UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

JAGUAR HEALTH, INC.

(Exact name of registrant as specified in its charter)

Delaware

46-2956775

(State or Other Jurisdiction of Incorporation or Organization)

(I.R.S. Employer Identification No.)

200 Pine Street, Suite 400 San Francisco, California 94104 (415) 371-8300

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Lisa A. Conte Chief Executive Officer and President Jaguar Health, Inc. 200 Pine Street, Suite 400 San Francisco, California 94104 (415) 371-8300

(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

Copies of all correspondence to:

Donald C. Reinke, Esq. Michael S. Lee, Esq. Reed Smith LLP 101 Second Street, Suite 1800 San Francisco, California 94105 (415) 543-8700

Approximate date of commencement of proposed sale of the securities to the public: From time to time after the effective date of this registration statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box: o

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: x

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. x File No. 333-248763

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. o

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer o

Accelerated filer o

Non-accelerated filer x

Smaller reporting company x Emerging growth company o

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. o

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)(2)		Amount of Registration Fee(3)	
Common Stock, par value \$0.0001 per share	\$	2,495,000.00	\$	272.20

- (1) Represents only the additional dollar amount of securities being registered, with an aggregate offering price not to exceed \$2,495,000. This does not include the securities that the registrant previously registered on the registration statement on Form S-3 (File No. 333-248763) ("Prior Registration Statement").
- 2) Calculated in accordance with Rule 457(o) under the Securities Act of 1933, as amended (the "Securities Act"). Based on the public offering price per share.
- The Registrant previously registered securities for a primary offering having a proposed maximum aggregate offering price of \$40,000,000 on the Prior Registration Statement. As of the date hereof, a balance of \$12,805,000 of such securities remains to be offered and sold under the Prior Registration Statement. In accordance with Rule 462(b) promulgated under the Securities Act, an additional amount of the registrant's securities having a proposed maximum aggregate offering price of \$2,495,000 is hereby registered, representing no more than 20% of the maximum aggregate offering price of unsold securities under the Prior Registration Statement.

This Registration Statement shall become effective upon filing with the Securities and Exchange Commission, in accordance with Rule 462(b) promulgated under the Securities Act, as amended.

EXPLANATORY NOTE AND INCORPORATION BY REFERENCE

This Registration Statement is being filed pursuant to Rule 462(b) as promulgated under the Securities Act of 1933, as amended, and includes the registration statement facing page, this page, the signature page, an exhibit index and the required opinion and consents solely to register up to an aggregate of \$2,495,000 of the Registrant's common stock, par value \$0.0001 per share. The contents of the Prior Registration Statement, including the exhibits and power of attorney thereto and all documents filed by the Registrant with the Securities and Exchange Commission and incorporated or deemed to be incorporated by reference in the Prior Registration Statement, are hereby incorporated by reference in this Registration Statement.

The required opinion, consents and powers of attorney are listed on an Exhibit Index attached hereto and filed herewith.

EXHIBIT INDEX

Exhibit No.	Description
5.1	Opinion of Reed Smith LLP as to validity of the securities being registered.
23.1	Consent of Mayer Hoffman McCann P.C., independent registered public accounting firm.
23.2	Consent of Reed Smith LLP (included in Exhibit 5.1).
24.1*	Power of Attorney.

^{*} Previously filed on the signature page of the Registrant's Registration Statement on Form S-3 (File No. 333-248763), filed with the Securities and Exchange Commission on September 11, 2020, and incorporated by reference herein.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Francisco, State of California, on this 9th day of April, 2021.

JAGUAR HEALTH, INC.,

By:	/s/ Lisa A. Conte			
	Lisa A. Conte			
	Chief Executive Officer and President			

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the date indicated.

