company has been presented, no order for the appointment of an administrator of the Company has been made and no administrative receiver, receiver or liquidator for the Company has been appointed.

## 5. **Qualifications**

### 5.1 *English Law as at today's date*

This Opinion is:

- 
- (a) based upon and limited to the laws of England and Wales in force at the date of this Opinion as applied by the English courts (“**English Law**”) and we do not undertake any obligation to take account of any change in law or circumstances after the date of this Opinion;
  - (b) given on the basis that this Opinion and any dispute, claim or obligation (whether contractual or non-contractual) arising out of or in connection with it, its subject matter or formation shall be governed by English Law; and
  - (c) given on the basis that we express no opinion on matters of fact. As to matters of fact which are material to this Opinion, we have relied entirely and without further enquiry on statements made in the Documents, except as necessary or appropriate for the purposes of giving this Opinion.

## 5.2 *Accuracy of information*

In relation to the Searches, it should be noted that the information revealed by the Searches may not be true, accurate, complete or up-to-date. In particular, but without limitation:

- (a) there may be matters which should have been registered but which have not been registered or there may be a delay between the registration of those matters and the relevant entries appearing on the relevant register;
- (b) there is no requirement to register with the Registrar of Companies notice of a petition for the winding-up of, or for an administration order in respect of, a company. Such a notice or notice of a winding-up or administration order having been made, a resolution having been passed for the winding-up of a company or a receiver, manager, administrative receiver, administrator or liquidator having been appointed may not be filed with the Registrar of Companies immediately and there may be a delay in any notice appearing on the register of the relevant party; and
- (c) the results of the Winding-Up Inquiry relate only to petitions for the compulsory winding up of, or for an administration order in respect of, the Company presented prior to the enquiry and entered on the records of the Central Registry of Winding-Up Petitions. The presentation of such a petition may not have been notified to the Central Registry or entered on its records immediately or, if presented to a County Court, at all,

in each case, further information might have become available on the relevant register after the Searches were made.

## 6. **Reliance and consent**

- 6.1 We hereby consent to the filing of this Opinion as an exhibit to the Registration Statement and to the references to this firm under the heading “Legal Matters” contained in the Registration Statement. In giving such consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the Rules.
- 6.2 This Opinion is delivered to the Company solely in connection with the Registration Statement.
- 6.3 No term of this Opinion is enforceable pursuant to the U.K. Contracts (Rights of Third Parties) Act 1999 by any person.



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7. **Governing law**

This Opinion shall be governed by and construed in accordance with the English Law.

Yours faithfully

/s/ Osborne Clarke LLP  
**Osborne Clarke LLP**

WILMERHALE

+1 212 230 8800 (t)  
+1 212 230 8888 (f)  
wilmerhale.com

September 25, 2018

Nightstar Therapeutics plc  
10 Midford Place, 2nd Floor  
London  
W1T 5BJ  
United Kingdom

Re: Nightstar Therapeutics plc

Ladies and Gentlemen:

In connection with the public offering of ordinary shares, nominal value £0.01 per share (the “Shares”), represented by American Depositary Shares (the “ADSs”) of Nightstar Therapeutics plc (the “Company”), pursuant to the registration statement on Form F-1 under the Securities Act of 1933, as amended (the “Securities Act”), originally filed by the Company with the Securities and Exchange Commission (the “Commission”) on September 25, 2018 (as so filed and as amended, the “Registration Statement”), you have requested our opinion concerning the statements in the Registration Statement under the heading “Material Income Tax Considerations — Material U.S. Federal Income Tax Considerations for U.S. Holders.”

In connection with rendering the opinion set forth below, we have examined and relied on the Registration Statement and such other documents as we have deemed necessary or relevant as a basis for the opinion set forth below. We have not independently verified any factual matters.

For purposes of rendering our opinion, we have assumed the authenticity of original documents, the accuracy of copies, the genuineness of all signatures and the legal capacity of all persons executing all instruments or documents examined or relied on by us.

Our opinion is based upon the relevant provisions of the U.S. Internal Revenue Code of 1986, as amended (the “Code”), the Treasury Regulations promulgated thereunder, and interpretations of the foregoing as expressed in court decisions and administrative determinations, all as in effect on the date of this opinion and all of which are subject to change at any time (possibly with retroactive effect). A change in the authorities upon which our opinion is based could affect the conclusions expressed herein. We undertake no obligation to update or supplement this opinion to reflect any changes of law or fact.

