
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

SCHEDULE 13D

**Under the Securities Exchange Act of 1934
(Amendment No. 2)***

Spruce Biosciences, Inc.
(Name of Issuer)

Common Stock, par value \$0.0001 per share
(Title of Class of Securities)

85209E 109
(CUSIP Number)

**Barbara Fiorini Due
Novo Holdings A/S
Tuborg Havnevej 19
Hellerup, Denmark DK-2900
+45 3527 6592**

Copy to:

**B. Shayne Kennedy, Esq.
Latham & Watkins LLP
650 Town Center Drive, 20th Floor
Costa Mesa, CA 92626
Telephone: (714) 540-1235**

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

November 8, 2021
(Date of Event which Requires Filing of this Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition which is subject of this Schedule 13D, and is filing this statement because of Rule 13d-1(e), 13d-1(f) or 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 Rule 13d-7(b) 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 (the "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).

1.	Name of Reporting Person: Novo Holdings A/S	
2.	Check the Appropriate Box if a Member of Group (See Instructions): (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3.	SEC Use Only:	
4.	Source of Funds: WC	
5.	Check if Disclosure of Legal Proceedings is Required Pursuant to <u>Items 2(d)</u> or <u>2(e)</u> : <input type="checkbox"/>	
6.	Citizenship or Place of Organization: Denmark	
Number of Shares Beneficially Owned By Each Reporting Person With:	7.	Sole Voting Power: 4,514,336
	8.	Shared Voting Power: 0
	9.	Sole Dispositive Power: 4,514,336
	10.	Shared Dispositive Power: 0
11.	Aggregate Amount Beneficially Owned by Each Reporting Person: 4,514,336	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares: <input type="checkbox"/>	
13.	Percent of Class Represented By Amount In Row (11): 19.2%(1)	
14.	Type of Reporting Person: CO	

- (1) Based upon 23,463,089 shares of the Issuer's Common Stock outstanding as of November 12, 2021, as reported in the Issuer's 10-Q filed with the Securities and Exchange Commission ("SEC") on November 15, 2021.

Item 1. Security and Issuer

This amendment (“Amendment No. 2”) amends the Schedule 13D originally filed with the SEC on October 16, 2020, as amended on May 21, 2021 (collectively, the “Schedule”), to report and reflect that effective November 8, 2021, Tiba Aynечи Ph.D, a board member of the Issuer, ceased employment with Novo Ventures (US), Inc. and thus is no longer affiliated with Novo Holdings A/S. Except as specifically amended by this Amendment No. 2, each Item of the Schedule remains unchanged. All capitalized terms contained herein but not otherwise defined shall have the meanings ascribed to such terms in the Schedule.

Item 2. Identity and Background

Item 2 of the Schedule is amended and replaced in its entirety as follows:

- (a) Novo Holdings A/S is a Danish corporation and an investment firm focused on life sciences and finance that is wholly owned by Novo Nordisk Foundation (the “Foundation”), a Danish commercial foundation. Novo Holdings A/S is the holding company in the group of Novo companies (currently comprised of Novo Nordisk A/S and Novozymes A/S) and is responsible for managing the Foundation’s assets, including its financial assets. Based on the governance structure of Novo Holdings A/S and the Foundation, the Foundation is not deemed to have any beneficial ownership of the securities of the Issuer held by Novo Holdings A/S. Tiba Aynечи, Ph.D., a director of the Issuer, ceased employment with Novo Ventures (US), Inc. effective as of November 8, 2021 and is no longer affiliated with Novo Holdings A/S. Dr. Aynечи is not, and has not been, deemed to be a beneficial owner of the securities held by Novo Holdings A/S.

The name of each director and executive officer of both Novo Holdings A/S and the Foundation is set forth on Schedule I to this Schedule 13D.

- (b) The business address of both Novo Holdings A/S and the Foundation is Tuborg Havnevej 19, 2900 Hellerup, Denmark.

The residence or business address of each director and executive officer of both Novo Holdings A/S and the Foundation is set forth on Schedule I to this Schedule 13D.

- (c) Novo Holdings A/S, a holding company that is responsible for managing the Foundation’s assets, provides seed and venture capital to development stage companies and invests in well-established companies within the life science and biotechnology sector.

The Foundation is a Danish self-governing and profit-making foundation, whose objectives are to provide a stable basis for commercial and research activities undertaken by the group of Novo companies and to support scientific, humanitarian and social purposes through grants.

- (d) Within the last five years, neither Novo Holdings A/S, the Foundation, nor any person named in Schedule I has been convicted in any criminal proceedings.

- (e) Within the last five years, neither Novo Holdings A/S, the Foundation, nor any person named in Schedule I was a party to a civil proceeding of a judicial or administrative body of competent jurisdiction and as a result of such proceeding was or is subject to a judgment, decree or final order enjoining future violations of, or prohibiting or mandating activities subject to, federal or state securities laws or finding any violation with respect to such laws.

Item 4. Purpose of Transaction

Item 4 of the Schedule is amended and replaced in its entirety as follows:

The acquisitions of Issuer securities made by Novo Holdings A/S, as described in this Schedule 13D, were for investment purposes. Novo Holdings A/S intends to review its investments in the Issuer on a continuing basis and any actions Novo Holdings A/S might undertake will be dependent upon its review of numerous factors from time to time, including, but not limited to: an ongoing evaluation of the Issuer’s business, financial condition, operations and prospects; price levels of the Issuer’s securities; general market, industry and economic conditions; the relative attractiveness of alternative business and investment opportunities; and other future developments. Novo Holdings A/S may, at any time and from time to time, acquire additional securities of the Issuer, or retain or sell all or a portion of the securities of the Issuer then held, in the open market or in privately negotiated transactions.

