



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

DIVISION OF  
CORPORATION FINANCE

October 21, 2014

Via E-mail

Jeffrey D. Marrazzo, Esq.  
Chief Executive Officer  
Spark Therapeutics, Inc.  
3501 Civic Center Boulevard  
Philadelphia, PA 19104

**Re: Spark Therapeutics, Inc.  
Draft Registration Statement on Form S-1  
Submitted September 24, 2014  
CIK No. 0001609351**

Dear Mr. Marrazzo:

We have reviewed your draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended draft registration statement or filed registration statement, we may have additional comments.

Prospectus Summary  
Product Candidates, page 1

1. Please describe the meaning and significance of the following terms at their first use in this section:
  - adeno-associated virus (AAV);
  - adeno-associated virus (AAV) vector;
  - autosomal recessive mutations;
  - orphan product designation; and
  - phenotypic.

2. Please describe the conditions “Leber’s congenital amaurosis (‘LCA’)” and “retinitis pigmentosa (‘RP’)” and the difference between the two conditions the first time you reference them in this section.
3. We note the inclusion of “various” programs in your pipeline table under “Inherited Retinal Dystrophies” and “Neurodegenerative Diseases.” If you have not yet identified a molecule and medical indications for these various programs, please eliminate them from the table. They are too preliminary to be considered true pipeline products.
4. For your product candidates that are still in ongoing preclinical trials, please revise your pipeline table to shorten the arrow so that it does not extend to the end of the preclinical stage column.

Technology, page 2

5. Please describe the meaning and significance of the term “lentiviral vectors” at its first use in the second paragraph of this section.

Risks associated with our business, page 3

6. Please include a bullet discussing the risk of adverse events or the perception that adverse events could occur because the registrant’s products use virus particles to deliver gene therapy.
7. Please include a bullet discussing the competitive nature of the field of gene therapy and disclose that you know of at least twelve other companies that are developing AAV-based gene therapy products.
8. Please include a bullet discussing the extent to which you may not be able to protect your intellectual property rights and identify the intellectual property rights that the owner may license to other parties.
9. Please expand your first bullet point in this section to disclose your accumulated deficit to date.
10. Please expand your fourth bullet point in this section to state that no manufacturer of gene therapy products in the U.S. has received cGMP status.

Risk factors

Risks related to our business operations

Product liability lawsuits against us could cause us to incur substantial..., page 39

11. Please expand your disclosure in this risk factor to quantify the amount of product liability insurance you carry. Also, for any other type of insurance coverage discussed in other risk factors, please quantify the amount of insurance you carry.

Use of proceeds, page 58

12. For the first two bullet points in this section regarding SPK-RPE65 and SPK-FIX, please disclose how far in the development process the allocated proceeds will enable you to reach.

Industry and other data, page 59

13. We note your statements, “While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. While we believe our internal estimates and research are reliable and the market definitions of our market and industry are appropriate, neither such research nor these definitions are appropriate, neither such research nor these definitions have been verified by any independent source. It is not appropriate to disclaim liability for information contained in your prospectus. Please revise your disclosure to delete these statements or, alternatively, state that you are liable for this information.

Management’s discussion and analysis of financial condition and results of operations

Financial operations overview

Revenue, page 67

14. Please describe the condition “rhodopsin-linked autosomal dominant retinitis pigmentosa” the first time you reference it in this section.

Critical accounting policies and significant judgments and estimates

Stock-based compensation and fair value of stock, page 71

15. We may have additional comments on your accounting for equity issuances, including stock compensation and beneficial conversion features. Once you have established an offering price, please provide us an analysis explaining the reasons for the differences between recent valuations of your common stock, leading up to the IPO and the estimated offering price. In your analysis, include the Series 1 Units issued to CHOP and UIRF in October 2013.

16. Please revise your disclosure to state that the valuations are highly subjective and that you will no longer be required to estimate the fair value of your common shares underlying equity awards once those shares begin trading.
17. Please provide us the information that served as the basis for your valuation of the issuance of 25 million Series 1 common units to CHOP and UIRF in consideration for your acquisition and in-license of certain rights and property. Include the material assumptions used in this valuation.

Funding requirements, page 75

18. Please expand the last sentence of this section to clarify whether you are referring to funding through the filing of a BLA. If not, please specifically identify the point in the process to which you are referring.

Business

19. Please disclose, where applicable in your business section, when an investigational new drug application (“IND”) was filed for the commencement of clinical trials SPK-RPE65, the name of the trial sponsor and the subject of the IND.

Overview, page 76

20. We note your disclosure in the last paragraph on page 1 and the second paragraph on page 83 regarding your desire to move away from disease based regulation to mutation/gene based regulation. We also note that you will attempt to expand your orphan designation to include other diseases caused by RPE65 mutations. Please expand your disclosure in this section to describe what you have done to date to effect these changes and what discussions you have had with the FDA and the feedback you have received from the FDA, if any. Also, please clarify whether your anticipated 2016 BLA application will cover just LCA or other IRDs. If the application will cover only LCA, please amend the first row of the pipeline table on pages 2 and 81 accordingly.

