Spark Therapeutics, Inc.
Form 8-K
December 19, 2017

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): December 19, 2017

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<br>Suite 1300<br>Philadelphia, PA | 19104 |
| (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 December 19, 2017, Spark Therapeutics, Inc., issued a press release announcing that the U.S. Food and Drug Administration has approved LUXTURNA™ (voretigene neparvovec-rzyl), a one-time gene therapy product indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. LUXTURNA should only be administered to patients with mutations on both copies of the RPE65 gene who have sufficient viable retinal cells as determined by their treating physicians.

LUXTURNA is the first FDA-approved gene therapy for a genetic disease, the first and only pharmacologic treatment for an inherited retinal disease (IRD) and the first adeno-associated virus (AAV) vector gene therapy approved in the U.S.

The U.S. Prescribing Information for LUXTURNA includes the following Warnings and Precautions: endophthalmitis; permanent decline in visual acuity; retinal abnormalities; increased intraocular pressure; expansion of intraocular air bubbles; and cataract. LUXTURNA is not recommended for patients younger than 12 months of age because the retina is still growing, which may affect how LUXTURNA works. LUXTURNA is administered by subretinal injection to each eye on separate days within a close interval, but no fewer than 6 days apart. Please see the Indication and Important Safety Information section below for more information regarding risks associated with LUXTURNA.

LUXTURNA will be manufactured at Spark Therapeutics' manufacturing facility located in West Philadelphia, which is the first licensed manufacturing facility in the U.S. for a gene therapy treating an inherited disease. The gene therapy will be administered at selected treatment centers in the U.S. by leading retinal surgeons, who will receive surgical training provided by Spark Therapeutics on the administration procedure. LUXTURNA is expected to be available for administration in these treatment centers late in the first quarter of 2018. Spark Therapeutics is committed to ensuring eligible patients have access to LUXTURNA. More details on the company's patient support programs, its commitment to access, and the price of the product will be shared in early January.

LUXTURNA was approved by FDA under Priority Review and previously received orphan drug and breakthrough therapy designations from FDA. With the approval of LUXTURNA, FDA will issue to Spark Therapeutics a Rare Pediatric Disease Priority Review Voucher for a Priority Review of a subsequent marketing application for a different product. Spark Therapeutics' Marketing Authorization Application (MAA) for LUXTURNA is currently under review with the European Medicines Agency (EMA). LUXTURNA also has received orphan product designations from EMA.

Genetic Testing and Obtaining a Genetic Diagnosis for Biallelic RPE65 Mutation-associated Retinal Dystrophy
A genetic test is the only way to verify the gene mutation(s) that is the underlying cause of an inherited retinal disease (IRD), including those associated with biallelic RPE65 mutations.

For people with IRDs, Spark Therapeutics will offer access to genetic testing designed to identify biallelic RPE65 mutations.

Genetic testing is also available through a variety of other channels, including as a covered service through a patient's insurance, through non-profit organizations, as well as through various commercial labs.

Patient Support for Accessing LUXTURNA

Spark Therapeutics is committed to helping ensure that appropriate patients in the U.S. with a confirmed genetic diagnosis of biallelic RPE65 mutation-associated retinal dystrophy have access to LUXTURNA. Spark has established Spark Therapeutics Generation Patient Services[SM] to support appropriate patients, their families and providers in the U.S. through the LUXTURNA treatment experience. The team at Spark Therapeutics Generation Patient Services will assist eligible and enrolled patients navigate the insurance process and provide options to support travel and logistics to and from treatment centers.

For patients who are underinsured or are insured through government programs like Medicare and Medicaid, Spark plans to support independent Patient Assistance Programs that may help cover their drug and treatment costs.

Indication and Important Safety Information

LUXTURNA (voretigene neparvovec-rzyl) 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 ≥ 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. 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.

Clinical Trial Overview of LUXTURNA™ (voretigene neparvovec-rzyl)

The safety and efficacy of LUXTURNA were assessed in one open-label, dose-exploration Phase 1 safety study (n=12) and one 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 dystrophy 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 crossover and receive LUXTURNA after one year of observation. All participants in these studies continue 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 has been previously reported in (The Lancet).

The efficacy of LUXTURNA in the Phase 3 study was established based on the 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.

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 median bilateral MLMT score change (intervention minus control group difference of 2; p=0.001) and median first-treated eye MLMT score change (intervention minus control group difference of 2; p=0.003). After crossing over to receive LUXTURNA, participants in the control group showed a similar response to those in the intervention group. The median bilateral MLMT score change of two was observed for the intervention group at the 30-day timepoint. This change score has been sustained for at least three years for the original intervention group and at least two years in the crossover group in 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 in the intervention group 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.

The U.S. Prescribing Information for LUXTURNA includes the following Warnings and Precautions: endophthalmitis; permanent decline in visual acuity; retinal abnormalities; increased intraocular pressure; expansion of intraocular air bubbles; and cataract. The most common adverse reactions (incidence ≥ 5%) were 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).

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-rzyl). The words ‘‘anticipate,’’ ‘‘believe,’’ ‘‘expect,’’ ‘‘intend,’’ ‘‘may,’’ ‘‘plan,’’ ‘‘predict,’’ ‘‘will,’’ ‘‘would,’’ ‘‘could,’’ ‘‘should,’’ ‘‘c expressions are 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: (i) our MAA submitted for LUXTURNA may not be approved by EMA; (ii) the data from our Phase 3 clinical trial of LUXTURNA may not support EU labeling for all biallelic RPE65 mutations other than Leber congenital amaurosis (LCA) or retinitis pigmentosa (RP); (iii) the improvements in functional vision demonstrated by LUXTURNA in our clinical trials may not be sustained over extended periods of time; and (iv) any one or more of our product candidates in preclinical or clinical development will not successfully be developed and commercialized. 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 Therapeutics 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: December 19, 2017 By: /s/ Joseph W. La Barge
Joseph W. La Barge
Chief Legal Officer