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

**POST-EFFECTIVE AMENDMENT NO. 3
to
FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

Cue Biopharma, Inc.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

47-3324577
(IRS Employer
Identification Number)

**21 Erie Street
Cambridge, MA 02139
(617) 949-2680**
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Daniel R. Passeri
Chief Executive Officer
Cue Biopharma, Inc.
21 Erie Street
Cambridge, MA 02139
(617) 949-2680**
(Name, address, including zip code, and telephone number, including area code, of agent for service)

**Please send copies of all communications to:
Cynthia T. Mazareas
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109
(617) 526-6000**

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement as determined by market conditions.

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

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.

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please 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 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.

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.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a 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 Accelerated filer
 Non-accelerated filer Smaller reporting company
 Emerging growth company

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.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered ⁽¹⁾	Proposed Maximum Offering Price per Unit ⁽¹⁾	Proposed Maximum Aggregate Offering Price ⁽¹⁾	Amount of Registration Fee
Common Stock				
Preferred Stock				
Debt Securities				
Warrants				
Rights				
Units ⁽²⁾				
Total			\$300,000,000 ⁽³⁾	\$38,940 ⁽⁴⁾

- (1) Pursuant to Form S-3 General Instruction II.D, this information is not required to be included. An indeterminate amount of the securities of each identified class is being registered as may from time to time be offered hereunder at indeterminate prices, along with an indeterminate number of securities that may be issued upon exercise, settlement, exchange or conversion of securities offered or sold hereunder as shall have an aggregate initial offering price not to exceed \$300,000,000. Pursuant to Rule 416 under the Securities Act of 1933, as amended (the “Securities Act”), this registration statement also covers any additional securities that may be offered or issued in connection with any stock split, stock dividend or pursuant to anti-dilution provisions of any of the securities. Separate consideration may or may not be received for securities that are issuable upon conversion, exercise or exchange of other securities.
- (2) Consisting of some or all of the securities listed above, in any combination.
- (3) The total amount to be registered and the proposed maximum aggregate offering price are estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act.
- (4) Previously paid.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

Post-Effective Amendment No. 1 to the Registration Statement on Form S-3 (File No. 333-239357) (the “Registration Statement”) of Cue Biopharma, Inc. (the “Registrant”) was filed because the Registrant expected that it would no longer be a well-known seasoned issuer (as such term is defined in Rule 405 of the Securities Act of 1933, as amended) upon the filing of its Annual Report on Form 10-K for the fiscal year ended December 31, 2020. Post-Effective Amendment No. 1 added disclosure to the Registration Statement required for a registrant other than a well-known seasoned issuer and made certain other amendments set forth therein. Post-Effective Amendment No. 2 was filed using EDGAR submission type POS AM to convert the Registration Statement to the proper EDGAR submission type for a non-automatic shelf registration statement and made certain other amendments. This Post-Effective Amendment No. 3 is being filed to state that documents filed by the Registrant under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, between the date of the initial Registration Statement and the effectiveness of the Registration Statement are incorporated by reference into the prospectus.

This registration statement contains two prospectuses:

- a base prospectus which covers the offering, issuance and sale by us of up to \$300,000,000 of the securities identified above, from time to time in one or more offerings; and
- a sales agreement prospectus covering the offering, issuance and sale by us of up to \$17,159,674 of our common stock that may be issued and sold from time to time under a sales agreement with Stifel, Nicolaus & Company, Incorporated.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered pursuant to the base prospectus will be specified in a prospectus supplement to the base prospectus. The sales agreement prospectus immediately follows the base prospectus. The common stock that may be offered, issued and sold by us under the sales agreement prospectus is included in the \$300,000,000 of securities that may be offered, issued and sold by us under the base prospectus.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated May 21, 2021



CUE BIOPHARMA, INC.

Prospectus

\$300,000,000

Common Stock

Preferred Stock

Debt Securities

Warrants

Rights

Units

We may offer and sell up to \$300,000,000 in the aggregate of securities from time to time in one or more offerings. These securities are inclusive of \$40,000,000 of shares of common stock that we may issue and sell pursuant to the previously announced At-the-Market Equity Offering Sales Agreement that we entered into with Stifel, Nicolaus & Company, Incorporated on June 22, 2020. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any applicable prospectus supplement before you invest.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement.

Our common stock is listed on the Nasdaq Capital Market under the symbol "CUE."

Investing in these securities involves certain risks. See "[Risk Factors](#)" on page 3 of this prospectus, included in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase these securities .

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is _____, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (the “SEC”) utilizing a “shelf” registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to \$300,000,000 (inclusive of \$40,000,000 of shares of common stock that we may issue and sell pursuant to the previously announced At-the-Market Equity Offering Sales Agreement that we entered into with Stifel, Nicolaus & Company, Incorporated on June 22, 2020).

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of the securities being offered. That prospectus supplement may include a discussion of any risk factors or other special consideration that apply to those securities. The prospectus supplement may also add, update or change information contained in this prospectus. If there is any inconsistency between the information in this prospectus and a prospectus supplement, you should rely on the information in that prospectus supplement. You should read both this prospectus and any applicable prospectus supplement together with additional information described above under the headings “Where You Can Find More Information” and “Incorporation by Reference.”

When acquiring any securities discussed in this prospectus, you should rely on the information provided in this prospectus and the prospectus supplement, including the information incorporated by reference. Neither we, nor any underwriters or agents, have authorized anyone to provide you with different information. We are not offering the securities in any state where such an offer is prohibited. You should not assume that the information in this prospectus, any prospectus supplement, or any document incorporated by reference, is truthful or complete at any date other than the date mentioned on the cover page of those documents. You should also carefully review the section entitled “Risk Factors,” which highlights certain risks associated with an investment in our securities, to determine whether an investment in our securities is appropriate for you.

Unless the context otherwise indicates, references in this prospectus to “we,” “our” and “us” refer, collectively, to Cue Biopharma, Inc., a Delaware corporation, and its consolidated subsidiaries

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC’s website at www.sec.gov. Our web site is located at www.cuebiopharma.com. The information contained on, or that may be obtained from, our web site is not part of this prospectus.

We will provide, upon written or oral request, without charge to you, including any beneficial owner to whom this prospectus is delivered, a copy of any or all of the documents incorporated herein by reference other than the exhibits to those documents, unless the exhibits are specifically incorporated by reference into the information that this prospectus incorporates. You should direct a request for copies to us at Cue Biopharma, Inc., 21 Erie Street, Cambridge, Massachusetts 02139 or you may call us at (617) 949-2680.

INCORPORATION BY REFERENCE

This prospectus “incorporates by reference” certain information that we have filed with the SEC under the Securities Exchange Act of 1934, as amended (the “Exchange Act”). This means we are disclosing important information to you by referring you to those documents. We incorporate by reference the documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of the initial registration statement and the effectiveness of the registration statement until the offering is terminated:

- Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2020 filed with the SEC on March 9, 2021, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our [definitive proxy statement](#) for the 2021 Annual Meeting of Stockholders;
- Quarterly Report on [Form 10-Q](#) for the fiscal quarter ended March 31, 2021, as filed with the SEC on May 10, 2021; and
- The description of our Common Stock contained in our Registration Statement on [Form 8-A](#), filed with the SEC pursuant to Section 12(g) of the Exchange Act on December 13, 2017, including any amendment or reports filed for the purpose of updating such description.

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To the extent that any information contained in any report on Form 8-K, or any exhibit thereto, was furnished to, rather than filed with, the SEC, such information or exhibit is specifically not incorporated by reference.

You should rely only on the information incorporated by reference or provided in this prospectus. We have authorized no one to provide you with different information. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of this document. All documents that we file pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of the initial registration statement and the effectiveness of the registration statement and prior to the termination of the offering will be deemed to be incorporated in this prospectus by reference and will be a part of this prospectus from the date of the filing of the document. Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus modifies or supersedes that statement. Any statement that is modified or superseded will not constitute a part of this prospectus, except as modified or superseded.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus and the information incorporated by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”), and Section 21E of the Exchange Act. All statements, other than statements of historical facts, contained in this herein and therein, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements include, among other things, statements about:

- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and our research and development programs;
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing;
- our expectations regarding our ability to fund our projected operating requirements with our existing cash resources and the period in which we expect that such cash resources will enable us to fund such operating requirements;
- our plans to develop our product candidates;
- the timing of and our ability to submit applications for, obtain and maintain regulatory approvals for our product candidates;
- the potential advantages of our product candidates;
- the rate and degree of market acceptance and clinical utility of our product candidates, if approved;
- our estimates regarding the potential market opportunity for our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- the impact of government laws and regulations;

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- our competitive position;
- developments relating to our competitors and our industry;
- our ability to establish collaborations or obtain additional funding; and
- the impacts of the COVID-19 pandemic.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. You are cautioned that these forward-looking statements are only predictions and are subject to risks, uncertainties and assumptions that are referenced in the section of any accompanying prospectus supplement entitled “Risk Factors.” You should also carefully review the risk factors and cautionary statements described in the other documents we file from time to time with the SEC, specifically our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

You should read this prospectus, the documents incorporated by reference in this prospectus and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this prospectus and incorporated by reference herein are made as of the date hereof, and we do not assume any obligation to update any forward-looking statements except as required by applicable law.

This prospectus and the information incorporated by reference in this prospectus include statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties as well as our own estimates. All of the market data used in this prospectus and the information incorporated by reference in this prospectus involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our drug candidates include several key assumptions based on our industry knowledge, industry publications, third-party research, and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

RISK FACTORS

Investing in our securities involves risk. See the risk factors described in our Annual Report on Form 10-K for our most recent fiscal year (together with any material changes thereto contained in subsequently filed Quarterly Reports on Form 10-Q) and those contained in our other filings with the SEC, which are incorporated by reference in this prospectus and any accompanying prospectus supplement.

The prospectus supplement applicable to each type or series of securities we offer may contain a discussion of risks applicable to the particular types of securities that we are offering under that prospectus supplement. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the caption “Risk Factors” in the applicable prospectus supplement, together with all of the other information contained in the prospectus supplement or appearing or incorporated by reference in this prospectus. These risks could materially affect our business, results of operations or financial condition and cause the value of our securities to decline. You could lose all or part of your investment.

THE COMPANY

Overview

We are a clinical-stage biopharmaceutical company engineering a novel class of injectable biologics to selectively engage and modulate targeted T cells directly within the patient's body. We believe our proprietary Immuno-STAT™ (*Selective Targeting and Alteration of T Cells*) platform will allow us to harness the fullest potential of an individual's intrinsic immune repertoire for restoring health while avoiding the deleterious side effects of broad immune activation (for immuno-oncology or infectious immunity) or broad immune suppression (for autoimmunity and inflammation). In addition to the selective modulation of T cell activity, we believe Immuno-STATs offer several key points of potential differentiation over competing approaches, including modularity and versatility providing broad disease coverage, manufacturability, and convenient administration.

