Spark Therapeutics, Inc.
Form 8-K
November 23, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)

of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): November 23, 2018

Spark Therapeutics, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**001-36819**	**46-2654405**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
3737 Market Street		**19104**

Suite 1300

Philadelphia, PA
(Address of Principal Executive Offices) (Zip Code)
Registrant s telephone number, including area code: (888) 772-7560

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, 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 13(a) of the Exchange Act.

Item 8.01. Other Events.

On November 23, 2018, Spark Therapeutics, Inc. (the Company) issued a press release announcing that the European Commission has granted marketing authorization for LUXTURNA® (voretigene neparvovec), a one-time gene therapy for the treatment of adult and pediatric patients with vision loss due to inherited retinal dystrophy caused by confirmed biallelic *RPE65* mutations and who have sufficient viable retinal cells. *RPE65*-mediated inherited retinal disease is a progressive condition leading to total blindness in most patients. This authorization is valid in all 28-member states of the EU, as well as Iceland, Liechtenstein and Norway. LUXTURNA is the first gene therapy for a genetic disease that has received regulatory approval in both the U.S. and EU. Under the terms of the License and Commercialization Agreement between the Company and Novartis Pharma AG (Novartis), upon receipt of the marketing authorization for LUXTURNA, the Company is entitled to a $25 million payment from Novartis.

Clinical Trial Overview of LUXTURNA® (voretigene neparvovec)

The safety and efficacy of LUXTURNA were assessed in one open-label, dose-exploration Phase 1 safety study (n=12), a second open-label Phase 1 follow-on study to assess the safety of injection of the contralateral eye (n=11) and an open-label, randomized, controlled Phase 3 efficacy and safety study (n=31) in pediatric and adult participants (range 4 to 44 years) with biallelic *RPE65* mutation-associated retinal disease and sufficient viable retinal cells.

Of the 31 participants enrolled in the Phase 3 study, 21 were randomized to receive subretinal injection of LUXTURNA and 10 were randomized to the control (non-intervention) group. One participant in the intervention group discontinued from the study prior to treatment and one participant in the control group withdrew consent and was discontinued from the study. All nine participants randomized to the control group elected to cross over to receive LUXTURNA after one year of observation. All participants in these studies planned to be followed for long-term safety and efficacy. LUXTURNA Phase 3 clinical trial data, including data from the intervention group of all randomized participants through the one-year time point, have been previously reported in *The Lancet*.

The efficacy of LUXTURNA in the Phase 3 study was established based on the binocular multi-luminance mobility test (MLMT) score change from baseline to one year. MLMT was designed to measure changes in functional vision as assessed by the ability of a participant to navigate a course accurately and at a reasonable pace at seven different levels of illumination, ranging from 400 lux (corresponding to a brightly lit office) to one lux (corresponding to a moonless summer night). Each light level was assigned a score ranging from zero to six, with a higher score indicating that a participant could pass MLMT at a lower light level. A score of negative one was assigned to participants who could not pass MLMT at a light level of 400 lux. MLMT score change was defined as the difference between the score at baseline and the score at one year with a positive score change indicating that a participant was able to complete MLMT at a lower light level. Additional clinical outcomes included white light full-field light sensitivity threshold (FST) testing and visual acuity, both averaged over both eyes.

LUXTURNA Phase 3 clinical study results showed a statistically significant difference between the intervention group (n=21) and control participants (n=10) at one year in mean binocular MLMT score change (intervention minus control group difference of 1.6; 95% CI, 0.72, 2.41; p=0.001). After crossing over to receive LUXTURNA, participants in the control group showed a similar response to those in the intervention group. This score change has been sustained for at least three years for the original intervention group and at least two years in the crossover group of the Phase 3 clinical study. In addition, participants who received LUXTURNA showed a statistically significant improvement from baseline to one year in white light FST averaged over both eyes (p<0.001) and first assigned eye MLMT change score (p=0.001) compared to the control group. The change in visual acuity from baseline to one year was not significantly different between the intervention and control participants.

Three ocular serious adverse events (SAEs) were reported in the clinical program. One SAE related to the surgical procedure in one eye of a Phase 3 participant, in which there was foveal thinning that resulted in unresolved loss of foveal function. One additional Phase 3 participant who continued into the long-term follow-up study reported an SAE of retinal detachment 4 years after vector administration assessed as related to the administration procedure. The third ocular SAE was reported in one eye of a Phase 1 participant in which the treatment for bacterial endophthalmitis led to elevated intraocular pressure and subsequent optic atrophy. There were three non-serious AEs of retinal deposits (subretinal precipitate) in three participants (three eyes) that were considered to be related to LUXTURNA. All three of these events were mild in intensity, transient in nature and resolved without consequences. No deleterious immune responses have been observed. The most common adverse reactions related to LUXTURNA reported in 5 percent or greater of the combined Phase 1 and Phase 3 trial participants included conjunctival hyperemia, cataract, increased intraocular pressure, retinal tear, dellen (thinning of the corneal stroma), macular hole, subretinal deposits, eye inflammation, eye irritation, eye pain and maculopathy (wrinkling on the surface of the macula).

