UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER
PURSUANT TO RULE 13a-16 OR 15d-16
UNDER THE SECURITIES EXCHANGE ACT OF 1934

For the Month of November 2018

Commission File Number: 001-38217

Nightstar Therapeutics plc

(Translation of registrant's name into English)

10 Midford Place, 2nd Floor
London W1T 5BJ United Kingdom
(Address of principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

☒ Form 20-F ☐ Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): ☐

Other Events

On November 13, 2018, Nightstar Therapeutics plc issued a press release announcing financial results for the three and nine months ended September 30, 2018. The press release is attached as Exhibit 99.1 hereto and is incorporated by reference herein.

Exhibit	Description
99.1	Press Release issued on November 13, 2018

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

NIGHTSTAR THERAPEUTICS PLC

Date: November 13, 2018

By: /s/ Bryan Yoon
Name: Bryan Yoon
Title: General Counsel and Secretary

Exhibit 99.1

Nightstar Announces Planned Initiation of Phase 2/3 Expansion Study in XIRIUS Trial for NSR-RPGR in XLRP and Reports Third Quarter 2018 Financial Results

Phase 2/3 Expansion Study to Include No-Sham Control Arm in Alignment with FDA Draft Guidance on Development of Gene Therapy Products for Retinal Disorders

Preliminary Efficacy Data from Phase 2/3 Expansion Study Expected in Mid-2019

WALTHAM, Mass. and LONDON, UK – November 13, 2018 (GLOBE NEWSWIRE) – Nightstar Therapeutics plc (NASDAQ: NITE), a clinical-stage gene therapy company developing treatments for rare inherited retinal diseases, today provided an update on recent achievements and upcoming clinical milestones and reported financial results for the quarter ended September 30, 2018.

"We are pleased with the upcoming initiation of the Phase 2/3 expansion study in line with our previous guidance after being the first sponsor to establish proof-of-concept in X-linked retinitis pigmentosa," said Dave Fellows, Chief Executive Officer. "The modified Phase 2/3 expansion study is designed to be consistent with recommendations in FDA's draft guidance on the development of gene therapy products for retinal disorders, which we believe will allow us to expedite the development of NSR-RPGR."

XIRIUS is a clinical trial consisting of an open-label, dose escalation study followed by an expansion study. Enrollment of the Phase 1 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, Nightstar 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. Six-month follow-up data on all 18 patients in the dose escalation study is expected to be available in the second quarter of 2019, with one-year follow-up data expected to be available in the fourth quarter of 2019.

The Phase 2/3 expansion study is designed to evaluate the safety and efficacy of NSR-RPGR in patients with a diagnosis of XLRP due to RPGR mutations, as confirmed by genetic testing. The primary efficacy endpoint will evaluate changes in retinal sensitivity following treatment with NSR-RPGR. Secondary endpoints include both anatomical and functional endpoints of efficacy and safety similar to those evaluated in the dose escalation study as well as exploratory efficacy endpoints such as mobility maze assessments. Approximately 45 patients across six surgical centers in both the United States and the United Kingdom will be enrolled. The eligibility criteria for the expansion study will include patients with functional impairment as measured by microperimetry and the presence of viable photoreceptors as indicated by ellipsoid zone measurements on optical coherence tomography. Patients will be randomized on a masked basis into one of three study arms: approximately 15 patients receiving a high-dose of NSR-RPGR in one-eye (2.5x10^11 genome particles, or gp); approximately 15 patients receiving a low-dose of NSR-RPGR in one-eye (5x10^10 gp); and approximately 15 patients receiving no treatment (no-sham, parallel control arm). The two treatment groups correspond to doses used in cohorts 5 and 3 of the dose escalation study, respectively. A standardized eight-week steroid

regimen will be included to maximize any potential treatment benefit. The Phase 2/3 expansion study is expected to begin by the end of 2018. Preliminary efficacy data is expected to be available in mid-2019, which would serve as the basis for discussions with regulatory agencies on potential Phase 3 requirements. One-year follow-up data from the expansion study is expected to be available in 2020.

