

INITIAL STATEMENT OF BENEFICIAL OWNERSHIP OF SECURITIES

OMB APPROVAL	
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Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporting Person* <u>Smith Cynthia</u> <hr/> (Last) (First) (Middle) C/O SPERO THERAPEUTICS, INC. 675 MASSACHUSETTS AVENUE, 14TH FLOOR <hr/> (Street) CAMBRIDGE MA 02139 <hr/> (City) (State) (Zip)	2. Date of Event Requiring Statement (Month/Day/Year) 03/19/2019	3. Issuer Name and Ticker or Trading Symbol <u>Spero Therapeutics, Inc. [SPRO]</u>	
		4. Relationship of Reporting Person(s) to Issuer (Check all applicable) <input checked="" type="checkbox"/> Director 10% Owner Officer (give title below) Other (specify below)	5. If Amendment, Date of Original Filed (Month/Day/Year) <hr/> 6. Individual or Joint/Group Filing (Check Applicable Line) <input checked="" type="checkbox"/> Form filed by One Reporting Person Form filed by More than One Reporting Person

Table I - Non-Derivative Securities Beneficially Owned

1. Title of Security (Instr. 4)	2. Amount of Securities Beneficially Owned (Instr. 4)	3. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)	4. Nature of Indirect Beneficial Ownership (Instr. 5)
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Table II - Derivative Securities Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 4)	2. Date Exercisable and Expiration Date (Month/Day/Year)		3. Title and Amount of Securities Underlying Derivative Security (Instr. 4)	4. Conversion or Exercise Price of Derivative Security	5. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)	6. Nature of Indirect Beneficial Ownership (Instr. 5)
	Date Exercisable	Expiration Date				

Explanation of Responses:

Remarks:

[Exhibit 24.1 - Power of Attorney](#)

No securities are beneficially owned.

/s/ Cynthia Smith 03/19/2019

** Signature of Reporting Person Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 5 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.

POWER OF ATTORNEY

Know all by these present, that the undersigned hereby constitutes and appoints each of Ankit Mahadevia, Chief Executive Officer of Spero Therapeutics, Inc. (the "Company"), and Joel Sendek, Chief Financial Officer of the Company, and Matthew J. Gardella, Matthew W. Tikonoff, Brian J. Shea, Kathryn Pajak, Anne T. Leland and Brenda L. Meyette of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., signing singly, with full power of substitution, the undersigned's true and lawful attorney-in-fact to:

- (1) execute for and on behalf of the undersigned, forms and authentication documents for EDGAR Filing Access;
- (2) do and perform any and all acts for and on behalf of the undersigned which may be necessary or desirable to complete and execute any such forms and authentication documents;
- (3) execute for and on behalf of the undersigned, in the undersigned's capacity as an officer, director and/or 10% shareholder of the Company, Forms 3, 4 and 5 in accordance with Section 16(a) of the Securities Exchange Act of 1934 and the rules thereunder;
- (4) do and perform any and all acts for and on behalf of the undersigned which may be necessary or desirable to complete and execute any such Form 3, 4 or 5 and timely file such form with the United States Securities and Exchange Commission and any stock exchange or similar authority; and
- (5) take any other action of any type whatsoever in connection with the foregoing which, in the opinion of such attorney-in-fact, may be of benefit to, in the best interest of, or legally required by, the undersigned, it being understood that the documents executed by such attorney-in-fact, on behalf of the undersigned pursuant to this Power of Attorney, shall be in such form and shall contain such terms and conditions as such attorney-in-fact may approve in such attorney-in-fact's discretion.

The undersigned hereby grants to each such attorney-in-fact full power and authority to do and perform any and every act and thing whatsoever requisite, necessary, or proper to be done in the exercise of any of the rights and powers herein granted, as fully to all intents and purposes as the undersigned might or could do if personally present, with full power of substitution or revocation, hereby ratifying and confirming all that such attorney-in-fact, or such attorney-in-fact's substitute or substitutes, shall lawfully do or cause to be done by virtue of this power of attorney and the rights and powers herein granted. The undersigned acknowledges that the foregoing attorneys-in-fact, in serving in such capacity at the request of the undersigned, is not assuming, nor is the Company assuming, any of the undersigned's responsibilities to comply with Section 16 of the Securities Exchange Act of 1934.

This Power of Attorney shall remain in full force and effect until the undersigned is no longer required to file Forms 3, 4 and 5 with respect to the undersigned's holdings of and transactions in securities issued by the Company, unless earlier revoked by the undersigned in a signed writing delivered to the foregoing attorneys-in-fact.

IN WITNESS WHEREOF, the undersigned has caused this Power of Attorney to be executed this 8th day of March, 2019.

/s/ Cynthia Smith

Cynthia Smith