Indication and Important Safety Information for LUXTURNA in the United States

LUXTURNA is an adeno-associated virus vector-based gene therapy indicated for the treatment of patients with confirmed biallelic *RPE65* mutation-associated retinal dystrophy.

Patients must have viable retinal cells as determined by the treating physicians.

Warnings and Precautions

Endophthalmitis may occur following any intraocular surgical procedure or injection. Use proper aseptic injection technique when administering LUXTURNA and monitor for and advise patients to report any signs or symptoms of infection or inflammation to permit early treatment of any infection.

Permanent decline in visual acuity may occur following subretinal injection of LUXTURNA. Monitor patients for visual disturbances.

Retinal abnormalities may occur during or following the subretinal injection of LUXTURNA, including macular holes, foveal thinning, loss of foveal function, foveal dehiscence, and retinal hemorrhage. Monitor and manage these retinal abnormalities appropriately. Do not administer LUXTURNA in the immediate vicinity of the fovea. Retinal abnormalities may occur during or following vitrectomy, including retinal tears, epiretinal membrane, or retinal detachment. Monitor patients during and following the injection to permit early treatment of these retinal abnormalities. Advise patients to report any signs or symptoms of retinal tears and/or detachment without delay.

Increased intraocular pressure may occur after subretinal injection of LUXTURNA. Monitor and manage intraocular pressure appropriately.

Expansion of intraocular air bubbles Instruct patients to avoid air travel, travel to high elevations or scuba diving until the air bubble formed following administration of LUXTURNA has completely dissipated from the eye. It may take one week or more following injection for the air bubble to dissipate. A change in altitude while the air bubble is still present can result in irreversible vision loss. Verify the dissipation of the air bubble through

ophthalmic examination.

Cataract Subretinal injection of LUXTURNA, especially vitrectomy surgery, is associated with an increased incidence of cataract development and/or progression.

Adverse Reactions

In clinical studies, ocular adverse reactions occurred in 66% of study participants (57% of injected eyes), and may have been related to LUXTURNA, the subretinal injection procedure, the concomitant use of corticosteroids, or a combination of these procedures and products.

The most common adverse reactions (incidence ³ 5% of study participants) were conjunctival hyperemia (22%), cataract (20%), increased intraocular pressure (15%), retinal tear (10%), dellen (thinning of the corneal stroma) (7%), macular hole (7%), subretinal deposits (7%), eye inflammation (5%), eye irritation (5%), eye pain (5%), and maculopathy (wrinkling on the surface of the macula) (5%).

Immunogenicity

Immune reactions and extra-ocular exposure to LUXTURNA in clinical studies were mild. No clinically significant cytotoxic T-cell response to either AAV2 or RPE65 has been observed. In clinical studies, the interval between the subretinal injections into the two eyes ranged from 7 to 14 days and 1.7 to 4.6 years. Study participants received systemic corticosteroids before and after subretinal injection of LUXTURNA to each eye, which may have decreased the potential immune reaction to either AAV2 or RPE65.

Pediatric Use

Treatment with LUXTURNA is not recommended for patients younger than 12 months of age, because the retinal cells are still undergoing cell proliferation, and LUXTURNA would potentially be diluted or lost during the cell proliferation. The safety and efficacy of LUXTURNA have been established in pediatric patients. There were no significant differences in safety between the different age subgroups.

Spark Therapeutics Cautionary note on forward-looking statements

This report contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the company s product LUXTURNA® (voretigene neparvovec). The words anticipate, believe, expect, intend, may, plan, predict, will, would, could, should, continue a intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Any forward-looking statements are based on management s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that the improvements in functional vision demonstrated by LUXTURNA in our clinical trials may not be sustained over extended periods of time. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the Risk Factors section, as well as discussions of potential risks, uncertainties and other important factors, in our Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and other filings we make with the Securities and Exchange Commission. All information in this report is as of the date of the report, and Spark undertakes no duty to update this information unless required by law.

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 hereunto duly authorized.

SPARK THERAPEUTICS, INC.

Date: November 23, 2018

By: /s/ Joseph W. La Barge
Joseph W. La Barge
Chief Legal Officer