Business Highlights Include

- **Appointment of Strategic Biotechnology Executive Paula Cobb to Board of Directors in September 2018.** Ms. Cobb currently serves as the executive vice president of corporate development at Decibel Therapeutics, Inc. and brings strategic, worldwide commercialization experience in rare diseases, having led teams to three new drug approvals and played key roles on four product launches, which will be invaluable as Nightstar evolves into a commercial-stage company.
- **Positive Proof-of-Concept Data from Dose Escalation Study in XIRIUS Trial for NSR-RPGR in XLRP in September 2018.** NSR-RPGR data presented at the EURETINA 2018 Congress demonstrated proof-of-concept with durable dose-related improvements seen as early as month 1 across multiple microperimetry analyses. Preliminary efficacy responses were observed in 5 out of 9 patients (56%) in cohorts 3, 4 and 5, including durable improvements in overall macula sensitivity, central 16 macula sensitivity and number of improved macula loci. NSR-RPGR was well-tolerated with no dose limiting toxicities or serious treatment-related adverse events.
- **Inaugural R&D Day in September 2018.** The R&D day featured presentations on XLRP endpoints, positive proof-of-concept data on NSR-RPGR from the XIRIUS dose escalation study, program updates on NSR-REP1 for the treatment of choroideremia and NSR-ABCA4 for the treatment of Stargardt disease, as well as an overview of Nightstar's hybrid manufacturing model for gene therapy.
- **Received Orphan Drug Designation for NSR-RPGR in September 2018.** NSR-RPGR was granted orphan drug designation for the treatment of inherited retinal dystrophies due to defects in the RPGR gene from the U.S. Food and Drug Administration, or FDA, in the United States.
- **Completion of Public Offering of 4,600,000 American Depository Shares, or ADSs, in October 2018.** The primary offering of 4,600,000 ADSs, including the full exercise by the underwriters of their overallotment option, at $18.00 per ADS, resulted in estimated net proceeds to Nightstar of approximately $77.1 million.

Anticipated Milestones for 2019 and 2020

- **NSR-RPGR for X-Linked Retinitis Pigmentosa**
  - **2Q 2019:** Six-Month Follow-up Data from Dose Escalation Study
  - **Mid-2019**: Preliminary Efficacy Data from Phase 2/3 Expansion Study
  - **4Q 2019:** One-Year Follow-up Data from Dose Escalation Study
  - **2020:** One-Year Follow-up Data from Phase 2/3 Expansion Study
- **NSR-REP1 for Choroideremia**
  - **1H 2019**: Completion of Enrollment for Phase 3 STAR Registrational Trial for Choroideremia
  - **2020:** One-year Follow-up Data from Phase 3 STAR Trial

Third Quarter 2018 Financial Results

Three Months Ended September 30, 2018 and 2017

Research and development expenses were $7.8 million for the three months ended September 30, 2018, compared to $4.0 million for the three months ended September 30, 2017. The increase of $3.8 million resulted primarily from increases in program-related expenses of $1.1 million for NSR-REP1 and $1.7 million for NSR-RPGR, as well as a $1.0 million increase in personnel-related costs and a $1.0 million increase in indirect research and development expenses. The increased expenses were partially offset by an increase of $1.0 million of research and development tax credits from Her Majesty's Revenue & Customs, or HMRC. Research and development personnel-related costs increased due to an increase in headcount to support our growth and to assist in the further development of our product candidates and pipeline. The increase in research and development personnel-related costs includes $0.2 million of additional non-cash share-based compensation compared to the same period in 2017.

General and administrative expenses were $3.0 million for the three months ended September 30, 2018, compared to $2.0 million for the three months ended September 30, 2017. The increase of $1.0 million is mainly due to an increase in personnel-related costs. General and administrative personnel-related costs increased due to an increase in headcount to support our increased research and development activities, growth of our company and our status as a public company. The increase in general and administrative personnel-related costs includes $0.3 million of additional non-cash share-based compensation compared to the same period in 2017.

