

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

**FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

Histogen Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

20-3183915
(I.R.S. Employer
Identification Number)

10655 Sorrento Valley Road, Suite 200
San Diego, CA 92121
(858) 526-3100

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Steven J. Mento, Ph.D.
Executive Chairman and Interim Chief Executive Officer and President
Histogen Inc.

10655 Sorrento Valley Road, Suite 200
San Diego, CA 92121
(858) 526-3100

(Name, address, including zip code, and telephone number, including area code, of agent for service)

With a copy to:

Larry W. Nishnick
DLA Piper LLP (US)
4365 Executive Drive, Suite 1100
San Diego, CA 92121
Tel: (858) 677-1400
Fax: (858) 677-1401

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

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

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 definition 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 13(a) of the Exchange Act.

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered(1)	Proposed maximum offering price per share(2)	Proposed maximum aggregate offering price(2)	Amount of registration fee
Common Stock, par value \$0.0001 per share	16,882,359	\$0.38	\$6,415,296.42	\$594.70

(1) Represents (i) 8,235,297 share of common stock, par value \$0.0001 per share, of the registrant ("Common Stock"), (ii) 8,235,297 shares of Common Stock that are issuable upon the exercise of certain warrants that were acquired by the selling stockholders in a private placement transaction and (iii) 411,765 shares of Common Stock that are issuable upon exercise of certain warrants issued to the placement agent pursuant to an engagement letter in connection with such private placement transaction, each of which may be sold by the selling stockholders named in this registration statement. Pursuant to Rule 416 of the Securities Act of 1933, as amended, this registration statement also covers such an indeterminate amount of shares of Common Stock as may become issuable to prevent dilution resulting from stock splits, stock dividends and similar events.

(2) Calculated pursuant to Rule 457(c), solely for the purpose of computing the amount of the registration fee, on the basis of the average of the high and low prices of the registrant's Common Stock quoted on The Nasdaq Capital Market on December 20, 2021.

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, as amended, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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 it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated _____, 2022

PRELIMINARY PROSPECTUS



HISTOGEN INC.

16,882,359 Shares of Common Stock

Pursuant to this prospectus, the selling stockholders identified herein (the “Selling Stockholders”) are offering on a resale basis an aggregate of 16,882,359 shares of common stock, par value \$0.0001 per share (the “Common Stock”), of Histogen Inc. (“Histogen,” “we,” “our” or the “Company”), a Delaware corporation. 16,470,594 shares of Common Stock offered for resale hereby were deemed acquired by certain Selling Stockholders pursuant to a securities purchase agreement by and among the Company and the Selling Stockholders, dated December 15, 2021 (the “Purchase Agreement”), of which 8,235,297 shares are outstanding and held by the Selling Stockholders and 8,235,297 shares are issuable upon the exercise of warrants (the “Common Warrants”) held by the Selling Stockholders and issued pursuant to the Purchase Agreement. 411,765 shares of Common Stock are issuable upon the exercise of warrants issued to the Company’s placement agent, H.C. Wainwright & Co., LLC (“Wainwright”), in connection with the Purchase Agreement (the “Placement Agent Warrants,” and collectively with the Common Warrants, the “Warrants”). The shares of Common Stock issued and the Common Stock issuable upon the exercise of the Warrants were issued pursuant to an exemption from the registration requirements of the Securities Act of 1933, as amended (the “Securities Act”) provided in Section 4(a)(2) thereof and/or Rule 506 of Regulations D promulgated thereunder. We are registering the resale of the shares of Common Stock covered by this prospectus as required by the Purchase Agreement and registration rights agreement entered into by and among the Company and the Selling Stockholders.

We will not receive any of the proceeds from the sale by the Selling Stockholders of the Common Stock. Upon any exercise of the Warrants by payment of cash, however, we will receive the exercise price of the Warrants. We intend to use those proceeds, if any, for general corporate purposes.

The Selling Stockholders may sell or otherwise dispose of the Common Stock covered by this prospectus in a number of different ways and at varying prices. We provide more information about how the Selling Stockholders may sell or otherwise dispose of the Common Stock covered by this prospectus in the section entitled “Plan of Distribution” on page 13. Discounts, concessions, commissions and similar selling expenses attributable to the sale of Common Stock covered by this prospectus will be borne by the Selling Stockholders. We will pay all expenses (other than discounts, concessions, commissions and similar selling expenses) relating to the registration of the Common Stock with the Securities and Exchange Commission, or SEC.