Through rational protein engineering, we leverage the modular and versatile nature of the Immuno-STAT platform to design drug product candidates for selective immune modulation in cancer, chronic infectious disease, and autoimmune disease. To address the needs of these clinical indications, we have developed four biologic series within the Immuno-STAT platform: CUE-100, CUE-200, CUE-300, and CUE-400, each specifically designed through rational engineering to possess distinct signaling modules for desired biological mechanisms that may be applied across many diseases. The CUE-100 series exploits rationally engineered IL-2 in context of the core Immuno-STAT framework for selective activation of targeted tumor-specific T cells, while the CUE-200 series is focused on cell surface receptors including CD80 and/or 4-1BBL to address T cell exhaustion associated with chronic infections. The CUE-300 series, being developed for autoimmune diseases, incorporates the inhibitory PD-L1 co-modulator for selective inhibition of the autoreactive T cell repertoire. This approach is pertinent for autoimmune diseases with known, well characterized, limited or few autoantigens, such as type 1 diabetes. The CUE-400 series, for autoimmune diseases with diverse or unknown autoantigens, represents a novel class of bispecific molecules that can selectively and effectively expand induced regulatory T cells, or iTregs. We categorize these molecules as "pathway-specific modulators," or PSM. The first candidate, CUE-401, incorporates the two key biological signals that are necessary for generation of iTregs, namely IL-2 and TGF-beta. Based on structure-based rational protein engineering, both IL-2 and TGF-beta have been affinity tuned (i.e. the binding strength has been optimized) to maintain on-target engagement while minimizing systemic toxicities.

Our drug product candidates are in various stages of clinical and preclinical development, and while we believe that these candidates hold potential value, our activities are subject to significant risks and uncertainties. We have not yet commenced any commercial revenue-generating operations, have limited cash flows from operations, and will need to access additional capital to fund our growth and ongoing business operations.

Corporate Information

We were incorporated as Imagen Biopharma, Inc. in Delaware on December 31, 2014. In October 2016, we changed our name to Cue Biopharma, Inc. The address of our corporate headquarters is 21 Erie Street, Cambridge, Massachusetts 02139 and our telephone number is (617) 949-2680. Our website can be accessed at www.cuebiopharma.com. The information contained on, or that may be obtained from, our website is not, and shall not be deemed to be, a part of this prospectus.

USE OF PROCEEDS

We currently intend to use the estimated net proceeds from the sale of these securities for general corporate and working capital purposes, including to fund ongoing research and development activities for our drug candidates and platform technologies. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds from the sale of these securities. Our plans to use the estimated net proceeds from the sale of these securities may change, and if they do, we will update this information in a prospectus supplement.

AUTHORIZED CAPITAL STOCK

Our certificate of incorporation currently provides us the authority to issue 100,000,000 shares of common stock, par value \$0.001 per share, and 10,000,000 shares of preferred stock, par value \$0.001 per share.

DESCRIPTION OF SECURITIES WE MAY OFFER

We may issue from time to time, in one or more offerings, the following securities:

- shares of common stock;
- shares of preferred stock;
- debt securities, which may include senior debt securities, subordinated debt securities or senior subordinated debt securities;
- warrants for the purchase of debt securities, preferred stock or common stock;
- units consisting of two or more of the foregoing; and
- rights to purchase our debt securities, common stock, preferred stock or other securities.

Set forth below is a general description of the securities that may be offered under this prospectus. We will set forth in the applicable prospectus supplement and/or free writing prospectus a specific description of the securities that are offered under this prospectus. The terms of the offering of our common stock, preferred stock or any such other securities, the initial offering price and the net proceeds to us will be contained in the prospectus supplement, and other offering material, relating to such offer.

We may sell the securities being offered pursuant to this prospectus directly to purchasers, to or through underwriters, through dealers or agents, or through a combination of such methods. The prospectus supplement with respect to the securities being offered will set forth the terms of the offering of those securities, including the names of any such underwriters, dealers or agents, the purchase price, the net proceeds to us, any underwriting discounts and other items constituting underwriters' compensation, the initial public offering price, any discounts or concessions allowed or reallocated or paid to dealers and any securities exchanges on which such securities may be listed.

DESCRIPTION OF COMMON STOCK WE MAY OFFER

The following summary description of our common stock is based on the provisions of our certificate of incorporation and bylaws and the applicable provisions of the General Corporation Law of the State of Delaware. This information may not be complete in all respects and is qualified entirely by reference to the provisions of our certificate of incorporation, bylaws and the General Corporation Law of the State of Delaware. For a description of provisions of our certificate of incorporation and bylaws that may have the effect of delaying, deferring or preventing a change in control, see the discussion below under the heading "Certain Provisions of Delaware Law and of the Company's Certificate of Incorporation and Bylaws." For information on how to obtain copies of our certificate of incorporation and bylaws, see the discussion above under the heading "Where You Can Find More Information."

We may offer our common stock issuable upon the conversion of debt securities or preferred stock and upon the exercise of warrants.

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Voting Rights

Each outstanding share of our common stock is entitled to one vote on all matters submitted to a vote of shareholders. There is no cumulative voting.

Dividend and Liquidation Rights

The holders of outstanding shares of our common stock are entitled to receive dividends out of assets legally available for the payment of dividends at the times and in the amounts as our board of directors may from time to time determine. The shares of our common stock are neither redeemable nor convertible. Holders of our common stock have no preemptive or subscription rights to purchase any of our securities and no sinking fund provisions apply to our common stock. Upon our liquidation, dissolution or winding up, the holders of our common stock are entitled to receive pro rata our assets which are legally available for distribution, after payment of all debts and other liabilities and subject to the prior rights of any holders of preferred stock then outstanding.

We have never paid any cash dividends on our common stock.

Fully Paid and Non-Assessable

All outstanding shares of our common stock are fully paid and non-assessable.

Nasdaq Listing

Our common stock is listed on the Nasdaq Capital Market under the symbol "CUE."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A..

DESCRIPTION OF PREFERRED STOCK WE MAY OFFER

This section describes the general terms and provisions of the preferred stock we may offer. This information may not be complete in all respects and is qualified entirely by reference to our certificate of incorporation with respect to each series of preferred stock. The specific terms of any series will be described in a prospectus supplement. Those terms may differ from the terms discussed below. Any series of preferred stock we issue will be governed by our certificate of incorporation and by the certificate of designations relating to that series. We will file the certificate of designations with the SEC and incorporate it by reference as an exhibit to our registration statement at or before the time we issue any preferred stock of that series.

Authorized Preferred Stock

We may issue preferred stock from time to time in one or more series, without shareholder approval, when authorized by our board of directors.

Upon issuance of a particular series of preferred stock, our board of directors is authorized, to specify:

- the number of shares to be included in the series;
- the annual dividend rate for the series, if any, and any restrictions or conditions on the payment of dividends;
- the redemption price, if any, and the terms and conditions of redemption;
- any sinking fund provisions for the purchase or redemption of the series;
- if the series is convertible, the terms and conditions of conversion;
- the amounts payable to holders upon our liquidation, dissolution or winding up; and
- any other rights, preferences and limitations relating to the series, including voting rights.

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Our board of directors' ability to authorize, without shareholder approval, the issuance of preferred stock with conversion and other rights, may adversely affect the rights of holders of our common stock or other series of preferred stock that may be outstanding.

No shares of our preferred stock are currently issued or outstanding.

Specific Terms of a Series of Preferred Stock

The preferred stock we may offer will be issued in one or more series. The preferred stock will have the dividend, liquidation, redemption and voting rights discussed below, unless otherwise described in a prospectus supplement relating to a particular series. A prospectus supplement will discuss the following features of the series of preferred stock to which it relates:

- the designations and stated value per share;
- the number of shares offered;
- the amount of liquidation preference per share;
- the public offering price at which the preferred stock will be issued;
- the dividend rate, the method of its calculation, the dates on which dividends would be paid and the dates, if any, from which dividends would cumulate;
- any redemption or sinking fund provisions;
- any conversion or exchange rights; and
- any additional voting, dividend, liquidation, redemption, sinking fund and other rights, preferences, privileges, limitations and restrictions.

Rank

Unless otherwise stated in the prospectus supplement, the preferred stock will have priority over our common stock with respect to dividends and distribution of assets, but will rank junior to all our outstanding indebtedness for borrowed money. Any series of preferred stock could rank senior, equal or junior to our other capital stock, as may be specified in a prospectus supplement, as long as our certificate of incorporation so permits.

Dividends

Holders of each series of preferred stock shall be entitled to receive cash dividends to the extent specified in the prospectus supplement when, as and if declared by our board of directors, from funds legally available for the payment of dividends. The rates and dates of payment of dividends of each series of preferred stock will be stated in the prospectus supplement. Dividends will be payable to the holders of record of preferred stock as they appear on our books on the record dates fixed by our board of directors. Dividends on any series of preferred stock may be cumulative or non-cumulative, as discussed in the applicable prospectus supplement.

Convertibility

Shares of a series of preferred stock may be exchangeable or convertible into shares of our common stock, another series of preferred stock or other securities or property. The conversion or exchange may be mandatory or optional. The prospectus supplement will specify whether the preferred stock being offered has any conversion or exchange features, and will describe all the related terms and conditions.

Redemption

The terms, if any, on which shares of preferred stock of a series may be redeemed will be discussed in the applicable prospectus supplement.

Liquidation

Upon any voluntary or involuntary liquidation, dissolution or winding up of our affairs, holders of each series of preferred stock will be entitled to receive distributions upon liquidation in the amount described in the related prospectus supplement. These distributions will be made before any distribution is made on any securities ranking junior to the preferred stock with respect to liquidation, including our common stock. If the liquidation amounts payable relating to the preferred stock of any series and any other securities ranking on a parity regarding liquidation rights are not paid in full, the holders of the preferred stock of that series will share ratably in proportion to the full liquidation preferences of each security. Holders of our preferred stock will not be entitled to any other amounts from us after they have received their full liquidation preference.

Voting

The holders of preferred stock of each series will have no voting rights, except as required by law and as described below or in a prospectus supplement. Our board of directors may, upon issuance of a series of preferred stock, grant voting rights to the holders of that series to elect additional board members if we fail to pay dividends in a timely fashion.

Without the affirmative vote of a majority of the shares of preferred stock of any series then outstanding, we may not:

- increase or decrease the aggregate number of authorized shares of that series;
- increase or decrease the par value of the shares of that series; or
- alter or change the powers, preferences or special rights of the shares of that series so as to affect them adversely.

No Other Rights

The shares of a series of preferred stock will not have any preferences, voting powers or relative, participating, optional or other special rights except:

- as discussed above or in the prospectus supplement;
- as provided in our certificate of incorporation and in the certificate of designations; and
- as otherwise required by law.

DESCRIPTION OF DEBT SECURITIES WE MAY OFFER

General

The debt securities that we may issue will constitute debentures, notes, bonds or other evidences of indebtedness of Cue Biopharma, to be issued in one or more series, which may include either senior debt securities, subordinated debt securities or senior subordinated debt securities. The particular terms of any series of debt securities we offer, including the extent to which the general terms set forth below may be applicable to a particular series, will be described in a prospectus supplement relating to such series.

Debt securities and any guarantees that we may issue will be issued under an indenture between us and a trustee qualified to act as such under the Trust Indenture Act of 1939. We have filed the form of the indenture as an exhibit to the registration statement of which this prospectus is a part. When we refer to the “indenture” in this prospectus, we are referring to the indenture under which the debt securities are issued as supplemented by any supplemental indenture applicable to the debt securities. We will provide the name of the trustee in any prospectus supplement related to the issuance of debt securities, and we will also provide certain other information related to the trustee, including describing any relationship we have with the trustee, in such prospectus supplement.

