

OMB APPROVAL	
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**STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP**

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

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

1. Name and Address of Reporting Person* <u>Larkin Cristina</u>  (Last) (First) (Middle) <u>C/O SPERO THERAPEUTICS, INC.</u> <u>675 MASSACHUSETTS AVENUE, 14TH FLOOR</u>  (Street) <u>CAMBRIDGE MA 02139</u>  (City) (State) (Zip)	2. Issuer Name and Ticker or Trading Symbol <u>Spero Therapeutics, Inc. [ SPRO ]</u>	5. Relationship of Reporting Person(s) to Issuer (Check all applicable)  Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) <u>Chief Operating Officer</u>
	3. Date of Earliest Transaction (Month/Day/Year) <u>12/16/2020</u>	
	4. If Amendment, Date of Original Filed (Month/Day/Year)	

**Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned**

1. Title of Security (Instr. 3)	2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any (Month/Day/Year)	3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5)			5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial Ownership (Instr. 4)
			Code	V	Amount	(A) or (D)	Price			
Common Stock	12/16/2020		M <sup>(1)</sup>		12,000	A	\$5.9	13,500	D	
Common Stock	12/16/2020		S <sup>(1)</sup>		12,000	D	\$19	1,500	D	

**Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)**

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transaction Code (Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4)	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)	
				Code	V	(A)	(D)	Date Exercisable	Expiration Date						Title
Stock Option (Right to Buy)	\$5.9	12/16/2020		M			12,000	(2)	07/05/2027	Common Stock	12,000	\$0.00	8,434	D	

**Explanation of Responses:**

- All transactions reported on this Form 4 were made pursuant to a previously adopted Rule 10b5-1 trading plan. Specifically, the transactions reported herein relate to option exercises and related sales (totaling 12,000 shares).
- All shares underlying this option were fully vested as of March 7, 2020.

**Remarks:**

/s/ Cristina Larkin 12/18/2020  
 \*\* 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 4 (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.