

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

SCHEDULE 13D

INFORMATION TO BE INCLUDED IN STATEMENTS FILED PURSUANT TO § 240.13d-1(a) AND AMENDMENTS  
THERE TO FILED PURSUANT TO 240.13d-2(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934  
(Amendment No. 5)\*

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SPERO THERAPEUTICS, INC.

(Name of Issuer)

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Common Stock, Par Value \$0.001

(Title of Class of Securities)

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84833T 10 3

(CUSIP Number)

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Victoria A. Whyte  
GlaxoSmithKline plc  
980 Great West Road  
Brentford, Middlesex TW8 9GS  
England  
Telephone: +44 (0)208 047 5000

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(Name, Address and Telephone Number of Person  
Authorized to Receive Notices and Communications)

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November 5, 2020

(Date of Event which Requires Filing of this Statement)

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If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of §§240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box.

**Note:** Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See §240.13d-7 for other parties to whom copies are to be sent.

\* The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act.

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1. NAMES OF REPORTING PERSONS I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

GlaxoSmithKline plc

2. CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP

(see instructions)

(a)

(b)

3. SEC USE ONLY

4. SOURCE OF FUNDS (see instructions)

WC

5. CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e)

6. CITIZENSHIP OR PLACE OF ORGANIZATION

England and Wales

7. SOLE VOTING POWER

1,740,606

NUMBER OF  
SHARES  
BENEFICIALLY  
OWNED BY  
EACH  
REPORTING  
PERSON WITH

8. SHARED VOTING POWER

-0-

9. SOLE DISPOSITIVE POWER

1,740,606

10. SHARED DISPOSITIVE POWER

-0-

11. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

1,740,606 shares of Common Stock (1)

12. CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES

(see instructions)

13. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)

6.4% of the shares of Common Stock (2)

14. TYPE OF REPORTING PERSON (see instructions)

CO

Footnotes:

(1) Common Stock are held of record by GSK Equity Investments, Limited, formerly S.R. One, Limited, an indirect, wholly-owned subsidiary of the Reporting Person.

(2) Based on 27,187,489 shares of the Issuer's Common Stock outstanding as of October 29, 2020, as reported in the Issuer's quarterly report for the quarter period ending September 30, 2020 on the Form 10-Q filed with the Securities and Exchange Commission (the "SEC") on November 5, 2020.

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**Item 1. Security and Issuer.**

This Amendment No. 5 to Schedule 13D (this “Statement”) amends and supplements the statement on Schedule 13D originally filed on November 16, 2017 and amended on July 17, 2018, September 19, 2018, February 14, 2020 and June 4, 2020 (the “Schedule 13D”) with respect to the shares of common stock, par value \$0.001 per share (the “Common Stock”), of Spero Therapeutics, Inc., a Delaware corporation (the “Issuer”). GlaxoSmithKline plc is filing this amendment to reflect its new percentage beneficial ownership in the Issuer, which has decreased as a result of an increase in the outstanding Common Stock of the Issuer. The Issuer’s principal executive offices are located at 675 Massachusetts Avenue, 14<sup>th</sup> Floor, Cambridge, Massachusetts 02139.

**Item 2. Identity and Background.**

The response set forth in Item 2 of the Schedule 13D is hereby amended by deleting Schedule 1 in its entirety and replacing it with Schedule 1 attached

**Item 5. Interest in Securities of the Issuer.**

The response set forth in Item 5 of the Schedule 13D is hereby amended by deleting the previous response in its entirety and replacing it with the following:

(a), (b) The information contained in rows 7, 8, 9, 10, 11, and 13 on each of the cover pages of this Statement is incorporated by reference in its entirety into this Item 5.

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**SIGNATURE**

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Date: December 7, 2020

GLAXOSMITHKLINE PLC

By: /s/ Victoria A. Whyte

Name: Victoria A. Whyte

Title: Authorized Signatory

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## Schedule 1

<u>Name</u>	<u>Business Address</u>	<u>Principal Occupation or Employment</u>	<u>Citizenship</u>
<b>Board of Directors</b>			
Emma Walmsley	980 Great West Road Brentford Middlesex, England TW8 9GS	Executive Director and Chief Executive Officer	British
Charles Bancroft	980 Great West Road Brentford Middlesex, England TW8 9GS	Company Director	US
Manvinder Singh Banga	980 Great West Road Brentford Middlesex, England TW8 9GS	Company Director	British & Indian
Dr. Hal Barron	269 E. Grand Avenue, South San Francisco, CA 94080	Chief Scientific Officer & President, R&D	US
Dr. Vivienne Cox	980 Great West Road Brentford Middlesex, England TW8 9GS	Company Director	British
Lynn Elsenhans	980 Great West Road Brentford Middlesex, England TW8 9GS	Company Director	US
Dr. Jesse Goodman	980 Great West Road Brentford Middlesex, England TW8 9GS	Company Director	US
Dr Laurie Glimcher	980 Great West Road Brentford Middlesex, England TW8 9GS	Company Director	US
Judy Lewent	980 Great West Road Brentford Middlesex, England TW8 9GS	Company Director	US
Iain MacKay	980 Great West Road Brentford Middlesex, England TW8 9GS	Executive Director & Chief Financial Officer	British

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Urs Rohner	980 Great West Road Brentford Middlesex, England TW8 9GS	Company Director	Swiss
Sir Jonathan Symonds	980 Great West Road Brentford Middlesex, England TW8 9GS	Chairman and Company Director	British
<b>Corporate Executive Team</b>			
Emma Walmsley	980 Great West Road Brentford Middlesex, England TW8 9GS	Executive Director and Chief Executive Officer	British
Dr. Hal Barron	269 E. Grand Avenue, South San Francisco, CA 94080	Chief Scientific Officer & President, R&D	US
Roger Connor	980 Great West Road Brentford Middlesex, England TW8 9GS	President, Global Vaccines	Irish
Diana Conrad	980 Great West Road Brentford Middlesex, England TW8 9GS	Senior Vice President, Human Resources	Canadian
James Ford	980 Great West Road Brentford Middlesex, England TW8 9GS	Senior Vice President & General Counsel	British & US
Nick Hirons	980 Great West Road Brentford Middlesex, England TW8 9GS	Senior Vice President, Global Ethics and Compliance	British & US
Sally Jackson	980 Great West Road Brentford Middlesex, England TW8 9GS	Senior Vice President, Global Communications and CEO Office	British
Iain MacKay	980 Great West Road Brentford Middlesex, England TW8 9GS	Executive Director & Chief Financial Officer	British

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Brian McNamara	184 Liberty Corner Road Warren NJ, 07059	Chief Executive Officer, GSK Consumer Healthcare	US
Luke Miels	980 Great West Road Brentford Middlesex, England TW8 9GS	President, Global Pharmaceuticals	Australian
David Redfern	980 Great West Road Brentford Middlesex, England TW8 9GS	Chief Strategy Officer	British
Regis Simard	980 Great West Road Brentford Middlesex, England TW8 9GS	President Pharmaceutical Supply Chain	French & British
Karenann Terrell	980 Great West Road Brentford Middlesex, England TW8 9GS	Chief Digital and Technology Officer	Canadian
Philip Thomson	980 Great West Road Brentford Middlesex, England TW8 9GS	President, Global Affairs	British
Deborah Waterhouse	980 Great West Road Brentford Middlesex, England TW8 9GS	Chief Executive Officer of ViiV Healthcare	British

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