Wilmer Cutler Pickering Hale and Dorr LLP, 7 World Trade Center, 250 Greenwich Street, New York, New York 10007  
Beijing Berlin Boston Brussels Denver Frankfurt London Los Angeles New York Palo Alto Washington

Nightstar Therapeutic plc  
September 25, 2018  
Page 2

Our opinion is not binding upon the Internal Revenue Service (the “IRS”) or any court. Thus, no assurance can be given that a position taken in reliance on our opinion will not be challenged by the IRS or rejected by a court.

On the basis of and subject to the foregoing and in reliance on the assumptions described above, subject to the limitations set forth in the Registration Statement, we are of the opinion that the statements of law or legal conclusions in the Registration Statement under the heading “Material Income Tax Considerations—Material U.S. Federal Income Tax Considerations for U.S. Holders” fairly summarize the material U.S. federal income tax consequences to U.S. Holders (as defined therein) of the acquisition, ownership and disposition of the ADSs and of the Shares.

This opinion is limited to the matters of federal income tax law of the United States set forth in the Registration Statement, and we express no opinion with respect to any other federal, state, local or foreign tax issues, consequences or matters related to the acquisition, ownership and disposition of the ADSs or of the Shares.

This opinion is furnished to you solely in connection with the Registration Statement and may not be relied upon by anyone else or used for any other purpose without our prior written consent, provided, however, that it may be relied upon by persons entitled to rely on it pursuant to applicable provisions of federal securities laws.

We hereby consent to the filing of this opinion as Exhibit 8.1 to the Registration Statement and to the use of our name under the caption “Legal Matters” in the Registration Statement. In giving such consent, we do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules or regulations of the Commission promulgated thereunder, nor do we thereby admit that we are experts with respect to any part of such Registration Statement within the meaning of the term “experts” as used in the Securities Act or the rules and regulations of the Commission promulgated thereunder.

Sincerely,

WILMER CUTLER PICKERING  
HALE AND DORR LLP

By: /s/ Richard E. Andersen  
Richard E. Andersen, a Partner

Nightstar Therapeutics plc  
10 Midford Place  
2nd Floor  
London  
W1T 5BJ  
United Kingdom

25 September 2018

Dear Sir/Madam,

**Nightstar Therapeutics plc — Form F-1 Registration Statement**

1. **Background**

1.1 ***Our role***

We act as English Law (as defined in paragraph 5.1(a)) legal advisers to Nightstar Therapeutics plc, a public limited company incorporated under the laws of England and Wales (the “**Company**” or “**you**”) in connection with the offering and issue by the Company (the “**Offering**”) of up to 4,600,000 new ordinary shares (including 600,000 new ordinary shares issuable upon exercise of the underwriters’ option granted by the Company) each of nominal value one penny per share of the Company (the “**New Ordinary Shares**”), each represented by one American Depositary Share of the Company (the “**ADSs**” and, together with the New Ordinary Shares, the “**Securities**”), all pursuant to the underwriting agreement to be made between the underwriters and the Company (the “**Underwriting Agreement**”).

1.2 ***English Law opinion***

We have been asked to provide you with this English Law opinion (this “**Opinion**”) in connection with a registration statement (as amended, the “**Registration Statement**”) on Form F-1 filed by the Company with the U.S. Securities and Exchange Commission (the “**SEC**”) pursuant to the U.S. Securities Act of 1933, as amended (the “**Securities Act**”) and the rules and regulations promulgated thereunder (the “**Rules**”).

1.3 ***Interpretation***

In this Opinion, headings are for ease of reference only and shall not affect the interpretation of this Opinion and all references to paragraphs and schedules are to paragraphs and schedules of this Opinion unless the context provides otherwise.

This Opinion is limited to the matters stated herein and no opinion is implied or may be inferred beyond the matters expressly stated herein.

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Osborne Clarke LLP  
One London Wall, London, EC2Y 5EB or DX 466 London Chancery Lane WC2 T +44 207 105 7000 F +44 207 105 7005

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The term ‘partner’ refers to a member of Osborne Clarke LLP. A list of members of Osborne Clarke LLP and their professional qualifications is available for inspection at the registered office. Any advice given by any individual member, employee, or consultant is the responsibility of Osborne Clarke LLP and not the individual.