THE FOLLOWING DESCRIPTION IS A SUMMARY OF THE MATERIAL PROVISIONS OF THE INDENTURE. IT DOES NOT RESTATE THE INDENTURE IN ITS ENTIRETY. THE INDENTURE IS GOVERNED BY THE TRUST INDENTURE ACT OF 1939. THE TERMS OF THE DEBT SECURITIES INCLUDE THOSE STATED IN THE INDENTURE AND THOSE MADE PART OF THE INDENTURE BY REFERENCE TO THE TRUST INDENTURE ACT. WE URGE YOU TO READ THE INDENTURE BECAUSE IT, AND NOT THIS DESCRIPTION, DEFINES THE RIGHTS OF A HOLDER OF THE DEBT SECURITIES.

Information You Will Find in the Prospectus Supplement

The indenture provides that we may issue debt securities from time to time in one or more series and that we may denominate the debt securities and make them payable in foreign currencies. The indenture does not limit the aggregate principal amount of debt securities that can be issued thereunder. The prospectus supplement for a series of debt securities will provide information relating to the terms of the series of debt securities being offered, which may include:

- the title and denominations of the debt securities of the series;
- any limit on the aggregate principal amount of the debt securities of the series;
- the date or dates on which the principal and premium, if any, with respect to the debt securities of the series are payable or the method of determination thereof;
- the rate or rates, which may be fixed or variable, at which the debt securities of the series shall bear interest, if any, or the method of calculating and/or resetting such rate or rates of interest;
- the dates from which such interest shall accrue or the method by which such dates shall be determined and the duration of the extensions and the basis upon which interest shall be calculated;
- the interest payment dates for the series of debt securities or the method by which such dates will be determined, the terms of any deferral of interest and any right of ours to extend the interest payment periods;
- the place or places where the principal and interest on the series of debt securities will be payable;
- the terms and conditions upon which debt securities of the series may be redeemed, in whole or in part, at our option or otherwise;
- our obligation, if any, to redeem, purchase, or repay debt securities of the series pursuant to any sinking fund or other specified event or at the option of the holders and the terms of any such redemption, purchase, or repayment;
- the terms, if any, upon which the debt securities of the series may be convertible into or exchanged for other securities, including, among other things, the initial conversion or exchange price or rate and the conversion or exchange period;
- if the amount of principal, premium, if any, or interest with respect to the debt securities of the series may be determined with reference to an index or formula, the manner in which such amounts will be determined;
- if any payments on the debt securities of the series are to be made in a currency or currencies (or by reference to an index or formula) other than that in which such securities are denominated or designated to be payable, the currency or currencies (or index or formula) in which such payments are to be made and the terms and conditions of such payments;
- any changes or additions to the provisions of the indenture dealing with defeasance, including any additional covenants that may be subject to our covenant defeasance option;
- the currency or currencies in which payment of the principal and premium, if any, and interest with respect to debt securities of the series will be payable, or in which the debt securities of the series shall be denominated, and the particular provisions applicable thereto in accordance with the indenture;
- the portion of the principal amount of debt securities of the series which will be payable upon declaration of acceleration or provable in bankruptcy or the method by which such portion or amount shall be determined;
- whether the debt securities of the series will be secured or guaranteed and, if so, on what terms;
- any addition to or change in the events of default with respect to the debt securities of the series;
- the identity of any trustees, authenticating or paying agents, transfer agents or registrars;
- the applicability of, and any addition to or change in, the covenants currently set forth in the indenture;
- the subordination, ranking or priority, if any, of the debt securities of the series and terms of the subordination;
- any other terms of the debt securities of the series which are not prohibited by the indenture; and

Holders of debt securities may present debt securities for exchange in the manner, at the places, and subject to the restrictions set forth in the debt securities, the indenture, and the prospectus supplement. We will provide these services without charge, other than any tax or other governmental charge payable in connection therewith, but subject to the limitations provided in the indenture, any board resolution establishing such debt securities and any applicable indenture supplement.

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Senior Debt

We may issue senior debt securities under the indenture. Unless otherwise set forth in the applicable indenture supplement and described in a prospectus supplement, the senior debt securities will be senior unsecured obligations, ranking equally with all of our existing and future senior unsecured debt. The senior debt securities will be senior to all of our subordinated debt and junior to any secured debt we may incur as to the assets securing such debt.

Subordinated Debt

We may issue subordinated debt securities under the indenture. These subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner set forth in the indenture and any applicable indenture supplement, to all of our senior indebtedness.

If this prospectus is being delivered in connection with a series of subordinated debt securities, the accompanying prospectus supplement or the information incorporated by reference will set forth the approximate amount of senior indebtedness outstanding as of a recent date.

Senior Subordinated Debt

We may issue senior subordinated debt securities under the indenture. These senior subordinated debt securities will be, to the extent and in the manner set forth in the applicable indenture supplement, subordinate and junior in right of payment to all of our “senior indebtedness” and senior to our other subordinated debt.

Interest Rate

Debt securities that bear interest will do so at a fixed rate or a variable rate. We may sell, at a discount below the stated principal amount, any debt securities which bear no interest or which bear interest at a rate that at the time of issuance is below the prevailing market rate. The relevant prospectus supplement will describe the special United States federal income tax considerations applicable to:

- any discounted debt securities; and
- any debt securities issued at par which are treated as having been issued at a discount for United States federal income tax purposes.

Registered Global Securities

We may issue registered debt securities of a series in the form of one or more fully registered global securities. We will deposit the registered global security with a depository or with a nominee for a depository identified in the prospectus supplement relating to such series. The global security or global securities will represent and will be in a denomination or aggregate denominations equal to the portion of the aggregate principal amount of outstanding registered debt securities of the series to be represented by the registered global security or securities. Unless it is exchanged in whole or in part for debt securities in definitive registered form, a registered global security may not be transferred, except as a whole in three cases:

- by the depository for the registered global security to a nominee of the depository;
- by a nominee of the depository to the depository or another nominee of the depository; and
- by the depository or any nominee to a successor of the depository or a nominee of the successor.

The prospectus supplement relating to a series of debt securities will describe the specific terms of the depository arrangement concerning any portion of that series of debt securities to be represented by a registered global security. We anticipate that the following provisions will generally apply to all depository arrangements.

Upon the issuance of a registered global security, the depository will credit, on its book-entry registration and transfer system, the principal amounts of the debt securities represented by the registered global security to the accounts of persons

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that have accounts with the depository. These persons are referred to as “participants.” Any underwriters, agents or dealers participating in the distribution of debt securities represented by the registered global security will designate the accounts to be credited. Only participants or persons that hold interests through participants will be able to beneficially own interests in a registered global security. The depository for a global security will maintain records of beneficial ownership interests in a registered global security for participants. Participants or persons that hold through participants will maintain records of beneficial ownership interests in a global security for persons other than participants. These records will be the only means to transfer beneficial ownership in a registered global security.

The laws of some states may require that specified purchasers of securities take physical delivery of the securities in definitive form. These laws may limit the ability of those persons to own, transfer or pledge beneficial interests in global securities.

So long as the depository, or its nominee, is the registered owner of a registered global security, the depository or its nominee will be considered the sole owner or holder of the debt securities represented by the registered global security for all purposes under the indenture. Except as set forth below, owners of beneficial interests in a registered global security:

- may not have the debt securities represented by a registered global security registered in their names;
- will not receive or be entitled to receive physical delivery of debt securities represented by a registered global security in definitive form; and
- will not be considered the owners or holders of debt securities represented by a registered global security under the indenture.

Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depository for the registered global security and, if the person is not a participant, on the procedures of the participant through which the person owns its interests, to exercise any rights of a holder under the indenture applicable to the registered global security.

We understand that, under existing industry practices, if we request any action of holders, or if an owner of a beneficial interest in a registered global security desires to give or take any action which a holder is entitled to give or take under the indenture, the depository for the registered global security would authorize the participants holding the relevant beneficial interests to give or take the action, and the participants would authorize beneficial owners owning through the participants to give or take the action or would otherwise act upon the instructions of beneficial owners holding through them.

Payment of Interest on and Principal of Registered Global Securities

We will make principal, premium, if any, and interest payments on debt securities represented by a registered global security registered in the name of a depository or its nominee to the depository or its nominee as the registered owner of the registered global security. None of Cue Biopharma, the trustee, or any paying agent for debt securities represented by a registered global security will have any responsibility or liability for:

- any aspect of the records relating to, or payments made on account of, beneficial ownership interests in such registered global security; or
- maintaining, supervising, or reviewing any records relating to beneficial ownership interests.

We expect that the depository, upon receipt of any payment of principal, premium or interest in respect of the global security, will immediately credit participants' accounts with payments in amounts proportionate to their beneficial interests in the principal amount of a registered global security as shown on the depository's records. We also expect that payments by participants to owners of beneficial interests in a registered global security held through participants will be governed by standing instructions and customary practices. This is currently the case with the securities held for the accounts of customers registered in “street name.” Such payments will be the responsibility of participants.

Exchange of Registered Global Securities

We may issue debt securities in definitive form in exchange for the registered global security if both of the following occur:

- the depository for any debt securities represented by a registered global security is at any time unwilling or unable to continue as depository or ceases to be a clearing agency registered under the Exchange Act; and

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- we do not appoint a successor depository within 90 days.

In addition, we may, at any time, determine not to have any of the debt securities of a series represented by one or more registered global securities. In this event, we will issue debt securities of that series in definitive form in exchange for all of the registered global security or securities representing those debt securities.

Covenants by Cue Biopharma

The indenture includes covenants by us, including among other things that we will make all payments of principal and interest at the times and places required. The supplemental indenture establishing each series of debt securities may contain additional covenants, including covenants which could restrict our right to incur additional indebtedness or liens and to take certain actions with respect to our businesses and assets.

Events of Default

Unless otherwise indicated in the applicable prospectus supplement, the following will be events of default under the indenture with respect to each series of debt securities issued under the indenture:

- failure to pay when due any interest on any debt security of that series, continued for 30 days;
- failure to pay when due the principal of, or premium, if any, on, any debt security of that series;
- failure to perform any other covenant or agreement of ours under the indenture or the supplemental indenture with respect to that series or the debt securities of that series, continued for 90 days after written notice to us by the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the series to which the covenant or agreement relates;
- certain events of bankruptcy, insolvency or similar proceedings affecting us; and
- any other event of default specified in any supplemental indenture under which such series of debt securities is issued.

Except as to certain events of bankruptcy, insolvency or similar proceedings affecting us and except as provided in the applicable prospectus supplement, if any event of default shall occur and be continuing with respect to any series of debt securities under the indenture, either the trustee or the holders of at least 25% in aggregate principal amount of outstanding debt securities of such series may accelerate the maturity of all debt securities of such series. Upon certain events of bankruptcy, insolvency or similar proceedings affecting us, the principal, premium, if any, and interest on all debt securities of each series shall be immediately due and payable.

After any such acceleration, but before a judgment or decree based on acceleration has been obtained by the trustee, the holders of a majority in aggregate principal amount of each affected series of debt securities may waive all defaults with respect to such series and rescind and annul such acceleration if all events of default, other than the non-payment of accelerated principal, have been cured, waived or otherwise remedied.

No holder of any debt securities will have any right to institute any proceeding with respect to the indenture or for any remedy under the indenture, unless such holder shall have previously given to the trustee written notice of a continuing event of default and the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the relevant series shall have made written request and offered indemnity satisfactory to the trustee to institute such proceeding as trustee, the trustee for 60 days after its receipt of such notice, request and the offer of indemnity has failed to institute any such proceedings, and the trustee shall not have received from the holders of a majority in aggregate principal amount of the outstanding debt securities of such series a direction inconsistent with such request and shall have failed to institute such proceeding within 60 days. However, such limitations do not apply to a suit instituted by a holder of a debt security for enforcement of payment of the principal of and premium, if any, or interest on such debt security on or after the respective due dates expressed in such debt security.

