

SCHEDULE 13G

Under the Securities Exchange Act of 1934

Amendment No.: 0*

Name of Issuer: Bicycle Therapeutics plc

Title of Class of Securities: American Depositary Shares

CUSIP Number: 088786108

Date of Event Which Requires Filing of this Statement: 12/31/2021

Check the appropriate box to designate the rule pursuant to which this Schedule is filed.

- Rule 13d-1(b)
 Rule 13d-1(c)
 Rule 13d-1(d)

* 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 the disclosures provided in a prior cover page.

The information required in 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 (however, see the Notes).

CUSIP No.: 088786108

1. NAME OF REPORTING PERSON
S.S. OR I.R.S. IDENTIFICATION NO. OF ABOVE PERSON
Janus Henderson Group plc
EIN #00-0000000
 2. CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
a.
b.
 3. SEC USE ONLY
 4. CITIZENSHIP OR PLACE OF ORGANIZATION
Jersey, Channel Islands
- NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:
5. SOLE VOTING POWER
0**
 6. SHARED VOTING POWER
1,695,409**
 7. SOLE DISPOSITIVE POWER
0**
 8. SHARED DISPOSITIVE POWER
1,695,409**
 9. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
1,695,409**
 10. CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES

Not applicable

11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)
5.8%**

12. TYPE OF REPORTING PERSON
IA, HC

** See Item 4 of this filing

Item 1.

(a). Name of Issuer: Bicycle Therapeutics plc ("Bicycle")

(b). Address of Issuer's Principal Executive Offices:

B900, Babraham Research Campus
Cambridge, United Kingdom CB22 3AT

Item 2.

(a)-(c). Name, Principal Business Address, and Citizenship of
Persons Filing:

(1) Janus Henderson Group plc
201 Bishopsgate
EC2M 3AE, United Kingdom
Citizenship: Jersey, Channel Islands

(d). Title of Class of Securities: American Depositary Shares

(e). CUSIP Number: 088786108

Item 3.

This statement is filed pursuant to Rule 13d-1 (b) or 13d-2(b) and the person filing, Janus Henderson Group plc ("Janus Henderson") is a parent holding company/control person in accordance with Section 240.13d-1(b)(ii)(G). See Item 4 for additional information.

Item 4. Ownership

The information in items 1 and 5 through 11 on the cover page(s) on Schedule 13G is hereby incorporated by reference.

Janus Henderson has an indirect 97% ownership stake in Intech Investment Management LLC ("Intech") and a 100% ownership stake in Janus Henderson Investors U.S. LLC ("JHIUS"), Henderson Global Investors Limited ("HGIL") and Janus Henderson Investors Australia Institutional Funds Management Limited ("JHIAIFML"), (each an "Asset Manager" and collectively as the "Asset Managers"). Due to the above ownership structure, holdings for the Asset Managers are aggregated for purposes of this filing. Each Asset Manager is an investment adviser registered or authorized in its relevant jurisdiction and each furnishing investment advice to various fund, individual and/or institutional clients (collectively referred to herein as "Managed Portfolios").

As a result of its role as investment adviser or sub-adviser to the Managed Portfolios, JHIUS may be deemed to be the beneficial owner of 1,695,409 shares or 5.8% of the shares outstanding of Bicycle American Depositary Shares held by such Managed Portfolios. However, JHIUS does not have the right to receive any dividends from, or the proceeds from the sale of, the securities held in the Managed Portfolios and disclaims any ownership associated with such rights.

Item 5. Ownership of Five Percent or Less of a Class

Not applicable.

Item 6. Ownership of More than Five Percent on Behalf of Another Person

The Managed Portfolios, set forth in Item 4 above, have the right to receive all dividends from, and the proceeds from the sale of, the securities held in their respective accounts.

The interest of any one such Managed Portfolio does not exceed 5% of the class of securities.

These shares were acquired in the ordinary course of business, and

not with the purpose of changing or influencing control of the Issuer.

Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on by the Parent Holding Company

Intech, JHIUS, HGIL and JHIAIFML are indirect subsidiaries of Janus Henderson and are registered investment advisers furnishing investment advice to Managed Portfolios.

Item 8. Identification and Classification of Members of the Group

Not applicable.

Item 9. Notice of Dissolution of Group

Not applicable.

Item 10. Certification

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired in the ordinary course of business and were not acquired for the purpose of and do not have the effect of changing or influencing the control of the issuer of such securities and were not acquired in connection with or as a participant in any transaction having such purposes or effect.

SIGNATURES

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.

JANUS HENDERSON GROUP PLC

By /s/ Kristin Mariani
Kristin Mariani, Head of North America Compliance, CCO
Date 2/11/2022

Name/Title Attorney-In-Fact

The original statement shall be signed by each person on whose behalf the statement is filed or his or her authorized representative. If the statement is signed on behalf of a person by his or her authorized representative other than an executive officer or general partner of the filing person, evidence of the representative's authority to sign on behalf of such person shall be filed with the statement (see Exhibit A), provided, however, that a power of attorney for this purpose which is already on file with the Commission may be incorporated by reference. The name and any title of each person who signs the statement shall be typed or printed beneath his or her signature.

EXHIBIT A

POWER OF ATTORNEY

The undersigned, Janus Henderson Group plc ("the Company"), does hereby make, constitute and appoint each of Kristin Mariani and Caroline Barotti acting severally, as its true and lawful attorneys-in-fact, for the purpose of, from time to time, executing in its name and on its behalf, whether the Company individually or as representative of others, any and all documents, certificates, instruments, statements, other filings and amendments to the foregoing (collectively, "documents") determined by such person to be necessary or appropriate to comply with ownership or control-person reporting requirements imposed by any United States or non-United States governmental or regulatory authority, including, without limitation, Forms 13D, 13F, 13G and 13H and any amendments to any of the foregoing as may be required to be filed with the Securities and Exchange Commission, and delivering, furnishing or filing any such documents with the appropriate governmental, regulatory authority or other person, and giving and granting to each such attorney-in-fact power and authority to act in the premises as fully and to all intents and purposes as the Company might or could do if personally present by one of its authorized signatories, hereby ratifying and confirming all that said attorney-in-fact shall lawfully do or cause to be done by virtue hereof. Any such determination by an

attorney-in-fact named herein shall be conclusively evidenced by such person's execution, delivery, furnishing or filing of the applicable document.

This power of attorney shall be valid from the date hereof and shall remain in full force and effect until either revoked in writing by the Company, or, in respect of any attorney-in-fact named herein, until such person ceases to be an employee of the Company or one of its affiliates.

IN WITNESS WHEREOF, the undersigned has caused this power of attorney to be executed as of this 30th day of September, 2021.

Janus Henderson Group plc

By: /s/ Bruce Koepfgen
Name: Bruce Koepfgen
Title: Executive Vice President, Head of North America