Net loss for the three-month period ended September 30, 2018 was $7.6 million, or $0.27 basic and diluted net loss per ordinary share, as compared to $8.2 million, or $0.38 basic and diluted net loss per ordinary share, for the three-month period ended September 30, 2017.

Nine Months Ended September 30, 2018 and 2017

Research and development expenses were $22.0 million for the nine months ended September 30, 2018, compared to $10.3 million for the nine months ended September 30, 2017. The increase of $11.7 million resulted primarily from increases in program-related expenses of $4.5 million for NSR-REP1 and $4.2 million for NSR-RPGR, as well as a $3.7 million increase in personnel-related costs and a $1.9 million increase in indirect research and development expenses. The increased expenses were partially offset by an increase of $2.6 million of research and development tax credits from HMRC. Research and development personnel-related costs increased due to an increase in headcount to support our growth and to assist in the further development of our product candidates and pipeline. The increase in research and development personnel-related costs includes $1.0 million of additional non-cash share-based compensation compared to the same period in 2017.

General and administrative expenses were $9.1 million for the nine months ended September 30, 2018, compared to $3.4 million for the nine months ended September 30, 2017. The increase of $5.7 million is mainly due to a $4.4 million increase in personnel-related costs and a $1.3 million increase in consulting and professional fees, including increased legal, accounting and audit fees and insurance costs. General and administrative personnel-related costs increased due to an increase in headcount to support our increased research and development activities, growth of our company and our status as a public company. The increase in general and administrative personnel-related costs includes $1.4 million of additional non-cash share-based compensation compared to the same period in 2017.

Net loss for the nine-month period ended September 30, 2018 was $30.0 million, or $1.07 basic and diluted net loss per ordinary share, as compared to $15.9 million, or $0.84 basic and diluted net loss per ordinary share, for the nine-month period ended September 30, 2017.

As of September 30, 2018, our cash, cash equivalents and marketable securities totaled $100.8 million, compared to $129.4 million at December 31, 2017. As of September 30, 2018, there were approximately 28.9 million ordinary shares outstanding. On October 2, 2018, Nightstar completed an underwritten public offering of 4,600,000 ADSs (representing the same number of ordinary shares), including the full exercise by the underwriters of their option to purchase additional ADSs, at a public offering price of $18.00 per ADS, resulting in estimated net proceeds to Nightstar of approximately $77.1 million, after deducting underwriting discounts and commissions and estimated offering expenses.

About Nightstar

Nightstar is 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. Nightstar's lead product candidate, NSR-REP1, is currently in Phase 3 development for the treatment of patients with choroideremia, a rare, degenerative, genetic retinal disorder that has no treatments currently available and affects approximately one in every 50,000 people. Positive results from a Phase 1/2 trial of NSR-REP1 were published in Nature Medicine in 2018, in The New England Journal of Medicine in 2016, and in The Lancet in 2014. Nightstar's second product candidate, NSR-RPGR, is currently being evaluated in a clinical trial known as the XIRIUS trial for the treatment of patients with X-linked retinitis pigmentosa, an inherited X-linked recessive retinal disease that affects approximately one in every 40,000 people. In September 2018, Nightstar 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.

For more information about Nightstar or its clinical trials, please visit www.nightstartx.com.

About X-Linked Retinitis Pigmentosa (XLRP)

XLRP, a form of retinitis pigmentosa, is a rare inherited X-linked recessive genetic retinal disorder primarily affecting males. 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 translates to approximately 17,000 patients in the United States and the five major European markets. There are no treatments currently available for XLRP. Nightstar is conducting a prospective, natural history observational study, referred to as the XOLARIS study, to better understand the progression of untreated XLRP in up to approximately 100 patients enrolled from approximately 23 centers in North America and Europe.