Our common stock is listed on The Nasdaq Capital Market under the symbol “HSTO.” On December 21, 2021, the last reported sale price for our common stock was \$0.378 per share.

Investing in our securities involves risks. See “[Risk Factors](#)” beginning on page 6 and “Item 1A—Risk Factors” of our most recent report on Form 10-K or 10-Q which is incorporated by reference in this prospectus before you invest in our securities.

Neither the SEC nor any state securities commission 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. The securities are not being offered in any jurisdiction where the offer is not permitted.

The date of this prospectus is _____, 2022.

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ABOUT THIS PROSPECTUS

This prospectus is part of the registration statement that we filed with the Securities and Exchange Commission (the “SEC”) pursuant to which the selling stockholders named herein may, from time to time, offer and sell or otherwise dispose of the shares of our common stock covered by this prospectus. As permitted by the rules and regulations of the SEC, the registration statement filed by us includes additional information not contained in this prospectus.

This prospectus and the documents incorporated by reference into this prospectus include important information about us, the securities being offered and other information you should know before investing in our securities. You should not assume that the information contained in this prospectus is accurate on any date subsequent to the date set forth on the front cover of this prospectus or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus is delivered or shares of common stock are sold or otherwise disposed of on a later date. It is important for you to read and consider all information contained in this prospectus, including the documents incorporated by reference therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you under “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” in this prospectus.

You should rely only on this prospectus and the information incorporated or deemed to be incorporated by reference in this prospectus. We have not, and the selling stockholders have not, authorized anyone to give any information or to make any representation to you other than those contained or incorporated by reference in this prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

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 in this prospectus 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 agreements, 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.

Unless otherwise indicated, information contained or incorporated by reference in this prospectus concerning our industry, including our general expectations and market opportunity, is based on information from our own management estimates and research, as well as from industry and general publications and research, surveys and studies conducted by third parties. Management estimates are derived from publicly available information, our knowledge of our industry and assumptions based on such information and knowledge, which we believe to be reasonable. In addition, assumptions and estimates of our and our industry’s future performance are necessarily uncertain due to a variety of factors, including those described in “Risk Factors” beginning on page 6 of this prospectus. These and other factors could cause our future performance to differ materially from our assumptions and estimates.

“Histogen,” the Histogen logo and other trademarks, service marks, and trade names of Histogen are registered and unregistered marks of Histogen Inc. Other third-party logos and product/trade names are registered trademarks or trade names of their respective companies.

PROSPECTUS SUMMARY

This summary highlights selected information from this prospectus and the documents incorporated herein by reference and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, including the risks of investing in our securities discussed under “Risk Factors” beginning on page 6 of this prospectus, the information incorporated herein by reference, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part. All references in this prospectus to “we,” “us,” “our,” “Histogen,” the “Company” and similar designations refer to Histogen Inc. and its consolidated subsidiaries, unless otherwise indicated or as the context otherwise requires.

Business Overview

We are a clinical-stage company focused on developing potential first-in-class restorative therapeutics that ignite the body’s natural process to repair and maintain healthy biological function.

Our technology is based on the discovery that growing fibroblast cells under simulated embryonic conditions induces them to become multipotent with stem cell-like properties without using embryonic stem cells or animal components. The environment created by our proprietary process is designed to mimic the conditions within the womb—very low oxygen and suspension. When cultured under these conditions, the fibroblast cells generate biological materials, growth factors and proteins, that have the potential to stimulate a person’s own stem cells to activate and replace/regenerate damaged cells and tissue. We believe our proprietary, reproducible manufacturing process provides targeted solutions that harness the body’s inherent regenerative power across a broad range of therapeutic indications including joint cartilage regeneration, spinal disc repair, and rejuvenation of other soft tissues such as tendon and ligament.

Our reproducible manufacturing process yields multiple biologic product candidates from a single bioreactor, including cell conditioned medium (CCM) and human extracellular matrix (hECM), creating a spectrum of product candidates for a variety of markets from one core technology.