Supplemental Indentures

We and the trustee may, at any time and from time to time, without prior notice to or consent of any holders of debt securities, enter into one or more indentures supplemental to the indenture, among other things:

- to add guarantees to or secure any series of debt securities;

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- to provide for the succession of another person pursuant to the provisions of the indenture relating to consolidations, mergers and sales of assets and the assumption by such successor of our covenants, agreements, and obligations, or to otherwise comply with the provisions of the indenture relating to consolidations, mergers, and sales of assets;
- to surrender any right or power conferred upon us under the indenture or to add to our covenants further covenants, restrictions, conditions or provisions for the protection of the holders of all or any series of debt securities;
- to cure any ambiguity or to correct or supplement any provision contained in the indenture, in any supplemental indenture or in any debt securities that may be defective or inconsistent with any other provision contained therein;
- to modify or amend the indenture in such a manner as to permit the qualification of the indenture or any supplemental indenture under the Trust Indenture Act;
- to add to or change any of the provisions of the indenture to supplement any of the provisions of the indenture in order to permit the defeasance and discharge of any series of debt securities pursuant to the indenture, so long as any such action does not adversely affect the interests of the holders of debt securities of any series in any material respect;
- to add to, change, or eliminate any of the provisions of the indenture with respect to one or more series of debt securities, so long as any such addition, change or elimination shall not apply to any debt securities of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision;
- to evidence and provide for the acceptance of appointment by a successor or separate trustee; and
- to establish the form or terms of debt securities of any series and to make any change that does not adversely affect the interests of the holders of debt securities.

With the consent of the holders of at least a majority in principal amount of debt securities of each series affected by such supplemental indenture (each series voting as one class), we and the trustee may enter into one or more supplemental indentures for the purpose of adding any provisions to or changing in any manner or eliminating any of the provisions of the indenture or modifying in any manner the rights of the holders of debt securities of each such series.

Notwithstanding our rights and the rights of the trustee to enter into one or more supplemental indentures with the consent of the holders of debt securities of the affected series as described above, no such supplemental indenture shall, without the consent of the holder of each outstanding debt security of the affected series, among other things:

- change the final maturity of the principal of, or any installment of interest on, any debt securities;
- reduce the principal amount of any debt securities or the rate of interest on any debt securities;
- change the currency in which any debt securities are payable;
- impair the right of the holders to conduct a proceeding for any remedy available to the trustee;
- reduce the percentage in principal amount of any series of debt securities whose holders must consent to an amendment or supplemental indenture;
- modify the ranking or priority of the securities; or
- reduce any premium payable upon the redemption of any debt securities.

Satisfaction and Discharge of the Indenture; Defeasance

Except to the extent set forth in a supplemental indenture with respect to any series of debt securities, we, at our election, may discharge the indenture and the indenture shall generally cease to be of any further effect with respect to that series of debt securities if (a) we have delivered to the trustee for cancellation all debt securities of that series (with certain limited exceptions) or (b) all debt securities of that series not previously delivered to the trustee for cancellation shall have become due and payable, or are by their terms to become due and payable within one year or are to be called for redemption within one year, and we have deposited with the trustee the entire amount sufficient to pay at maturity or upon redemption all such debt securities.

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In addition, we have a “legal defeasance option” (pursuant to which we may terminate, with respect to the debt securities of a particular series, all of our obligations under such debt securities and the indenture with respect to such debt securities) and a “covenant defeasance option” (pursuant to which we may terminate, with respect to the debt securities of a particular series, our obligations with respect to such debt securities under certain specified covenants contained in the indenture). If we exercise our legal defeasance option with respect to a series of debt securities, payment of such debt securities may not be accelerated because of an event of default. If we exercise our covenant defeasance option with respect to a series of debt securities, payment of such debt securities may not be accelerated because of an event of default related to the specified covenants.

We may exercise our legal defeasance option or our covenant defeasance option with respect to the debt securities of a series only if we irrevocably deposit in trust with the trustee cash or U.S. government obligations (as defined in the indenture) for the payment of principal, premium, if any, and interest with respect to such debt securities to maturity or redemption, as the case may be. In addition, to exercise either of our defeasance options, we must comply with certain other conditions, including the delivery to the trustee of an opinion of counsel to the effect that the holders of debt securities of such series will not recognize income, gain or loss for Federal income tax purposes as a result of such defeasance and will be subject to Federal income tax on the same amounts, in the same manner and at the same times as would have been the case if such defeasance had not occurred (and, in the case of legal defeasance only, such opinion of counsel must be based on a ruling from the Internal Revenue Service or other change in applicable Federal income tax law).

The trustee will hold in trust the cash or U.S. government obligations deposited with it as described above and will apply the deposited cash and the proceeds from deposited U.S. government obligations to the payment of principal, premium, if any, and interest with respect to the debt securities of the defeased series.

Mergers, Consolidations and Certain Sales of Assets

Unless otherwise indicated in the applicable prospectus supplement, while we have outstanding debt securities, we may not:

- consolidate with or merge into any other person or entity or permit any other person or entity to consolidate with or merge into us in a transaction in which we are not the surviving entity, or
- sell, convey, transfer or otherwise dispose of all or substantially all of our assets to any other person or entity,

unless:

- the resulting, surviving or transferee entity shall be a corporation organized and existing under the laws of the United States or any state thereof and such resulting, surviving or transferee entity shall expressly assume, by supplemental indenture, executed and delivered in form satisfactory to the trustee, all of our obligations under the debt securities and the indenture;
- immediately after giving effect to such transaction (and treating any indebtedness which becomes an obligation of the resulting, surviving or transferee entity as a result of such transaction as having been incurred by such entity at the time of such transaction), no default or event of default would occur or be continuing; and
- we shall have delivered to the trustee an officers’ certificate and an opinion of counsel, each stating that such consolidation, merger or transfer and such supplemental indenture (if any) comply with the indenture.

The phrase “substantially all” of our assets will likely be interpreted under applicable state law and will be dependent upon particular facts and circumstances. As a result, there may be a degree of uncertainty in ascertaining whether a sale or transfer of “substantially all” of our assets has occurred.

Governing Law

The indenture and the debt securities will be governed by the laws of the State of New York.

No Personal Liability of Directors, Officers, Employees and Stockholders

No director, officer, incorporator or stockholder of Cue Biopharma, as such, shall have any liability for any obligations of Cue Biopharma under the debt securities or the indenture or for any claim based on, in respect of, or by reason of, such obligations or their creation, solely by reason of his, her, or its status as director, officer, incorporator or stockholder of Cue Biopharma. By accepting a debt security, each holder waives and releases all such liability, but only such liability. The waiver and release are part of the consideration for issuance of the debt securities. Nevertheless, such waiver may not be effective to waive liabilities under the federal securities laws and it has been the view of the SEC that such a waiver is against public policy.

Conversion or Exchange Rights

Any debt securities offered hereby may be convertible into or exchangeable for shares of our equity or other securities. The terms and conditions of such conversion or exchange will be set forth in the applicable prospectus supplement. Such terms may include, among others, the following:

- the conversion or exchange price;
- the conversion or exchange period;
- provisions regarding our ability or that of the holder to convert or exchange the debt securities;
- events requiring adjustment to the conversion or exchange price; and
- provisions affecting conversion or exchange in the event of our redemption of such debt securities.

Concerning the Trustee

The indenture provides that there may be more than one trustee with respect to one or more series of debt securities. If there are different trustees for different series of debt securities, each trustee will be a trustee of a trust under a supplemental indenture separate and apart from the trust administered by any other trustee under such indenture. Except as otherwise indicated in this prospectus or any prospectus supplement, any action permitted to be taken by a trustee may be taken by the trustee only with respect to the one or more series of debt securities for which it is the trustee under an indenture. Any trustee under the indenture or a supplemental indenture may resign or be removed with respect to one or more series of debt securities. All payments of principal of, premium, if any, and interest on, and all registration, transfer, exchange authentication and delivery (including authentication and delivery on original issuance of the debt securities) of, the debt securities of a series will be effected by the trustee with respect to such series at an office designated by the trustee.

The indenture contains limitations on the right of the trustee, should it become a creditor of Cue Biopharma, to obtain payment of claims in certain cases or to realize on certain property received in respect of any such claim as security or otherwise. If the trustee acquires an interest that conflicts with any duties with respect to the debt securities, the trustee is required to either resign or eliminate such conflicting interest to the extent and in the manner provided by the indenture.

DESCRIPTION OF WARRANTS WE MAY OFFER

We may issue warrants for the purchase of debt securities, preferred stock or common stock. Warrants may be issued independently or together with debt securities, preferred stock or common stock and may be attached to or separate from any offered securities. Any issue of warrants will be governed by the terms of the applicable form of warrant and any related warrant agreement, which we will file with the SEC, and they will be incorporated by reference to the registration statement of which this prospectus is a part on or before the time we issue any warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the title of such warrants;
- the aggregate number of such warrants;
- the price or prices at which such warrants will be issued;
- the currency or currencies (including composite currencies) in which the price of such warrants may be payable;

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- the terms of the securities purchasable upon exercise of such warrants and the procedures and conditions relating to the exercise of such warrants;
- the price at which the securities purchasable upon exercise of such warrants may be purchased;
- the date on which the right to exercise such warrants will commence and the date on which such right shall expire;
- any provisions for adjustment of the number or amount of securities receivable upon exercise of the warrants or the exercise price of the warrants;
- if applicable, the minimum or maximum amount of such warrants that may be exercised at any one time;
- if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;
- if applicable, the date on and after which such warrants and the related securities will be separately transferable;
- information with respect to book-entry procedures, if any; and
- any other terms of such warrants, including terms, procedures and limitations relating to the exchange or exercise of such warrants.

The prospectus supplement relating to any warrants to purchase equity securities may also include, if applicable, a discussion of certain U.S. federal income tax and ERISA considerations.

Warrants for the purchase of preferred stock and common stock will be offered and exercisable for U.S. dollars only.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement.

After the close of business on the expiration date, unexercised warrants will become void. We will specify the place or places where, and the manner in which, warrants may be exercised in the applicable prospectus supplement.

Prior to the exercise of any warrants to purchase debt securities, preferred stock or common stock, holders of the warrants will not have any of the rights of holders of the debt securities, preferred stock or common stock purchasable upon exercise.

DESCRIPTION OF RIGHTS WE MAY OFFER

We may issue rights to purchase our debt securities, common stock, preferred stock or other securities. These rights may be issued independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the rights in such offering. In connection with any offering of such rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering.

Each series of rights will be issued under a separate rights agreement which we will enter into with a bank or trust company, as rights agent, all which will be set forth in the relevant offering material. The rights agent will act solely as our agent in connection with the certificates relating to the rights and will not assume any obligation or relationship of agency or trust with any holders of rights certificates or beneficial owners of rights.

The following description is a summary of selected provisions relating to rights that we may offer. The summary is not complete. When rights are offered in the future, a prospectus supplement, information incorporated by reference or a free writing prospectus, as applicable, will explain the particular terms of those securities and the extent to which these general provisions may apply. The specific terms of the rights as described in a prospectus supplement or free writing prospectus will supplement and, if applicable, may modify or replace the general terms described in this section.