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## 2. **Examinations and enquiries**

For the purposes of giving this Opinion, we have only examined the text in the Registration Statement under the heading “*U.K. Taxation*”. We have not conducted any independent research or investigation into, nor examined any other contracts, instruments or other documents entered into by or affecting the Company nor any other corporate records of the Company. We have made no further enquiries concerning the Company or the Offering or any other matter in connection with the giving of this Opinion (including not making any searches or enquiries of any other public register or records to obtain information or to verify any information given to us).

## 3. **Assumptions**

### 3.1 **General statement regarding assumptions**

The opinion set out in paragraph 4 is given on the basis of the assumptions set out in the remainder of this paragraph 3.

### 3.2 **Signatures and documents**

- (a) That all documents submitted to us as photocopies, portable document format (PDF) copies, facsimile copies or e-mail conformed copies (or any other means) are complete and conform to the original document.
- (b) That all documents referred to in paragraph 3.2(a) are authentic and complete copies of all such original documents.
- (c) That where a document has been examined by us in draft or specimen form, it will be or has been executed in the form of that draft or specimen.
- (d) That all representations and statements as to factual matters expressed in the documents referred to in paragraph 3.2(a) are true and accurate.
- (e) That all signatures, seals and stamps on such documents referred to in paragraph 3.2(a) are genuine.
- (f) That the Registration Statement has been or will have been filed with the SEC in the form referred to in this Opinion.

## 4. **Opinion**

### 4.1 **General statement regarding opinions**

- (a) The opinion set out in the remainder of this paragraph 4 is given on the basis of the examination and enquiries referred to in paragraph 2 and the assumptions made in paragraph 3 and subject to the qualifications set out in paragraph 5.
- (b) This Opinion is strictly limited to the matters expressly stated in the remainder of this paragraph 4 and subject to the provisions of paragraph 6 and is not to be construed as extending by implication to any other matter.

### 4.2 **Opinion**

Based on the foregoing and subject to the assumptions and qualifications set out in this Opinion, we are of the opinion that the statements in the Registration Statement under the heading “*U.K. Taxation*” insofar as such statements purport to summarise matters of United Kingdom tax laws, fairly present in all material respects such United Kingdom tax laws.

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5. **Qualifications**

5.1 ***English Law as at today's date***

This Opinion is:

- (a) based upon and limited to the laws of England and Wales as applied by the English courts ("**English Law**") and the generally published practice of Her Majesty's Revenue and Customs in each case in force at the date of this Opinion and we do not undertake any obligation to take account of any change in law, practice or circumstances after the date of this Opinion;
- (b) given on the basis that this Opinion and any dispute, claim or obligation (whether contractual or non-contractual) arising out of or in connection with it, its subject matter or formation shall be governed by English Law; and
- (c) given on the basis that we express no opinion on matters of fact.

6. **Reliance and consent**

- 6.1 We hereby consent to the filing of this Opinion as an exhibit to the Registration Statement and to the references to this firm under the heading "*Legal Matters*" contained in the Registration Statement. In giving such consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the Rules.
- 6.2 This Opinion is delivered to the Company solely in connection with the Registration Statement.
- 6.3 No term of this Opinion is enforceable pursuant to the U.K. Contracts (Rights of Third Parties) Act 1999 by any person.

7. **Governing law**

This Opinion shall be governed by and construed in accordance with the English Law.

Yours faithfully

/s/ Osborne Clarke LLP

**Osborne Clarke LLP**

September 25, 2018

Securities and Exchange Commission  
100 F Street, N.E.  
Washington, DC 20549

Dear Commissioners:

We have read the Registration Statement on Form F-1 dated September 25, 2018, of Nightstar Therapeutics plc and are in agreement with the statements contained in paragraphs one, two, three and four of Changes in Registrant's Certifying Accountant on page 73 therein. We have no basis to agree or disagree with other statements of the registrant contained therein.

Regarding the registrant's statement concerning the previously identified material weakness in its internal control over financial reporting, included in Changes in Registrant's Certifying Accountant on page 73 therein, we had considered such matter in determining the nature, timing and extent of procedures performed in our audit of the registrant's 2016 consolidated financial statements.

/s/ Ernst & Young LLP  
Cambridge, United Kingdom

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” in the Registration Statement (Form F-1) and related Prospectus of Nightstar Therapeutics plc for the registration of its American Depositary Shares and to the incorporation by reference therein of our report dated April 3, 2018, with respect to the consolidated financial statements of Nightstar Therapeutics plc included in its Annual Report (Form 20-F) for the year ended December 31, 2017, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Cambridge, United Kingdom

September 25, 2018