Tiba Aynechi, Ph.D. was appointed to the board of directors of the Issuer in May 2016. Effective as of November 8, 2021, Dr. Aynechi is no longer employed by Novo Ventures (US), Inc., and is no longer affiliated with Novo Holdings A/S. Dr. Aynechi is not, and has not been, deemed to be a beneficial owner of the securities held by Novo Holdings A/S. Other than as described herein, Novo Holdings A/S currently does not have any plans or proposals that relate to, or would result in, any of the matters listed in Items 4(a)–(j) of Schedule 13D, although, depending on the factors discussed herein, Novo Holdings A/S may review or reconsider or change its purpose or formulate different plans, strategies, or proposals with respect thereto at any time.

Item 5. Interest in Securities of the Issuer

Item 5 of the Schedule is amended and replaced in its entirety as follows:

(a) Novo Holdings A/S beneficially owns 4,514,336 shares of Common Stock (the “Novo Shares”) representing approximately 19.2% of the Issuer’s outstanding shares of Common Stock, based upon 23,463,089 shares of the Issuer’s Common Stock outstanding as of November 12, 2021, as reported in the Issuer’s Form 10-Q filed with the SEC on November 15, 2021.

(b) Novo Holdings A/S is a Danish corporation wholly owned by the Novo Nordisk Foundation. Novo Holdings A/S has the sole power to vote and dispose of the Novo Shares. Neither the Foundation nor any person listed on Schedule I has the power to direct the vote as to, or the disposition of the Novo Shares.

(c) Novo Holdings A/S has not effected any transactions in the Issuer’s Common Stock within the past 60 days and neither the Foundation nor any person listed on Schedule I has effected any transactions in the Issuer’s Common Stock within the past 60 days.

(d) Novo Holdings A/S does not know of any other person having the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the Novo Shares.

(e) Not applicable.

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.

Dated: November 22, 2021

Novo Holdings A/S

/s/ Barbara Fiorini Due

By: Barbara Fiorini Due

Its: General Counsel

Schedule I

Information regarding each director and executive officer of both Novo Holdings A/S and the Novo Nordisk Foundation is set forth below.

<i>Novo Holdings A/S</i>			
Name, Title	Address	Principal Occupation	Citizenship
Lars Rebien Sørensen, Chairman of the Board	Christianholms Tværvej 27, 2930 Klampenborg Denmark	Professional Board Director	Denmark
Steen Riisgaard, Vice Chairman of the Board	Hestetangsvej 155, 3520 Farum, Denmark	Professional Board Director	Denmark
Jean-Luc Butel, Director	235 Arcadia Road unit # 10-3 289843 Singapore	Global Healthcare Advisor, President, K8 Global Pte Ltd.	Singapore
Jeppe Christiansen, Director	c/o Kasper Fonager Christiansen Classensgade 59, 5. th. 2100 København Ø Denmark	Chief Executive Officer, Fondsmæglerselskabet Maj Invest A/S	Denmark
Francis Michael Cyprian Cuss, Director	111 Rippling Brook Way, Bernardsville, NJ 07924 USA	Former Executive Vice President and Chief Scientific Officer of Bristol-Myers Squibb	United Kingdom
Viviane Monges, Director	Chemin de Craivavers 32, 1012 Lausanne, Switzerland	Professional Board Director	France
Henrik Poulsen, Director	Emiliekildevej 36 2930 Klampenborg Denmark	Professional Board Director and Senior Advisor, A.P. Møller Holding A/S,	Denmark
Poul Carsten Stendevad, Director	3220 Idaho Ave NW Washington, DC 20016 USA	Co-Chief Investment Officer for Sustainability, Bridgewater Associates	Denmark
Kasim Kutay, Chief Executive Officer of Novo Holdings A/S	Bredgade 65, 3.tv. 1260 Copenhagen K. Denmark	Chief Executive Officer of Novo Holdings A/S	United Kingdom

<i>Novo Nordisk Foundation</i>			
Name, Title	Address	Principal Occupation	Citizenship
Lars Rebien Sørensen, Chairman of the Board	Christianholms Tværvej 27 2930 Klampenborg Denmark	Professional Board Director	Denmark
Marianne Philip, Vice Chairman of the Board	Annasvej 28 2900 Hellerup Denmark	Attorney	Denmark

Novo Nordisk Foundation

Name, Title	Address	Principal Occupation	Citizenship
Steen Riisgaard, Director	Hestetangsvej 155 3520 Farum Denmark	Professional Board Director	Denmark
Mads Krogsgaard Thomsen, Chief Executive Officer	Præstevejen 38 3230 Græsted Denmark	Chief Executive Officer, Novo Nordisk Foundation	Denmark
Anne Marie Kverneland, Director	Nybrovej 216 2800 Kgs. Lyngby Denmark	Laboratory technician, Novo Nordisk A/S	Denmark
Lars Bo Køppler, Director	Anemonevej 7 3550 Slangerup Denmark	Technician, Novozymes A/S	Denmark
Lars Henrik Fugger, Director	72 Staunton Road, Headington Great Britain	Professor, John Radcliffe Hospital, University of Oxford, Oxford, Great Britain	Denmark
Lars Henrik Munch, Director	Galionsvej 46 1437 Copenhagen K Denmark	Professional Board Director	Denmark
Mads Boritz Grøn, Director	Horsevænget 4 3400 Hillerød Denmark	Senior Lead Auditor	Denmark
Liselotte Højgaard, Director	Grønningen 21 1270 Copenhagen K Denmark	Professor	Denmark