The specific terms of any rights offered will be set forth in a rights agreement and the rights certificate, as applicable. We will file each of these documents, as applicable, with the SEC and they will be incorporated by reference to the registration statement of which this prospectus is a part on or before the time we issue a series of rights. See “Where You Can Find More Information” and “Incorporation by Reference” above for information on how to obtain a copy of a document when it is filed.

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The applicable prospectus supplement or free writing prospectus may describe:

- in the case of a distribution of rights to our stockholders, the date of determining the stockholders entitled to the rights distribution;
- in the case of a distribution of rights to our stockholders, the number of rights issued or to be issued to each stockholder;
- the exercise price payable for the underlying debt securities, common stock, preferred stock or other securities upon the exercise of the rights;
- the number and terms of the underlying debt securities, common stock, preferred stock or other securities which may be purchased per each right;
- the extent to which the rights are transferable;
- the date on which the holder's ability to exercise the rights shall commence, and the date on which the rights shall expire;
- the extent to which the rights may include an over-subscription privilege with respect to unsubscribed securities;
- if applicable, the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering of such rights; and
- any other terms of the rights, including, but not limited to, the terms, procedures, conditions and limitations relating to the exchange and exercise of the rights.

The provisions described in this section, as well as those described under “— Description of Debt Securities We May Offer,” “— Description of Common Stock We May Offer” and “— Description of Preferred Stock We May Offer” above, will apply, as applicable, to any rights we offer.

DESCRIPTION OF UNITS WE MAY OFFER

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information incorporated by reference and included in any applicable prospectus supplement or free writing prospectus, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement or free writing prospectus, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain United States federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

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The applicable provisions described in this section, as well as those described under “Description of Debt Securities We May Offer,” “Description of Common Stock We May Offer,” “Description of Preferred Stock We May Offer,” “Description of Warrants We May Offer” and “Description of Rights We May Offer” above, will apply to each unit and to each security included in each unit, respectively.

CERTAIN PROVISIONS OF DELAWARE LAW AND OF THE COMPANY’S CERTIFICATE OF INCORPORATION AND BYLAWS

The following paragraphs regarding certain provisions of the General Corporation Law of the State of Delaware (the “DGCL”), our certificate of incorporation, and our bylaws are summaries of the material terms thereof and do not purport to be complete. We urge you to read the applicable prospectus supplements, any related free writing prospectuses related to a security that we may offer under this prospectus, the DGCL, and our certificate of incorporation and bylaws. Copies of the certificate of incorporation and bylaws are on file with the SEC as exhibits to filings previously made by us. See “Where You Can Find More Information.”

General

The provisions of the DGCL and our certificate of incorporation and bylaws could have the effect of discouraging others from attempting an unsolicited offer to acquire our company. Such provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Authorized but Unissued Shares

The authorized but unissued shares of our common stock and our preferred stock are available for future issuance without any further vote or action by our stockholders. These additional shares may be utilized for a variety of corporate purposes, including future public or private offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of our common stock and our preferred stock could render more difficult or discourage an attempt to obtain control over us by means of a proxy contest, tender offer, merger or otherwise.

Actions at Meetings of Stockholders; Special Meeting of Stockholders and Advance Notice Requirements for Stockholder Proposals

Our certificate of incorporation and bylaws require that any action required or permitted to be taken by our stockholders may be effected by a consent in writing; however, stockholders pursuing an action by written consent will be required to comply with certain notice and record date requirements that are set forth in the DGCL. Our certificate of incorporation and bylaws also provide that special meetings of stockholders may be called from time to time only by the Chairman of our board of directors, our President, our Chief Executive Officer or a majority of our board of directors for the purpose or purposes specified in the notice of meeting, or by the request of the holders of record of at least 20% of outstanding shares of our common stock. In addition, the bylaws provide that candidates for director may be nominated and other business brought before an annual meeting only by the Board of Directors or by a stockholder who gives written notice to us not less than 90 days, nor more than 120 days, prior to the first anniversary of the preceding year’s annual meeting, subject to certain exceptions. Such stockholder’s notice must set forth certain information required by the bylaws. These provisions may have the effect of deterring unsolicited offers to acquire our company or delaying stockholder actions, even if they are favored by the holders of a majority of our outstanding voting securities.

Delaware Business Combination Statute

We must comply with Section 203 of the Delaware General Corporation Law, an anti-takeover law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a period of three years following the date the person became an interested stockholder, unless the business combination or the transaction in which the person became an interested stockholder is approved in a prescribed manner or certain other exceptions are met. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to an interested stockholder. An “interested stockholder” includes a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation’s voting stock. The existence of this provision generally will have an anti-takeover effect for transactions not approved in advance by the board of directors, including discouraging attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

Other Supermajority Voting Requirements

In addition to the supermajority requirement for certain business combinations discussed above, our certificate of incorporation and bylaws also contain other supermajority requirements, including the affirmative vote of the holders of at least 66 2/3% of the voting power of the shares of our then outstanding voting stock, voting together as a single class, is required to amend or repeal, or adopt any provisions in our certificate of incorporation inconsistent with certain designated provisions relating to (1) our board of directors, (2) indemnification of certain indemnitees of the Company, (3) venue for internal corporate claims, and (4) amendments to our certificate of incorporation or bylaws.

Directors, and Not Stockholders, Fix the Size of Our Board

Our certificate of incorporation and bylaws provide that the number of directors will be fixed from time to time exclusively pursuant to a resolution adopted by our board of directors.

Board Vacancies to Be Filled by Remaining Directors

Under our certificate of incorporation and bylaws, any vacancy on the board of directors created by any reason prior to the expiration of the term in which the vacancy occurs will be filled by a majority of the remaining directors, even if less than a quorum. A director elected to fill a vacancy will be elected for the unexpired term of his or her predecessor or until his or her successor is elected and qualified.

PLAN OF DISTRIBUTION

We may sell the securities offered by this prospectus to one or more underwriters or dealers for public offering, through agents, directly to purchasers or through a combination of any such methods of sale. The name of any such underwriters, dealers or agents involved in the offer and sale of the securities, the amounts underwritten and the nature of its obligation to take the securities will be specified in the applicable prospectus supplement. We have reserved the right to sell the securities directly to investors on our own behalf in those jurisdictions where we are authorized to do so. The sale of the securities may be effected in transactions (a) on any national or international securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, (b) in the over-the-counter market, (c) in transactions otherwise than on such exchanges or in the over-the-counter market or (d) through the writing of options.

We and our agents and underwriters may offer and sell the securities at a fixed price or prices that may be changed, at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices. The securities may be offered on an exchange, which will be disclosed in the applicable prospectus supplement. We may, from time to time, authorize dealers, acting as our agents, to offer and sell the securities upon such terms and conditions as set forth in the applicable prospectus supplement. We may also sell the securities offered by any applicable prospectus supplement in “at-the-market offerings” within the meaning of Rule 415 of the Securities Act of 1933, to or through a market maker or into an existing trading market, on an exchange or otherwise.

We may enter into agreements with underwriters to sell our securities. In connection with the sale of the securities, underwriters may receive compensation from us in the form of underwriting discounts or commissions and may also receive commissions from purchasers of the securities for whom they may act as agent. Any underwriting compensation paid by us to underwriters or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers, will be set forth in the applicable prospectus supplement to the extent required by applicable law. Underwriters may sell the securities to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions (which may be changed from time to time) from the purchasers for whom they may act as agents.

Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions under the Securities Act. Unless otherwise indicated in the applicable prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase debt securities as a principal, and may then resell the debt securities at varying prices to be determined by the dealer.

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If so indicated in the prospectus supplement, we will authorize underwriters, dealers or agents to solicit offers by certain specified institutions to purchase offered securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. Such contracts will be subject to any conditions set forth in the applicable prospectus supplement and the prospectus supplement will set forth the commission payable for solicitation of such contracts. The underwriters and other persons soliciting such contracts will have no responsibility for the validity or performance of any such contracts.

Underwriters, dealers and agents may be entitled, under agreements entered into with us, to indemnification against and contribution towards certain civil liabilities, including any liabilities under the Securities Act.

To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain, or otherwise affect the price of the securities. These may include over-allotment, stabilization, syndicate short covering transactions and penalty bids. Over-allotment involves sales in excess of the offering size, which creates a short position. Stabilizing transactions involve bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Syndicate short covering transactions involve purchases of securities in the open market after the distribution has been completed in order to cover syndicate short positions. Penalty bids permit the underwriters to reclaim selling concessions from dealers when the securities originally sold by the dealers are purchased in covering transactions to cover syndicate short positions. These transactions may cause the price of the securities sold in an offering to be higher than it would otherwise be. These transactions, if commenced, may be discontinued by the underwriters at any time.

Any securities other than our common stock issued hereunder may be new issues of securities with no established trading market. Any underwriters or agents to or through whom such securities are sold for public offering and sale may make a market in such securities, but such underwriters or agents will not be obligated to do so and may discontinue any market making at any time without notice. No assurance can be given as to the liquidity of the trading market for any such securities. The amount of expenses expected to be incurred by us in connection with any issuance of securities will be set forth in the applicable prospectus supplement. Certain of the underwriters, dealers or agents and their associates may engage in transactions with, and perform services for, us and certain of our affiliates in the ordinary course of business.

During such time as we may be engaged in a distribution of the securities covered by this prospectus we are required to comply with Regulation M promulgated under the Exchange Act. With certain exceptions, Regulation M precludes us, any affiliated purchasers, and any broker-dealer or other person who participates in such distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase, any security which is the subject of the distribution until the entire distribution is complete. Regulation M also restricts bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of our shares of common stock.

LEGAL MATTERS

The validity and legality of the securities offered hereby and certain other legal matters will be passed upon for the Company by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts.

EXPERTS

The consolidated financial statements of Cue Biopharma, Inc. as of December 31, 2020 and 2019 and for the years then ended incorporated in this prospectus by reference from the Cue Biopharma, Inc. Annual Report on Form 10-K for the year ended December 31, 2020 have been audited by RSM US LLP, an independent registered public accounting firm, as stated in their report thereon incorporated herein by reference, and have been incorporated in this prospectus and Registration Statement in reliance upon such report and upon the authority of such firm as experts in accounting and auditing.

\$300,000,000



**Common Stock
Preferred Stock
Debt Securities
Warrants
Rights
Units**

Prospectus

, 2021

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated May 21, 2021

PROSPECTUS



**Up to \$17,159,674
Common Stock**

Cue Biopharma, Inc. has entered into an At-the-Market Equity Offering Sales Agreement (the “Sales Agreement”), dated June 22, 2020, with Stifel, Nicolaus & Company, Incorporated (“Stifel”) to offer and sell up to \$40,000,000 of our common stock, \$0.001 par value per share, offered by this prospectus. We originally filed a prospectus supplement, dated June 22, 2020 (the “Prior Prospectus Supplement”), for the offer and sale of up to \$40,000,000 of shares of our common stock pursuant to the Sales Agreement under the shelf registration statement on Form S-3 (Registration Statement No. 333-239357). The Prior Prospectus Supplement provided for sales of shares of our common stock having an aggregate offering price of up to \$40,000,000. As of the date of this prospectus, we have issued and sold an aggregate of 1,192,000 shares of common stock pursuant to the Sales Agreement and the Prior Prospectus Supplement, for which we had received gross proceeds of approximately \$22.8 million. Accordingly, this prospectus covers the offer and sale of up to \$17.2 million of our common stock that may be sold under the Sales Agreement as of the date of this prospectus.