- *Human Multipotent Cell Conditioned Media, or CCM:* A soluble multipotent CCM that is the starting material for products for skin care and other applications. The liquid complex produced through Histogen’s manufacturing process contains soluble biologicals with a diverse range of embryonic-like proteins. Because the cells produce and secrete these factors while developing the extracellular matrix, or ECM, these proteins are naturally infused into the liquid media in a stabilized form. The CCM contains a diverse mixture of cell-signaling materials, including human growth factors such as Keratinocyte Growth Factor, soluble human ECM proteins such as collagen, and vital proteins which support the epidermal stem cells that renew skin throughout life.
- *Human Extracellular Matrix, or hECM:* An insoluble hECM for applications such as orthopedics and soft tissue augmentation, which can be fabricated into a variety of structural or functional forms for tissue engineering and clinical applications. The hECM produced through our proprietary process is a novel, all-human, naturally secreted material. It is most similar to early embryonic structural tissue which provides the framework and signals necessary for cell in-growth and tissue development. By producing similar ECM materials to those that aided in the original formation of these tissues in the embryo, regenerative cells are supported in vitro and have shown potential as therapeutics in vivo.

Under our core technology platform, our pipeline of novel therapeutics focused on orthopedic indications includes two candidates in development; HST 003, a treatment for joint cartilage repair, and HST 004, a treatment for spinal disc repair. In addition, we retained development and commercialization rights to emricasan,

an asset previously developed by Conatus Pharmaceuticals Inc. (“Conatus”), which is being jointly developed with our collaboration partner, Amerimmune, for the potential treatment of COVID-19.

- **HST 003** is a human extracellular matrix, or hECM, intended for regenerating hyaline cartilage for the treatment of articular cartilage defects in the knee, with a novel, malleable scaffold that stimulates the body’s own stem cells. In September 2020, we were awarded a \$2.0 million grant by the Peer Reviewed Orthopedic Research Program (“PRORP”) of the U.S. Department of Defense (“DoD”) to partially fund a Phase 1/2 clinical trial of HST 003 for regeneration of cartilage in the knee. The U.S. Army Medical Research Acquisition Activity, 820 Chandler Street, Fort Detrick MD, 21702, is the awarding and administering acquisition office. The views expressed in this filing are ours and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government. In December 2020, we filed an investigational new drug application (“IND”) for the initiation of a Phase 1/2 clinical trial to evaluate the safety and efficacy of HST 003, implanted within microfracture interstices and the cartilage defect in the knee to regenerate hyaline cartilage in combination with a microfracture procedure. In January 2021, we announced that the FDA had notified the Company that the IND for the planned Phase 1/2 clinical trial of HST 003 was placed on clinical hold. The hold was due to additional chemistry, manufacturing, and controls (“CMC”) information required for the FDA to complete their review. Following the receipt of the written clinical hold letter on February 3, 2021, we submitted a complete response letter to the FDA on February 19, 2021. In March 2021, the FDA confirmed that Histogen had satisfactorily addressed all clinical hold questions and could proceed with initiation of the planned Phase 1/2 clinical trial of HST 003 and in June 2021, we initiated the trial and anticipate top line results in the first quarter of 2023.
- **HST 004** is a CCM solution intended to be administered through an intradiscal injection for spinal disc repair. Initial preclinical research has shown that the growth- and repair-factor enriched HST 004 stimulates stem cells from the spinal disc to proliferate and secrete aggrecan and collagen II, regenerate normal matrix and cell tissue structure, and restore disc height. HST 004 was also shown to both reduce inflammation and protease activity and upregulate aggrecan production in an ex vivo spinal disc model. In the second quarter of 2021, we initiated IND enabling activities for HST 004 and expect to file an IND in the third quarter of 2022.
- **Emricasan** is an orally available pan-caspase inhibitor being jointly developed with our partner Amerimmune for the potential treatment of COVID-19. On October 26, 2020, we entered into a Collaborative Development and Commercialization Agreement with Amerimmune, pursuant to which Amerimmune, at its expense and in collaboration with us, shall use commercially reasonable efforts to lead the development activities for emricasan. We filed and received permission from the FDA for an IND to initiate a Phase 1 study of emricasan in mild COVID-19 patients to assess safety and tolerability. In March 2021, we, together with our partner, Amerimmune, announced dosing the first patient in the Phase 1 study and in June 2021, we, and our partner Amerimmune, announced top line results from the Phase 1 study of emricasan in mild symptomatic COVID-19 patients to assess safety, tolerability, and preliminary efficacy. The study demonstrated that emricasan was safe and well-tolerated during the 14 days of dosing and at the day 45 follow-up, as compared to placebo with no reports of serious adverse events. Patients who completed treatment with emricasan had a complete resolution of the symptoms most commonly associated with mild COVID-19, such as cough, headache, and fatigue at day 7 and continued through day 45. Patients in the placebo arm who completed the study did not experience COVID-19 associated symptom resolution at any time point out to day 45. In September 2021, we, together with our partner Amerimmune, finalized a Phase 2 trial design for emricasan and initiated a process on strategic partnering options.
- **Other Pipeline Product Candidates**—Our pipeline also includes pre-clinical candidates focused on soft tissues such as tendon and ligament. In December of 2021, we received the initial data from our

pre-clinical proof of concept studies focused on tendon and ligament. We will continue to evaluate the data and any related pre-clinical development activities.