Signature	Title	Date
/s/ Lisa A. Conte Lisa A. Conte	Chief Executive Officer, President and Director (Principal Executive Officer)	April 9, 2021
/s/ Carol Lizak Carol Lizak	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	April 9, 2021
James J. Bochnowski	Chairman of the Board	
John Micek III	Director	
* Jonathan B. Siegel	Director	April 9, 2021
* Greg J. Divis	Director	April 9, 2021
*By: /s/ LISA A. CONTE Name: Lisa A. Conte Title: Attorney-in-fact		
	II-3	



Reed Smith LLP 101 Second Street Suite 1800 San Francisco, CA 94105-3659 Tel +1 415 543 8700 Fax +1 415 391 8269 reedsmith.com

April 9, 2021

Jaguar Health, Inc. 200 Pine Street, Suite 400 San Francisco, California 94104

Ladies and Gentlemen:

We have acted as counsel to Jaguar Health, Inc., a Delaware corporation (the "Company"), in connection with the preparation and filing of a registration statement on Form S-3 (such registration statement, including the documents incorporated by reference therein, the "462(b) Registration Statement") filed by the Company with the Securities and Exchange Commission (the "Commission") pursuant to Rule 462(b) promulgated under the Securities Act of 1933, as amended (the "Securities Act"). The 462(b) Registration Statement relates to the offer and sale by the Company from time to time of up to an aggregate of \$2,495,000 of shares (the "Shares") of the Company's common stock, par value \$0.0001 per share (the "Common Stock"), pursuant to that certain At the Market Offering Agreement, dated as of October 5, 2020, by and between the Company and Ladenburg Thalmann Co. Inc. as sales agent (the "Sales Agreement"). The 462(b) Registration Statement is filed in connection with, and incorporates by reference the information contained in, the Shelf Registration Statement on Form S-3 (Registration No. 333-248763) filed with the Commission on September 11, 2020 and declared effective on September 23, 2020 (the "Shelf Registration Statement" and together with the 462(b) Registration Statement, the "Registration Statements"). This opinion letter is furnished in accordance with the requirements of Item 601(b)(5) of Regulation S-K, 17 C.F.R. § 229.601(b)(5).

We have reviewed originals or copies of the Registration Statements, the certificate of incorporation and bylaws of the Company, as amended through the date hereof, and such other corporate records, agreements and documents of the Company, certificates or comparable documents of public officials and officers of the Company and have made such other investigations as we have deemed necessary as a basis for the opinion set forth below.

In rendering the opinion set forth below, we have assumed:

- a. the genuineness of all signatures;
- b. the legal capacity of natural persons;
- c. the authenticity of all documents submitted to us as originals;
- d. the conformity to original documents of all documents submitted to us as duplicates or conformed copies;

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- e. as to matters of fact, the truthfulness of the representations made in certificates or comparable documents of public officials and officers of the Company; and
- f. the amount of valid consideration paid in respect of such Shares will equal or exceed the par value of such Shares.

We have not independently established the validity of the foregoing assumptions.

Based upon the foregoing, and subject to the qualifications, assumptions and limitations stated herein, we are of the opinion that the Shares have been duly authorized by all necessary corporate action on the part of the Company, and when issued and delivered by the Company pursuant to the Sales Agreement against payment of the requisite consideration therefor, will be validly issued, fully paid and nonassessable.

Our opinion is limited to the General Corporation Law of the State of Delaware, and we do not express any opinion herein concerning any other law. This opinion letter speaks only as of its date.

We hereby consent to the filing of this opinion letter as Exhibit 5.1 to the 462(b) Registration Statement and to the use of our name under the caption "Legal Matters" in the prospectus included in the Registration Statements. In giving such consent, we do not hereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act, and the rules and regulations of the Commission promulgated thereunder.

Very truly yours,

/s/ REED SMITH LLP
Reed Smith LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in this Registration Statement on Form S-3 dated April 9, 2021, of our report dated March 31, 2021, relating to the consolidated financial statements of Jaguar Health, Inc. as of December 31, 2020 and 2019, and the related consolidated statements of operations, changes in convertible preferred stock and stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2020.

/s/ Mayer Hoffman McCann P.C.
San Diego, California
April 9, 2021