In accordance with the terms of the Sales Agreement, we may offer and sell shares of our common stock at any time and from time to time through Stifel as our sales agent. Sales of the common stock, if any, will be made at market prices by any method that is deemed to be an “at the market offering” as defined in Rule 415 under the Securities Act of 1933, as amended (the “Securities Act”). Stifel may also sell our common stock in negotiated transactions with our prior approval.

The aggregate compensation payable to Stifel shall be equal to up to 3.0% of the gross sales price of the shares sold through Stifel pursuant to the Sales Agreement. In connection with the sale of the common stock on our behalf, Stifel will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Stifel will be deemed to be underwriting commissions or discounts.

Subject to the terms and conditions of the Sales Agreement, Stifel will use its commercially reasonable efforts consistent with its normal trading and sales practices to sell on our behalf any shares to be offered by us under the Sales Agreement. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

We are an “emerging growth company” as that term is defined in the Jumpstart Our Business Startups Act of 2012 and, as such, are subject to certain reduced public company reporting requirements. See “The Company— Implications of Being an Emerging Growth Company” in the accompanying prospectus.

Our common stock is listed on the Nasdaq Capital Market under the symbol “CUE.” The last reported sale price of our common stock on the Nasdaq Capital Market on March 8, 2021 was \$13.27 per share.

Investing in our common stock involves risks. See “[Risk Factors](#)” beginning on page SA-7.

Neither the Securities and Exchange Commission (the “SEC”), nor any state securities commission, or any other regulatory body has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

STIFEL

The date of this prospectus is _____, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the “SEC,” utilizing a “shelf” registration process. Under this shelf registration process, we may from time to time sell shares of our common stock having an aggregate offering price of up to \$300,000,000. Under this prospectus, we may from time to time sell shares of our common stock having an aggregate offering price of up to \$17,159,674, at prices and on terms to be determined by market conditions at the time of the offering. The \$17,159,674 of shares of our common stock that may be sold under this prospectus are included in the \$300,000,000 of shares of common stock that may be sold under the registration statement.

Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus and all of the information contained in the documents incorporated by reference in this prospectus, as well as the additional information described under the headings “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference.” These documents contain important information that you should consider when making your investment decision.

To the extent there is a conflict between the information contained in this prospectus, on the one hand, and the information contained in any document incorporated by reference in this prospectus, on the other hand, you should rely on the information in this prospectus, provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreement, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We have not, and Stifel has not, authorized anyone to provide you with any information other than that contained in or incorporated by reference in this prospectus, any prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not, and Jefferies has not, authorized anyone to provide you with different information. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to “Cue Biopharma” “we,” “our,” “us” and “the Company” refer, collectively, to Cue Biopharma, Inc., a Delaware corporation, and its consolidated subsidiaries.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus and the information incorporated by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). All statements, other than statements of historical facts, contained in this herein and therein, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements include, among other things, statements about:

- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and our research and development programs;
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing;
- our expectations regarding our ability to fund our projected operating requirements with our existing cash resources and the period in which we expect that such cash resources will enable us to fund such operating requirements;
- our plans to develop our product candidates;
- the timing of and our ability to submit applications for, obtain and maintain regulatory approvals for our product candidates;
- the potential advantages of our product candidates;
- the rate and degree of market acceptance and clinical utility of our product candidates, if approved;
- our estimates regarding the potential market opportunity for our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- the impact of government laws and regulations;
- our competitive position;
- developments relating to our competitors and our industry;
- our ability to establish collaborations or obtain additional funding; and
- the impacts of the COVID-19 pandemic.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. You are cautioned that these forward-looking statements are only predictions and are subject to risks, uncertainties and assumptions that are referenced in the section of any accompanying prospectus supplement entitled “Risk Factors.” You should also carefully review the risk

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factors and cautionary statements described in the other documents we file from time to time with the SEC, specifically our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

You should read this prospectus, the documents incorporated by reference in this prospectus and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this prospectus and incorporated by reference herein are made as of the date hereof, and we do not assume any obligation to update any forward-looking statements except as required by applicable law.

This prospectus and the information incorporated by reference in this prospectus include statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties as well as our own estimates. All of the market data used in this prospectus and the information incorporated by reference in this prospectus involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our drug candidates include several key assumptions based on our industry knowledge, industry publications, third-party research, and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus and in the documents we incorporate by reference. This summary does not contain all of the information you should consider before making an investment decision. You should read this entire prospectus carefully, especially the risks of investing in our common stock discussed under “Risk Factors” beginning on page SA-7 of this prospectus, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus.

Cue Biopharma, Inc.

We are a clinical-stage biopharmaceutical company engineering a novel class of injectable biologics to selectively engage and modulate targeted T cells directly within the patient’s body. We believe our proprietary Immuno-STAT™ (*Selective Targeting and Alteration of T Cells*) platform will allow us to harness the fullest potential of an individual’s intrinsic immune repertoire for restoring health while avoiding the deleterious side effects of broad immune activation (for immuno-oncology or infectious immunity) or broad immune suppression (for autoimmunity and inflammation). In addition to the selective modulation of T cell activity, we believe Immuno-STATs offer several key points of potential differentiation over competing approaches, including modularity and versatility providing broad disease coverage, manufacturability, and convenient administration.

Through rational protein engineering, we leverage the modular and versatile nature of the Immuno-STAT platform to design drug product candidates for selective immune modulation in cancer, chronic infectious disease, and autoimmune disease. To address the needs of these clinical indications, we have developed four biologic series within the Immuno-STAT platform: CUE-100, CUE-200, CUE-300, and CUE-400, each specifically designed through rational engineering to possess distinct signaling modules for desired biological mechanisms that may be applied across many diseases. The CUE-100 series exploits rationally engineered IL-2 in context of the core Immuno-STAT framework for selective activation of targeted tumor-specific T cells, while the CUE-200 series is focused on cell surface receptors including CD80 and/or 4-1BBL to address T cell exhaustion associated with chronic infections. The CUE-300 series, being developed for autoimmune diseases, incorporates the inhibitory PD-L1 co-modulator for selective inhibition of the autoreactive T cell repertoire. This approach is pertinent for autoimmune diseases with known, well characterized, limited or few autoantigens, such as type 1 diabetes. The CUE-400 series, for autoimmune diseases with diverse or unknown autoantigens, represents a novel class of bispecific molecules that can selectively and effectively expand induced regulatory T cells, or iTregs. We categorize these molecules as “pathway-specific modulators,” or PSM. The first candidate, CUE-401, incorporates the two key biological signals that are necessary for generation of iTregs, namely IL-2 and TGF-beta. Based on structure-based rational protein engineering, both IL-2 and TGF-beta have been affinity tuned (i.e. the binding strength has been optimized) to maintain on-target engagement while minimizing systemic toxicities.

Our drug product candidates are in various stages of clinical and preclinical development, and while we believe that these candidates hold potential value, our activities are subject to significant risks and uncertainties. We have not yet commenced any commercial revenue-generating operations, have limited cash flows from operations, and will need to access additional capital to fund our growth and ongoing business operations.

Corporate Information

We were incorporated as Imagen Biopharma, Inc. in Delaware on December 31, 2014. In October 2016, we changed our name to Cue Biopharma, Inc. The address of our corporate headquarters is 21 Erie Street, Cambridge, Massachusetts 02139 and our telephone number is (617) 949-2680. Our website can be accessed at www.cuebiopharma.com. The information contained on, or that may be obtained from, our website is not, and shall not be deemed to be, a part of this prospectus.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

As a company with less than \$1.07 billion of revenue during our last fiscal year, we qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an emerging growth company for up to five years from the date of the closing of our initial public offering, or until such earlier time as we

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have more than \$1.07 billion in annual revenue, the market value of our stock held by non-affiliates is more than \$700 million or we issue more than \$1 billion of non-convertible debt over a three-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure and other requirements that are applicable to other public companies that are not emerging growth companies.

We are also a “smaller reporting company,” meaning that the market value of our stock held by non-affiliates is less than \$700 million and our annual revenue was less than \$100 million during our most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than \$250 million or (ii) our annual revenue was less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. For so long as we remain a smaller reporting company, we are permitted and intend to rely on exemptions from certain disclosure and other requirements that are applicable to other public companies that are not smaller reporting company.

THE OFFERING

Common stock offered by us	Shares of our common stock having an aggregate offering price of up to \$17,159,674.
Manner of offering	“At the market offering,” as defined in Rule 415(a)(4) of the Securities Act, that may be made from time to time by Stifel. See “Plan of Distribution” on page SA-14 of this prospectus. Stifel may also sell our common stock in negotiated transactions with our prior approval.
Use of proceeds	We intend to use the net proceeds from this offering to support clinical studies for our CUE-100 series biologics and for general corporate and working capital purposes, including ongoing research and development activities for our drug candidates and platform technologies. See “Use of Proceeds” on page SA-9 for additional information.
Risk factors	See the section entitled “Risk Factors” beginning on page SA-7 and the other information included or incorporated by reference in this prospectus for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock.
Nasdaq Capital Market symbol	Our common stock is currently listed on the Nasdaq Capital Market under the symbol “CUE.”

RISK FACTORS

You should carefully consider the following risk factors and the risk factors discussed under “Item 1A—Risk Factors” contained in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 and in Part II, Item 1A, Risk Factors of any subsequently filed Quarterly Reports on Form 10-Q, which are incorporated by reference in this prospectus in their entirety, together with all of the other information contained in this prospectus or incorporated by reference in this prospectus. The risks described in any document incorporated by reference are not the only ones we face, but are considered to be the most material. Additional risks of which we are not presently aware or that we currently believe are immaterial may also harm our business and results of operations. If any of these risks actually occur, our business, financial condition and results of operations would likely suffer. In that case, the market price of our common stock could decline, and you may lose part or all of your investment in our company.

Risks Related to this Offering of Our Common Stock

Sales of our common stock in this offering, or the perception that such sales may occur, could cause the market price of our common stock to fall.

We may issue and sell shares of our common stock for aggregate gross proceeds of up to \$17.2 million from time to time in connection with this offering. The issuance and sale from time to time of these new shares of common stock, or our ability to issue these new shares of common stock in this offering, could have the effect of depressing the market price of our common stock.

Purchasers will experience immediate dilution in the book value per share of the common stock purchased in the offering.

The shares sold in this offering, if any, will be sold from time to time at various prices. However, we expect that the offering price of our common stock will be substantially higher than the net tangible book value per share of our outstanding common stock. After giving effect to the sale of shares of our common stock in the aggregate amount of \$17,159,674 at an assumed offering price of \$13.27 per share, the last sale price of our common stock on March 8, 2021 on The Nasdaq Capital Market, and after deducting estimated commissions and estimated offering expenses, our as adjusted net tangible book value as of December 31, 2020 would have been approximately \$95.4 million, or approximately \$3.01 per share. This represents an immediate increase in as adjusted net tangible book value of approximately \$0.42 per share to our existing stockholders and an immediate dilution in as adjusted net tangible book value of approximately \$10.26 per share to purchasers of our common stock in this offering. See “Dilution” for more information.