Phase 1 proof-of-concept trials  
Study design, page 87

21. Please disclose the three doses of SPK-RPE65 that were evaluated during the 101 trial.

Pivotal Phase 3 clinical trial  
Trial design, page 90

22. We note that the Phase 3 trial for SPK-RPE65 uses the same dose level used in the 102 trial. Please revise your disclosure to quantify the dose level used in the Phase 3 trial.

Collaboration agreements

The Children's Hospital of Philadelphia, page 97

23. Please expand your disclosure regarding your license agreement with CHOP to describe the nature and scope of the "certain other know-how" for which CHOP granted you a non-exclusive worldwide license.
24. We note that your license agreement with CHOP requires you to pay milestones ranging from \$125,000 to \$5 million. Please revise your disclosure to provide the aggregate milestone payments to be paid under the agreement.
25. We note that the term of the license agreement with CHOP continues until the expiration of the last to expire of the licensed patent rights. Please expand your disclosure to provide the expiration date of the last to expire patent under the agreement.

University of Pennsylvania, page 98

26. Please expand your disclosure regarding your license agreement with Penn to disclose the material terms of the agreement, including the duration of the agreement, termination provisions and any payment provisions under the agreement including upfront payments, aggregate amounts paid to date under the agreement, aggregate future potential milestones to be paid under the agreement and royalty rates.

University of Iowa Research Foundation, page 99

27. Please expand your disclosure regarding your license agreement with UIRF to quantify the amount of the up-front cash payment you made to UIRF.

Genable, page 99

28. Please expand your disclosure regarding your license agreement with Genable to provide the aggregate amount of milestones that Genable is obligated to pay you under the agreement.
29. We note that the duration of the license agreement is conditioned upon the later of expiration of all of the patents subject to the license or 10 years after first commercial sale of the licensed product. Please expand your disclosure to provide the expiration date of the last to expire patent licensed to Genable. Also please provide the duration of the development consultancy agreement with Genable.

Principal stockholders, page 133

30. Please update your beneficial ownership table so that it is as of the most recent practicable date.

Notes to financial statements

(6) Members' equity, page F-11

31. You issued 5.1 million Series 2 Units to founders and .8 million Series 3 Units to employees. Please provide us your computation of the \$4.5 million grant date fair value of these units. Explain any difference between the fair value used for stock compensation purposes and the fair value of the 25 million Series 1 Units to CHOP in October 2013.

Notes to unaudited interim financial statements

(3) Summary of significant accounting policies, page F-19

32. Disclose your accounting policy for leases including free rent periods and explain the amount of deferred rent on the balance sheet.

(h) Revenue recognition, page F-21

33. Please provide all of the disclosure for your contractual arrangements with CHOP and Genable as required by ASC 605-25-50. Disclose the terms governing the initial payment from Genable and your accounting basis for deferral and recognition of revenue related to this payment.

(6) Stockholders' equity, page F-24

34. Please explain your consideration of the terms governing adjustments to the initial conversion price in determining your accounting treatment for the Series A and Series B convertible preferred stock. Refer us to the authoritative literature upon which you relied.
35. Tell us how you determined the fair value of 1.2 million units granted in 2014 which resulted in a weighted-average grant date fair value of \$0.32 as compared to the weighted-average grant date fair value of \$0.76 in 2013 (page F-13) and what caused the decline in fair value.
36. Tell us how you accounted for each outstanding Series 3 Unit converting into 0.19418865 share of common stock and the basis for your accounting.

General

37. We note that there are a number of additional exhibits that still need to be filed. Please provide these exhibits as promptly as possible. Please note that we may have comments on these materials once they are provided.

Jeffrey D. Marrazzo, Esq.  
Spark Therapeutics, Inc.  
October 21, 2014  
Page 7

38. Please confirm that the graphics included in your registration statement are the only graphics you will use in your prospectus. If those are not the only graphics, please provide any additional graphics prior to their use for our review.
39. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.

If you intend to respond to these comments with an amended draft registration statement, please submit it and any associated correspondence in accordance with the guidance we provide in the Division's October 11, 2012 announcement on the SEC website at <http://www.sec.gov/divisions/corpfin/cfannouncements/drsfilingprocedures101512.htm>.

Please keep in mind that we may publicly post filing review correspondence in accordance with our December 1, 2011 policy (<http://www.sec.gov/divisions/corpfin/cfannouncements/edgarcorrespondence.htm>). If you intend to use Rule 83 (17 CFR 200.83) to request confidential treatment of information in the correspondence you submit on EDGAR, please properly mark that information in each of your confidential submissions to us so we do not repeat or refer to that information in our comment letters to you.

You may contact Franklin Wyman at (202) 551-3660 or Lisa Vanjoske at (202) 551-3614 if you have questions regarding comments on the financial statements and related matters. Please contact Johnny Gharib at (202) 551-3170 or me at (202) 551-3715 with any other questions.

Sincerely,

/s/ Jeffrey P. Riedler

Jeffrey P. Riedler  
Assistant Director

cc: Via E-mail  
Lia Der Marderosian, Esq.  
Wilmer Cutler Pickering Hale and Dorr LLP