We have also developed a non-prescription topical skin care ingredient utilizing CCM that we believe harnesses the power of growth factors and other cell signaling molecules to support our epidermal stem cells, which renew skin throughout life. The CCM ingredient for skin care is licensed to Allergan PLC (“Allergan Agreements”), who formulates the ingredient into their skin care product lines.

Corporate Information

We were incorporated under the laws of Delaware under the name Conatus Pharmaceuticals, Inc. as a private company in July 2005. We completed our initial public offering in July 2013. In May 2020, we acquired Histogen Therapeutics, Inc. (formerly known as Histogen Inc.) through its merger with a wholly owned subsidiary of ours, with Histogen Therapeutics surviving as our wholly-owned subsidiary. As part of that transaction, Conatus Pharmaceuticals, Inc. changed its name to Histogen Inc. Our principal executive offices are located at 10655 Sorrento Valley Road, Suite 200, San Diego, CA 92121 and our telephone number is (858) 526-3100. Our website is www.histogen.com. Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus, and you should not consider information on our website to be part of this prospectus. We have included our website address as an inactive textual reference only.

THE OFFERING

Pursuant to this prospectus, the Selling Stockholders are offering on a resale basis an aggregate of 16,882,359 shares of Common Stock. 16,470,594 shares of Common Stock offered for resale hereby were acquired by certain Selling Stockholders pursuant to the Purchase Agreement by and among the Company and the Selling Stockholders, dated December 15, 2021, of which 8,235,297 shares are outstanding and held by the Selling Stockholders and 8,235,297 shares are issuable upon the exercise of the Common Warrants held by the Selling Stockholders and issued pursuant to the Purchase Agreement. 411,765 shares of Common Stock are issuable upon the exercise of Placement Warrants issued to Wainwright, the Company's placement agent, in connection with the Purchase Agreement.

Common Stock to be offered by the Selling Stockholders	8,235,297 shares of Common Stock and 8,647,062 shares of Common Stock issuable upon the exercise of Warrants.
Common Stock outstanding prior to this offering	58,597,274 shares (assuming the exercise of all Warrants).
Common Stock to be outstanding after this offering	41,714,915 shares (assuming the sale of all Common Stock and Warrants held by the Selling Securityholders).
Use of proceeds:	We will not receive any of the proceeds from the sale by the Selling Stockholders of the Common Stock. Upon any exercise of the Warrants by payment of cash, however, we will receive the exercise price of the Warrants. See "Use of Proceeds" on page 10 of this prospectus.
Risk factors:	You should read the "Risk Factors" section beginning on page 6 of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our securities.
Nasdaq Capital Market symbol:	Our common stock is listed on The Nasdaq Capital Market under the symbol "HSTO." We do not intend to apply for listing of the Warrants on any securities exchange or nationally recognized trading system.

RISK FACTORS

An investment in our securities involves certain risks. Before deciding to invest in our common stock, you should consider carefully the following discussion of risks and uncertainties affecting us and our securities, together with other information in this prospectus and the other information and documents incorporated by reference in this prospectus, including the risks, uncertainties and assumptions discussed under the heading “Risk Factors” in our most recent Annual Report on Form 10-K for the fiscal year ended December 31, 2020, or any updates in our Quarterly Reports on Form 10-Q or Current Reports on Form 8-K. Our business, business prospects, financial condition or results of operations could be seriously harmed as a result of these risks. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may materially and adversely affect our business, financial condition and results of operations. Please also read carefully the section below entitled “Special Note Regarding Forward-Looking Statements.”

Risks Related to Our Common Stock and this Offering

Our failure to meet the continued listing requirements of the Nasdaq could result in a delisting of our common stock.

We must continue to satisfy the Nasdaq Capital Market’s continued listing requirements, including, among other things, the corporate governance requirements, and the minimum closing bid price requirement. If we fail to satisfy the continued listing requirements of the Nasdaq, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so.