In addition to this offering, subject to market conditions and other factors, we may pursue additional equity financings in the future, including future public offerings or future private placements of equity securities or securities convertible into or exchangeable for equity securities at prices that may be higher or lower than the price per share in this offering. Further, the exercise of outstanding options could result in further dilution to investors and any additional shares issued in connection with acquisitions will result in dilution to investors. In addition, the market price of our common stock could fall as a result of resales of any of these shares of common stock due to an increased number of shares available for sale in the market.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by any investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by any investors in this offering.

Our management will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and our stockholders will not have the opportunity as part of their investment decisions to assess whether the net proceeds are being used

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appropriately. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our failure to apply the net proceeds of this offering effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, in our investment of these net proceeds. You will not have the opportunity to influence our decisions on how to use our net proceeds from this offering.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

We have never declared nor paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate gross proceeds of up to \$17,159,674 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions paid to Stifel and proceeds to us, if any, are not determinable at this time. We estimate that the net proceeds from the sale of the shares of common stock that we are offering may be up to approximately \$16.6 million, after deducting commissions payable to Stifel and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering to support clinical studies for our CUE-100 series biologics and for general corporate and working capital purposes, including ongoing research and development activities for our drug candidates and platform technologies. The amounts and timing of our actual use of the net proceeds from this offering will vary depending on numerous factors, including the factors described under “Risk Factors” located elsewhere in this prospectus or in the information incorporated by reference herein. As a result, our management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds from this offering.

Pending application of the net proceeds as discussed above, we plan to invest any remaining proceeds from this offering in a variety of capital preservation instruments, including short-term, interest-bearing obligations, investment-grade instruments, or direct or guaranteed obligations of the U.S. government.

DIVIDEND POLICY

We have not declared or paid any cash dividends on our capital stock. We currently intend to retain any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

DILUTION

If you purchase shares of common stock in this offering, you will experience dilution to the extent of the difference between the public offering price per share in this offering and our pro forma as adjusted net tangible book value per share after this offering.

Net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of common stock outstanding. Our historical net tangible book value as of December 31, 2020 was \$78.8 million, or \$2.59 per share of common stock. After giving effect to our sale of common stock in this offering in the aggregate amount of \$17,159,674 at an assumed public offering price of \$13.27 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on March 8, 2021, and after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2020 would have been approximately \$95.4 million, or approximately \$3.01 per share. This represents an immediate increase in net tangible book value of approximately \$0.42 per share to existing stockholders and immediate dilution in as adjusted net tangible book value of approximately \$10.26 per share to new investors in this offering.

The following table illustrates this dilution on a per share basis. The as adjusted information is illustrative only and will adjust based on the actual public offering price, the actual number of shares sold and other terms of the offering determined at the time shares of our common stock are sold pursuant to this prospectus. The as adjusted information assumes that all of our common stock in the aggregate amount of \$17,159,674 is sold at the assumed public offering price of \$13.27 per share. The shares sold in this offering, if any, will be sold from time to time at various prices.

Assumed public offering price per share	\$13.27
Historical net tangible book value per share as of December 31, 2020	\$2.59
Increase in net tangible book value per share attributable to this offering	<u>\$0.42</u>
As adjusted net tangible book value per share, after giving effect to this offering	<u>\$ 3.01</u>
Dilution per share to new investors in this offering	<u><u>\$10.26</u></u>

The above discussion and table are based on 30,351,366 shares of common stock outstanding as of December 31, 2020, and excludes the following:

- 5,030,899 shares of our common stock issuable upon exercise of outstanding stock options issued pursuant to our 2016 Omnibus Incentive Plan and 2016 Non-Employee Equity Incentive Plan as of December 31, 2020 at a weighted average exercise price of \$9.10 per share;
- 230,002 shares of our common stock issuable upon vesting of outstanding restricted stock units issued pursuant to our 2016 Omnibus Incentive Plan as of December 31, 2020;
- 861,969 shares of common stock reserved for issuance under outstanding warrants as of December 31, 2020 at a weighted average exercise price of \$8.82 per share;
- 750,325 shares of our common stock reserved for future issuance under our 2016 Omnibus Incentive Plan as of December 31, 2020; and
- 5,400 shares of our common stock reserved for future issuance under our 2016 Non-Employee Equity Incentive Plan as of December 31, 2020.

DESCRIPTION OF COMMON STOCK

The following description of our common stock is intended as a summary only and therefore is not a complete description of our common stock. This description is based upon, and is qualified by reference to, our certificate of incorporation, our bylaws and applicable provisions of Delaware corporate law. You should read our certificate of incorporation and bylaws, which are filed as exhibits to the registration statement of which this prospectus forms a part, for the provisions that are important to you.

Voting Rights

Each outstanding share of our common stock is entitled to one vote on all matters submitted to a vote of shareholders. There is no cumulative voting.

Dividend and Liquidation Rights

The holders of outstanding shares of our common stock are entitled to receive dividends out of assets legally available for the payment of dividends at the times and in the amounts as our board of directors may from time to time determine. The shares of our common stock are neither redeemable nor convertible. Holders of our common stock have no preemptive or subscription rights to purchase any of our securities and no sinking fund provisions apply to our common stock. Upon our liquidation, dissolution or winding up, the holders of our common stock are entitled to receive pro rata our assets which are legally available for distribution, after payment of all debts and other liabilities and subject to the prior rights of any holders of preferred stock then outstanding.

We have never paid any cash dividends on our common stock.

Fully Paid and Non-Assessable

All outstanding shares of our common stock are fully paid and non-assessable.

Nasdaq Listing

Our common stock is listed on the Nasdaq Capital Market under the symbol “CUE.”

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A..

Provisions of Our Certificate of Incorporation and Bylaws and Delaware Law That May Have Anti-Takeover Effects

General

The provisions of the General Corporation Law of the State of Delaware (the “DGCL”) and our certificate of incorporation and bylaws could have the effect of discouraging others from attempting an unsolicited offer to acquire our company. Such provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Authorized but Unissued Shares

The authorized but unissued shares of our common stock and our preferred stock are available for future issuance without any further vote or action by our stockholders. These additional shares may be utilized for a variety of corporate purposes, including future public or private offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of our common stock and our preferred stock could render more difficult or discourage an attempt to obtain control over us by means of a proxy contest, tender offer, merger or otherwise.

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Actions at Meetings of Stockholders; Special Meeting of Stockholders and Advance Notice Requirements for Stockholder Proposals

Our certificate of incorporation and bylaws require that any action required or permitted to be taken by our stockholders may be effected by a consent in writing; however, stockholders pursuing an action by written consent will be required to comply with certain notice and record date requirements that are set forth in the DGCL. Our certificate of incorporation and bylaws also provide that special meetings of stockholders may be called from time to time only by the Chairman of our board of directors, our President, our Chief Executive Officer or a majority of our board of directors for the purpose or purposes specified in the notice of meeting, or by the request of the holders of record of at least 20% of outstanding shares of our common stock. In addition, the bylaws provide that candidates for director may be nominated and other business brought before an annual meeting only by the Board of Directors or by a stockholder who gives written notice to us not less than 90 days, nor more than 120 days, prior to the first anniversary of the preceding year's annual meeting, subject to certain exceptions. Such stockholder's notice must set forth certain information required by the bylaws. These provisions may have the effect of deterring unsolicited offers to acquire our company or delaying stockholder actions, even if they are favored by the holders of a majority of our outstanding voting securities.

Delaware Business Combination Statute

We must comply with Section 203 of the Delaware General Corporation Law, an anti-takeover law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years following the date the person became an interested stockholder, unless the business combination or the transaction in which the person became an interested stockholder is approved in a prescribed manner or certain other exceptions are met. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to an interested stockholder. An "interested stockholder" includes a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock. The existence of this provision generally will have an anti-takeover effect for transactions not approved in advance by the board of directors, including discouraging attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

Other Supermajority Voting Requirements

In addition to the supermajority requirement for certain business combinations discussed above, our certificate of incorporation and bylaws also contain other supermajority requirements, including the affirmative vote of the holders of at least 66 2/3% of the voting power of the shares of our then outstanding voting stock, voting together as a single class, is required to amend or repeal, or adopt any provisions in our certificate of incorporation inconsistent with certain designated provisions relating to (1) our board of directors, (2) indemnification of certain indemnitees of the Company, (3) venue for internal corporate claims, and (4) amendments to our certificate of incorporation or bylaws.

Directors, and Not Stockholders, Fix the Size of Our Board

Our certificate of incorporation and bylaws provide that the number of directors will be fixed from time to time exclusively pursuant to a resolution adopted by our board of directors.

Board Vacancies to Be Filled by Remaining Directors

Under our certificate of incorporation and bylaws, any vacancy on the board of directors created by any reason prior to the expiration of the term in which the vacancy occurs will be filled by a majority of the remaining directors, even if less than a quorum. A director elected to fill a vacancy will be elected for the unexpired term of his or her predecessor or until his or her successor is elected and qualified.

PLAN OF DISTRIBUTION

We have entered into the Sales Agreement, dated June 22, 2020, with Stifel under which we may offer and sell shares of our common stock having an aggregate gross sales price of up to \$40.0 million from time to time through Stifel. We originally filed a prospectus supplement, dated June 22, 2020 (the “Prior Prospectus Supplement”), for the offer and sale of up to \$40,000,000 of shares of our common stock pursuant to the Sales Agreement under the shelf registration statement on Form S-3 (Registration Statement No. 333-239357). The Prior Prospectus Supplement provided for sales of shares of our common stock having an aggregate offering price of up to \$40,000,000. As of the date of this prospectus, we have issued and sold an aggregate of 1,192,000 shares of common stock pursuant to the Sales Agreement and the Prior Prospectus Supplement, for which we had received gross proceeds of approximately \$22.8 million. Accordingly, this prospectus covers the offer and sale of up to \$17.2 million of our common stock that may be sold under the Sales Agreement as of the date of this prospectus. The Sales Agreement has been filed as an exhibit to a Current Report on Form 8-K filed under the Exchange Act and is incorporated by reference in this prospectus.

Upon delivery of a placement notice and subject to the terms and conditions of the Sales Agreement, Stifel may sell our common stock by any method permitted by law deemed to be an “at the market offering” as defined in Rule 415 promulgated under the Securities Act. Stifel may also sell our common stock in negotiated transactions with our prior approval. We may instruct Stifel not to sell common stock if the sales cannot be effected at or above the price designated by us from time to time. We or Stifel may suspend the offering of common stock upon notice and subject to other conditions.

We will pay Stifel commissions, in cash, for its services in acting as agent in the sale of our common stock. Stifel will be entitled to compensation at a commission rate equal to up to 3.0% of the aggregate gross proceeds from each sale of our common stock. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions paid to Stifel and proceeds to us, if any, are not determinable at this time. We have also agreed to reimburse Stifel for certain expenses incurred in connection with the offering of our common stock pursuant to the Sales Agreement, up to a maximum of \$50,000. We estimate that the total expenses for the offering, excluding compensation and reimbursements payable to Stifel under the terms of the Sales Agreement, will be approximately \$200,000.

Settlement for sales of common stock will occur on the second business day, or such earlier day as is industry practice for regular-way trading, following the date on which any sales are made, or on some other date that is agreed upon by us and Stifel in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our common stock as contemplated in this prospectus will be settled through the facilities of The Depository Trust Company or by such other means as we and Stifel may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Subject to the terms and conditions of the Sales Agreement, Stifel will use its commercially reasonable efforts consistent with its normal trading and sales practices to sell on our behalf any shares to be offered by us under the Sales Agreement. In connection with the sale of the common stock on our behalf, Stifel will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Stifel will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Stifel against certain civil liabilities, including liabilities under the Securities Act.