Cautionary Language Concerning Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. The words "believe," "anticipate," "could," "intend,"

"estimate," "will," "would," "may," "should," "project," "target," "track," "expect" or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. All statements contained in this press release other than statements of historical facts are forward-looking statements, including, without limitation: statements about our cash position and sufficiency of capital resources to fund our operating requirements, trends and other factors that may affect our financial results; our planned and ongoing clinical trials for NSR-REP1 and NSR-RPGR, including our Phase 3 STAR trial in choroideremia and our XIRIUS trial in X-linked retinitis pigmentosa; potential results and timelines relating to the dose escalation study and the Phase 2/3 expansion study in the XIRIUS trial; the continued clinical development of our pipeline; the timelines associated with our research and development programs including the timing of patient enrollment and the release of data from ongoing clinical trials and studies; timelines, pathway and prerequisite activities, including additional trials or studies, to filing for and receiving marketing authorization for any of our product candidates from any regulatory agency; the prevalence of patient populations for our targeted indications; and the utility of the endpoints, including any exploratory endpoints, in our clinical trials and the prior preclinical and clinical data in determining future clinical results. These forward-looking statements are based on management's current expectations of future events as of the date of this release and are subject to a number of substantial known and unknown risks, uncertainties and other 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, including those related to the timing and costs involved in commercializing any product candidate that receives regulatory approval; the initiation, timing and conduct of clinical trials; the availability of data from clinical trials and expectations for regulatory submissions and approvals; whether interim results of a clinical trial will be predictive of the final results of the trial; whether results of small or early stage clinical trials will be predictive of the results of later-stage trials; our scientific approach and general development progress; the availability or commercial potential of the our product candidates; the sufficiency of our cash resources; and other risks and uncertainties set forth in our Report of Foreign Private Issuer on Form 6-K furnished to the U.S. Securities and Exchange Commission on September 25, 2018 and subsequent reports that we file with the U.S. Securities and Exchange Commission. We may not actually achieve the plans, intentions, estimates or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions, estimates and expectations disclosed in the forward-looking statements we make. We anticipate that subsequent events and developments will cause our views to change. We are under no duty to update any of these forward-looking statements after the date of this press release to conform these statements to actual results or revised expectations, except as required by law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this press release. Any reference to our website address in this press release is intended to be an inactive textual reference only and not an active hyperlink.

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Investors:

Senthil Sundaram, Chief Financial Officer
Brian Luque, Sr. Manager, Investor Relations
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NIGHTSTAR THERAPEUTICS PLC

Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except per share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Operating expenses:				
Research and development	$ 7,845	$ 3,983	$ 21,961	$ 10,275
General and administrative	3,019	2,025	9,119	3,432
Total operating expenses	10,864	6,008	31,080	13,707
Other income (expense):				
Interest and other income	798	55	1,887	61
Other Income (expense), net	2,564	(2,258)	(1,097)	(2,258)
Total other income (expense), net	3,362	(2,203)	790	(2,197)
Loss before benefit for income taxes	(7,502)	(8,211)	(30,290)	(15,904)
Provision for (benefit from) income taxes	83	—	(251)	—
Net loss	(7,585)	(8,211)	(30,039)	(15,904)
Other comprehensive income (loss)	(2,733)	1,848	932	3,570
Total comprehensive loss	$(10,318)	$ (6,363)	$(29,107)	$(12,334)
Basic and diluted net loss per ordinary share	$ (0.27)	$ (0.38)	$ (1.07)	$ (0.84)
Weighted average basic and diluted ordinary shares	28,139	21,514	27,975	18,858

NIGHTSTAR THERAPEUTICS PLC

Consolidated Balance Sheets
(In thousands)

	September 30, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 45,974	$ 129,404
Marketable securities	54,800	—
Prepaid expenses and other assets	12,531	5,438
Total current assets	113,305	134,842
Property and equipment, net	534	355
Other assets	632	—
Total assets	$ 114,471	$ 135,197
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 4,423	$ 3,196
Accrued expenses and other liabilities	10,340	6,189
Total current liabilities	14,763	9,385
Total liabilities	14,763	9,385
Total shareholders' equity	99,708	125,812
Total liabilities and shareholders' equity	$ 114,471	$ 135,197