On August 18, 2021, we received a letter from the Listing Qualifications Department of the Nasdaq Stock Market (“Nasdaq”) indicating that, based upon the closing bid price of our common stock for the 30 consecutive business day period between July 7, 2021, through August 17, 2021, we did not meet the minimum bid price of \$1.00 per share required for continued listing on The Nasdaq Capital Market pursuant to Nasdaq Listing Rule 5550(a)(2). The letter also indicated that we will be provided with a compliance period of 180 calendar days, or until February 14, 2022 (the “Compliance Period”), in which to regain compliance pursuant to Nasdaq Listing Rule 5810(c)(3)(A).

If we fail to regain compliance with the minimum bid price requirement our stock may be delisted. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with Nasdaq’s listing requirements. Delisting from the Nasdaq Capital Market or any Nasdaq market could make trading our common stock more difficult for investors, potentially leading to declines in our share price and liquidity. Without a Nasdaq market listing, stockholders may have a difficult time getting a quote for the sale or purchase of our stock, the sale or purchase of our stock would likely be made more difficult and the trading volume and liquidity of our stock could decline. Delisting from Nasdaq could also result in negative publicity and could also make it more difficult for us to raise additional capital. The absence of such a listing may adversely affect the acceptance of our common stock as currency or the value accorded by other parties. Further, if we are delisted, we would also incur additional costs under state blue sky laws in connection with any sales of our securities. These requirements could severely limit the market liquidity of our common stock and the ability of our stockholders to sell our common stock in the secondary market.

There may be future sales of our securities or other dilution of our equity, which may adversely affect the market price of our common stock.

We are generally not restricted from issuing additional common stock, including any securities that are convertible into or exchangeable for, or that represent the right to receive, common stock. The market price of

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our common stock could decline as a result of sales of common stock or securities that are convertible into or exchangeable for, or that represent the right to receive, common stock after this offering or the perception that such sales could occur.

A more active, liquid trading market for our common stock may not develop, and the price of our common stock may fluctuate significantly.

Historically, the market price of our common stock has fluctuated over a wide range. During the 12-month period prior to the date of this prospectus, our common stock traded as high as \$1.98 per share and as low as \$0.366 per share. There has been relatively limited trading volume in the market for our common stock, and a more active, liquid public trading market may not develop or may not be sustained. Limited liquidity in the trading market for our common stock may adversely affect a stockholder's ability to sell its shares of common stock at the time it wishes to sell them or at a price that it considers acceptable. If a more active, liquid public trading market does not develop we may be limited in our ability to raise capital by selling shares of common stock and our ability to acquire other companies or assets by using shares of our common stock as consideration. In addition, if there is a thin trading market or "float" for our stock, the market price for our common stock may fluctuate significantly more than the stock market as a whole. Without a large float, our common stock would be less liquid than the stock of companies with broader public ownership and, as a result, the trading prices of our common stock may be more volatile and it would be harder for a stockholder to liquidate any investment in our common stock. Furthermore, the stock market is subject to significant price and volume fluctuations, and the price of our common stock could fluctuate widely in response to several factors, including:

- our quarterly or annual operating results;
- changes in our earnings estimates;
- investment recommendations by securities analysts following our business or our industry;
- additions or departures of key personnel;
- changes in the business, earnings estimates or market perceptions of our competitors;
- our failure to achieve operating results consistent with securities analysts' projections;
- changes in industry, general market or economic conditions; and
- announcements of legislative or regulatory changes.

The stock market has experienced extreme price and volume fluctuations in recent years that have significantly affected the quoted prices of the securities of many companies, including companies in the staffing industry. The changes often appear to occur without regard to specific operating performance. The price of our common stock could fluctuate based upon factors that have little or nothing to do with us and these fluctuations could materially reduce our stock price.

Sales of a substantial number of shares of our common stock by our stockholders in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities. We are unable to predict the effect that such sales may have on the prevailing market price of our common stock. As of December 21, 2021, we have outstanding warrants to purchase an aggregate of approximately 23,726,140 shares of our common stock, and options to purchase an aggregate of approximately 2,407,785 shares of our common stock, which, if exercised, may further increase the number of shares of our common stock outstanding and the number of shares eligible for resale in the public market.

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Our internal control over financial reporting may not meet the standards required by Section 404 of the Sarbanes-Oxley Act, and failure to achieve and maintain effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act, could have a material adverse effect on our business and share price.