The offering of our common stock pursuant to the Sales Agreement will terminate upon the earlier of (i) the sale of all of our common stock subject to the Sales Agreement or (ii) the termination of the Sales Agreement as permitted therein. We and Stifel may each terminate the Sales Agreement at any time upon written notice.

Stifel and its affiliates may in the future provide various investment banking, commercial banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, Stifel will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus.

LEGAL MATTERS

Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts, will pass upon the validity of the shares of common stock offered by this prospectus. Goodwin Procter LLP, New York, New York, has acted as counsel to Stifel in connection with certain legal matters related to this offering.

EXPERTS

The consolidated financial statements of Cue Biopharma, Inc. as of December 31, 2020 and 2019 and for the years then ended incorporated in this prospectus by reference from the Cue Biopharma, Inc. Annual Report on Form 10-K for the year ended December 31, 2020 have been audited by RSM US LLP, an independent registered public accounting firm, as stated in their report thereon incorporated herein by reference, and have been incorporated in this prospectus in reliance upon such report and upon the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC's website at www.sec.gov. Our web site is located at www.cuebiopharma.com. The information contained on, or that may be obtained from, our web site is not part of this prospectus.

We will provide, upon written or oral request, without charge to you, including any beneficial owner to whom this prospectus is delivered, a copy of any or all of the documents incorporated herein by reference other than the exhibits to those documents, unless the exhibits are specifically incorporated by reference into the information that this prospectus incorporates. You should direct a request for copies to us at Cue Biopharma, Inc., 21 Erie Street, Cambridge, Massachusetts 02139 or you may call us at (617) 949-2680.

INCORPORATION BY REFERENCE

This prospectus "incorporates by reference" certain information that we have filed with the SEC under the Exchange Act. This means we are disclosing important information to you by referring you to those documents. We incorporate by reference the documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of the initial registration statement and the effectiveness of the registration statement until the offering is terminated:

- Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2020 filed with the SEC on March 9, 2021, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our [definitive proxy statement](#) for the 2021 Annual Meeting of Stockholders;
- Quarterly Report on [Form 10-Q](#) for the fiscal quarter ended March 31, 2021, as filed with the SEC on May 10, 2021; and
- The description of our Common Stock contained in our Registration Statement on [Form 8-A](#), filed with the SEC pursuant to Section 12(g) of the Exchange Act on December 13, 2017, including any amendment or reports filed for the purpose of updating such description.

To the extent that any information contained in any report on Form 8-K, or any exhibit thereto, was furnished to, rather than filed with, the SEC, such information or exhibit is specifically not incorporated by reference.

You should rely only on the information incorporated by reference or provided in this prospectus. We have authorized no one to provide you with different information. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of this document. All documents that we file pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of the initial registration statement and the effectiveness of the registration statement and prior to the termination of the offering will be deemed to be incorporated in this prospectus by reference and will be a part of this prospectus from the date of the filing of the document. Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus modifies or supersedes that statement. Any statement that is modified or superseded will not constitute a part of this prospectus, except as modified or superseded.



**Up to \$17,159,674
Common Stock**

PROSPECTUS

, 2021

STIFEL

PART II**INFORMATION NOT REQUIRED IN PROSPECTUS****Item 14. Other Expenses of Issuance and Distribution.**

The following is an itemized statement of expenses of the Company in connection with the issuance and delivery of the securities being registered hereby, other than underwriting discounts and commissions.

SEC Registration Fee	\$38,940
Printing Expenses	*
NASDAQ Listing Fees	*
Trustee Fees and Expenses	*
Accounting fees and expenses	*
Legal fees and expenses	*
Miscellaneous	*
Total	

* These fees will be dependent on the types of securities offered and number of offerings and, therefore, cannot be estimated at this time.

Item 15. Indemnification of Directors and Officers.

The following summary is qualified in its entirety by reference to the complete text of any statutes referred to below and the certificate of incorporation of Cue Biopharma, Inc., a Delaware corporation.

Section 145 of the General Corporation Law of the State of Delaware (the "DGCL") permits a Delaware corporation to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe the person's conduct was unlawful.

In the case of an action by or in the right of the corporation, Section 145 of the DGCL permits a Delaware corporation to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses that the Court of Chancery or such other court shall deem proper.

Section 145 of the DGCL also permits a Delaware corporation to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any

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liability asserted against such person and incurred by such person in any such capacity, or arising out of such person's status as such, whether or not the corporation would have the power to indemnify such person against such liability under Section 145 of the DGCL.

Article VI of our Amended and Restated Certificate of Incorporation states that our directors shall not be personally liable to us or to our stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability. Under Section 102(b) (7) of the DGCL, the personal liability of a director to the corporation or its stockholders for monetary damages for breach of fiduciary duty can be limited or eliminated except (i) for any breach of the director's duty of loyalty to the corporation or its stockholders; (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law; (iii) under Section 174 of the DGCL (relating to unlawful payment of dividend or unlawful stock purchase or redemption); or (iv) for any transaction from which the director derived an improper personal benefit.

Article V of our Amended and Restated Certificate of Incorporation provides that we shall indemnify (and advance expenses to) our officers and directors to the full extent permitted by the DGCL.

We have directors' and officers' liability insurance insuring our directors and officers against liability for acts or omissions in their capacities as directors or officers, subject to certain exclusions. Such insurance also insures us against losses which we may incur in indemnifying our officers and directors. As permitted by the DGCL, we have entered into indemnification agreements with each of our directors and executive officers that require us to indemnify such persons against various actions including, but not limited to, third-party actions where such director or executive officer, by reason of his or her corporate status, is a party or is threatened to be made a party to an action, or by reason of anything done or not done by such director in any such capacity. We intend to indemnify directors and executive officers against all costs, judgments, penalties, fines, liabilities, amounts paid in settlement by or on behalf such directors or executive officers and for any expenses actually and reasonably incurred by such directors or executive officers in connection with such action, if such directors or executive officers acted in good faith and in a manner they reasonably believed to be in or not opposed to the best interests of the Company, and with respect to any criminal proceeding, had no reasonable cause to believe their conduct was unlawful. We also intend to advance to our directors and executive officers expenses (including attorney's fees) incurred by such directors and executive officers in advance of the final disposition of any action after the receipt by the Company of a statement or statements from directors or executive officers requesting such payment or payments from time to time, provided that such statement or statements are accompanied by an undertaking, by or on behalf of such directors or executive officers, to repay such amount if it shall ultimately be determined that they are not entitled to be indemnified against such expenses by the Company.

The indemnification agreements also set forth certain procedures that will apply in the event of a claim for indemnification or advancement of expenses, including, among others, provisions about providing notice to the Company of any action in connection with which a director or executive officer seeks indemnification or advancement of expenses from the Company and provisions concerning the determination of entitlement to indemnification or advancement of expenses.

Item 16. Exhibits.

Exhibit Number	Exhibit Description	Incorporated by Reference				
		Filed Herewith	Form	Exhibit	Filing Date	Registration /File No.
1.1*	Form of Underwriting Agreement					
1.2	At-the-Market Equity Offering Sales Agreement by and between Cue Biopharma, Inc. and Stifel, Nicolaus & Company, Incorporated, dated June 22, 2020		8-K	1.1	6/22/20	001-38327
4.1	Amended and Restated Certificate of Incorporation, as amended, of the Registrant		10-Q	3.1	11/9/20	001-38327
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4.2	Amended and Restated Bylaws of the Registrant	S-1	3.5	12/05/17	333-220550
4.3	Specimen Certificate representing shares of common stock of the Registrant	S-1	4.1	12/05/17	333-220550
4.4*	Form of certificate representing preferred stock				
4.5*	Form of certificate of designations for preferred stock				
4.6	Form of Indenture relating to the issuance from time to time in one or more series of debentures, notes, bonds or other evidences of indebtedness	S-3ASR	4.6	6/22/20	333-239357
4.7*	Form of Senior Debt Security				
4.8*	Form of Subordinated Debt Security				
4.9*	Form of Warrant				
5.1	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP	POSASR	5.1	3/9/21	333-239357
23.1	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (contained in Exhibit 5.1)	POSASR	5.1	3/9/21	333-239357
23.2	Consent of RSM US LLP, Independent Registered Public Accounting Firm	X			
24.1	Power of Attorney (included on signature page)	S-3ASR	24.1	6/22/20	333-239357
24.2	Power of Attorney	POSASR	24.2	3/9/21	333-239357
25.1**	Form T-1 Statement of Eligibility of Trustee under the Trust Indenture Act of 1939, as amended				

* To be filed, if necessary, with a Current Report on Form 8-K or a Post-Effective Amendment to the registration statement.

** To be filed, if necessary, pursuant to Section 305(b)(2) of the Trust Indenture Act of 1939.

Item 17. Undertakings.

The undersigned registrant hereby undertakes:

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(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act;

(ii) to reflect in the prospectus any facts or events arising after the effective date of this registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in this registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement); and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in this registration statement or any material change to such information in this registration statement;

provided, however, that the undertakings set forth in subparagraphs (i), (ii) and (iii) above do not apply if the information required to be included in a post-effective amendment by those subparagraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934, that are incorporated by reference in this registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration, by means of a post-effective amendment, any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser: (A) each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and (B) each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser: (i) any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424; (ii) any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant; (iii) the portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and (iv) any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

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(6) That, for purposes of determining any liability under the Securities Act of 1933, (i) the information omitted from the form of prospectus filed as part of the registration statement in reliance upon Rule 430A and contained in the form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of the registration statement as of the time it was declared effective; and (ii) each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(7) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(8) The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the Securities and Exchange Commission under Section 305(b)(2) of the Trust Indenture Act.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant, pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

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 Post-Effective Amendment No. 3 to the Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on May 21, 2021.

CUE BIOPHARMA, INC.

By: /s/ Daniel R. Passeri
Daniel R. Passeri
Chief Executive Officer and Director

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, this Post-Effective Amendment No. 3 to the Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Name	Title	Date
<u>/s/ Daniel R. Passeri</u> Daniel R. Passeri	Chief Executive Officer and Director (Principal Executive Officer)	May 21, 2021
<u>/s/ Kerri-Ann Millar</u> Kerri-Ann Millar	Chief Financial Officer (Principal Financial and Accounting Officer)	May 21, 2021
* <u>Frederick Driscoll</u>	Director	May 21, 2021
* <u>Aaron Fletcher</u>	Director	May 21, 2021
* <u>Cameron Gray</u>	Director	May 21, 2021
* <u>Tamar Howson</u>	Director	May 21, 2021
* <u>Peter A. Kiener</u>	Director	May 21, 2021
* <u>Frank Morich</u>	Director	May 21, 2021
* <u>Barry Simon</u>	Director	May 21, 2021

* By: /s/ Kerri-Ann Millar
Kerri-Ann Millar
Attorney-in-fact

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in this Post-Effective Amendment No. 3 to the Registration Statement (No. 333-239357) on Form S-3 and related Prospectus of Cue Biopharma, Inc. of our report dated March 9, 2021 relating to the consolidated financial statements of Cue Biopharma, Inc. and Subsidiary appearing in the Annual Report on Form 10-K of Cue Biopharma, Inc. for the year ended December 31, 2020.

We also consent to the reference to our firm under the heading “Experts” in such Prospectus.

/s/ RSM US LLP

Boston, Massachusetts

May 21, 2021