



This free writing prospectus relates only to the offering described below and should be read together with the preliminary prospectus dated January 28, 2015 (the "**Preliminary Prospectus**") included in Amendment No. 2 ("**Amendment No. 2**") to the Registration Statement on Form S-1 (File No. 333-201318) (the "**Registration Statement**"). The Preliminary Prospectus can be accessed through the following link: <http://www.sec.gov/Archives/edgar/data/1609351/000119312515022513/d776249ds1a.htm>.

References to "Spark," "the company," "we," "us" and "our" are used in the manner described in the Preliminary Prospectus. The following reflects updated information set forth in the Preliminary Prospectus contained in Amendment No. 2.

Updated offering information

Common stock offered by us	6,500,000 shares
Option to purchase additional shares	The underwriters have an option for a period of 30 days to purchase up to 975,000 additional shares of our common stock.
Common stock to be outstanding after this offering	22,990,367 shares (23,965,367 shares if the underwriters exercise their option to purchase additional shares in full)
Expected Initial Public Offering Price	Between \$19 and \$21 per share
Net Proceeds	<p>We estimate that the net proceeds to us of the sale of the common stock that we are offering will be approximately \$117.9 million, assuming an initial public offering price of \$20.00 per share, which is the midpoint of the price range set forth on the cover page of the Preliminary Prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds will be approximately \$136.0 million.</p> <p>We intend to use the net proceeds from this offering as follows: approximately \$11.0 million to fund external research and development expenses for SPKRPE65; approximately \$8.0 million to fund external research and development expenses for SPK-CHM; approximately \$5.0 million to fund external research and development expenses for our SPK-FIX program; approximately \$14.0 million to fund external research and development expenses for preclinical product candidates; and the remainder for working capital, general and administrative expenses, internal research and development expenses and other general corporate purposes, including pre-commercial activities, in-licenses or potential acquisitions.</p>
NASDAQ Global Select Market Symbol	ONCE

Updated summary balance sheet data

The balance sheet data presented under the section of the Preliminary Prospectus captioned “Prospectus summary—Summary financial information” has been revised as follows:

	As of September 30, 2014		
	Actual	Pro forma(1) (unaudited) (in thousands)	Pro forma as adjusted(2)
Balance Sheet Data:			
Cash and cash equivalents	\$67,273	\$ 67,273	\$ 185,446
Working capital	\$62,281	\$ 62,281	\$ 180,181
Total assets	\$80,914	\$ 80,914	\$ 197,753
Total preferred stock(3)	\$82,437	\$ —	\$ —
Total stockholders' equity	\$62,725	\$ 62,725	\$ 180,625

- (1) The pro forma balance sheet data give effect to (a) the issuance of 200,000 shares of restricted stock that are subject to certain milestone-based vesting conditions and were issued to Penn in connection with entry into our license agreement in December 2014 and (b) the automatic conversion of all outstanding shares of our preferred stock, including shares of preferred stock issuable as accrued dividends, into an aggregate of 10,200,050 shares of common stock upon the closing of this offering assuming the closing occurs on February 4, 2015.
- (2) The pro forma as adjusted balance sheet data give further effect to our issuance and sale of 6,500,000 shares of common stock in this offering (assuming no exercise by the underwriters of their option to purchase additional shares) at an assumed initial public offering price of \$20.00 per share, the midpoint of the price range listed on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.
- (3) The balance of total preferred stock is included in total stockholders' equity.

A \$1.00 increase (decrease) in the assumed initial public offering price of \$20.00 per share, which is the midpoint of the range listed on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents and working capital, total assets and total stockholders' equity by approximately \$6.0 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Update to “Capitalization”

The disclosure set forth in the first paragraph, the second paragraph, the table following the second paragraph and the third paragraph in the section of the Preliminary Prospectus captioned “Capitalization” has been revised as follows:

The following table sets forth our cash and cash equivalents and capitalization as of September 30, 2014, as follows:

- on an actual basis;
- on a pro forma basis to reflect (1) the issuance of 200,000 shares of restricted stock that are subject to certain milestone-based vesting conditions and were issued to Penn in connection with entry into our license agreement in December 2014; (2) the automatic conversion of all outstanding shares of our preferred stock, including shares of our preferred stock issuable as accrued stock dividends, into 10,200,050 shares of common stock upon the closing of this offering, assuming the closing occurs on February 4, 2015; and (3) the filing of our restated certificate of incorporation as of the closing date of this offering; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of 6,500,000 shares of common stock in this offering (assuming no exercise by the underwriters of the option to purchase additional shares) at an assumed initial public offering price of \$20.00 per share, the midpoint of the price range listed on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of the offering determined at pricing. You should read the information in this “Capitalization” section in conjunction with our financial statements and the related notes appearing at the end of this prospectus and the “Management’s discussion and analysis of financial condition and results of operations” section and other financial information contained in this prospectus.

	As of September 30, 2014		
	Actual	Pro forma (unaudited)	Pro forma as adjusted
	(in thousands, except share and per share data)		
Cash and cash equivalents	\$ 67,273	\$ 67,273	\$ 185,446
Series A preferred stock, par value \$0.001 per share; 5,000,000 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	\$ 10,000	\$ —	\$ —
Series B preferred stock, par value \$0.001 per share; 45,186,334 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	72,437	—	—
Preferred Stock, \$0.001 par value per share; no shares authorized, issued or outstanding, actual; 5,000,000 shares authorized, no shares issued or outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, par value \$0.001 per share; 95,700,000 shares authorized, 6,090,317 shares issued and outstanding, actual; 150,000,000 shares authorized, pro forma and pro forma as adjusted; 16,490,367 shares issued and outstanding, pro forma; 22,990,367 shares issued and outstanding pro forma as adjusted	6	16	23
Additional paid-in capital	52,869	135,296	253,189
Accumulated deficit	(72,587)	(72,587)	(72,587)
Total stockholders' equity	62,725	62,725	180,625
Total capitalization	\$ 62,725	\$ 62,725	\$ 180,625

A \$1.00 increase (decrease) in the assumed initial public offering price of \$20.00 per share, which is the midpoint of the range listed on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by approximately \$6.0 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Update to "Dilution"

The disclosure set forth in the fourth paragraph, the table immediately following the fourth paragraph, the fifth paragraph and the sixth paragraph in the section of the Preliminary Prospectus captioned "Dilution" has been revised as follows:

After giving effect to the sale of 6,500,000 shares of common stock that we are offering at an assumed initial public offering price of \$20.00 per share, which is the midpoint of the range listed on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of September 30, 2014 would have been approximately \$180.6 million, or approximately \$7.86 per share. This amount represents an immediate increase in pro forma net tangible book value of \$4.06 per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of approximately \$12.14 per share to new investors purchasing shares of common stock in this offering. We determine dilution by subtracting the pro forma, as adjusted net tangible book value per share after this offering from the amount of cash that a new investor paid for a share of common stock. The following table illustrates this dilution:

Assumed initial public offering price per share	\$20.00
Net tangible book value per share as of September 30, 2014	\$10.30
Pro forma decrease in net tangible book value per share as of September 30, 2014 attributable to the conversion of outstanding preferred stock, including shares issued as accrued dividends, as well as shares issued in December 2014	6.50
Pro forma net tangible book value per share as of September 30, 2014 before giving effect to this offering	3.80
Increase per share attributable to new investors	4.06
Pro forma as adjusted net tangible book value per share after this offering	7.86
Dilution per share to new investors	\$12.14

A \$1.00 increase (decrease) in the assumed initial public offering price of \$20.00 per share, which is the midpoint of the range listed on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per share after this offering by approximately \$0.26, and dilution in pro forma net tangible book value per share to new investors by approximately \$0.74, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase additional shares of our common stock in full in this offering, the pro forma as adjusted net tangible book value after the offering would be \$8.29 per share, the increase in pro forma net tangible book value per share to existing stockholders would be \$4.49 and the dilution to new investors would be \$11.71 per share, in each case assuming an initial public offering price of \$20.00 per share, which is the midpoint of the range listed on the cover page of this prospectus.

Spark Therapeutics, Inc. (“Spark”) has filed a registration statement (including a prospectus) with the Securities and Exchange Commission (the “SEC”) for the offering to which this communication relates. Before you invest, you should read the prospectus in that registration statement and other documents Spark has filed with the SEC for more complete information about Spark and this offering. You may get these documents for free by visiting EDGAR on the SEC web site at www.sec.gov. Alternatively, Spark, any underwriter or any dealer participating in the offering will arrange to send you the prospectus if you request it by contacting: J.P. Morgan Securities LLC, c/o Broadridge Financial Solutions, 1155 Long Island Avenue, Edgewood, NY 11717, or by telephone at (866) 803-9204; or Credit Suisse Securities (USA) LLC, Attention: Prospectus Department, One Madison Avenue, New York, NY 10010, or by telephone at (800) 221-1037, by facsimile at (212) 325-8057, or by email at newyork.prospectus@credit-suisse.com.