Our management is required to report on the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for our management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation.

We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begins our Section 404 audits, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Our executive officers, directors and principal stockholders own a significant percentage of our stock and, if they choose to act together, will be able to exert control or significantly influence over matters subject to stockholder approval.

As of December 31, 2021, our executive officers, directors and greater than 5% stockholders, in the aggregate, own approximately 14.87% of our outstanding common stock. As a result, such persons, or their appointees to our board of directors, acting together, will be able to exert control or significantly influence over all matters submitted to our board of directors or stockholders for approval, including the appointment of our management, the election and removal of directors and approval of any significant transaction, as well as our management and business affairs. This concentration of ownership may have the effect of delaying, deferring, or preventing a change in control, impeding a merger, consolidation, takeover or other business combination involving us, or discouraging a potential acquiror from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders.

SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

This prospectus and the documents incorporated herein by reference contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements are based on our management's current beliefs, expectations and assumptions about future events, conditions and results and on information currently available to us. Discussions containing these forward-looking statements may be found, among other places, in the Sections entitled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" incorporated by reference from our most recent Annual Report on Form 10-K and in our Quarterly Reports on Form 10-Q, as well as any amendments thereto, filed with the SEC. This prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

All statements, other than statements of historical fact, included or incorporated herein regarding our strategy, future operations, financial position, future revenues, projected costs, plans, prospects and objectives are forward-looking statements. Words such as "expect," "anticipate," "intend," "plan," "believe," "seek," "estimate," "think," "may," "could," "will," "would," "should," "continue," "potential," "likely," "opportunity" and similar expressions or variations of such words are intended to identify forward-looking statements, but are not the exclusive means of identifying forward-looking statements. These forward-looking statements include, but are not limited to, statements about:

- any impact of the COVID-19 pandemic, or responses to the pandemic, on our business, clinical trials or personnel;
- our expectations regarding the potential benefits of our strategy, platform, product candidates, and technology;
- our expectations regarding our product candidates, collaborations, and related benefits;
- our beliefs regarding our industry;
- our beliefs regarding the success, cost and timing of our product candidate development and collaboration activities and current and future clinical trials and studies;
- our beliefs regarding the potential markets for our product candidates and collaborations and our ability to serve those markets;
- our ability to attract and retain key personnel;
- our estimates regarding the sufficiency of our cash and cash equivalents to fund our operations and our ability to obtain funding for our operations, including funding necessary to complete further development and any commercialization of our product candidates;
- our expected use of the net proceeds to us from this offering; and
- regulatory developments in the United States, or U.S. and foreign countries, with respect to our product candidates.

Such statements are based on currently available operating, financial and competitive information and are subject to various risks, uncertainties and assumptions that could cause actual results to differ materially from those anticipated or implied in our forward-looking statements due to a number of factors including, but not limited to, those set forth above under the section entitled "Risk Factors" in this prospectus and any accompanying prospectus supplement. Given these risks, uncertainties and other factors, many of which are beyond our control, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to revise any forward-looking statements to reflect events or developments occurring after the date of this prospectus, even if new information becomes available in the future.

USE OF PROCEEDS

All shares of our common stock offered by this prospectus are being registered for the accounts of the Selling Stockholders, and we will not receive any proceeds from the sale of these shares. However, we will receive proceeds from the exercise of the Warrants if such Warrants are exercised for cash. We intend to use those proceeds, if any, for general corporate purposes.

SELLING STOCKHOLDERS

On December 15, 2021, we entered into the Purchase Agreement with each of the Selling Stockholders (except Wainwright) pursuant to which we issued and sold in a private placement an aggregate of (i) 8,235,297 shares of Common Stock and (ii) Common Warrants to purchase up to an aggregate of 8,235,297 shares of Common Stock. The combined purchase price of one share of Common Stock and accompanying Common Warrant was \$0.425. We also issued Placement Warrants to purchase up to an aggregate of 411,765 shares of Common Stock.

The Common Stock being offered by the Selling Stockholders are those previously issued to the Selling Stockholders, and those issuable to the Selling Stockholders, upon exercise of the Warrants. The Selling Stockholders acquired the Common Stock and the Warrants pursuant to the Purchase Agreement or in the case of the Placement Agent Warrants, in connection with an engagement letter with the Wainwright entered into in connection with the private place transaction. We are registering the shares of Common Stock in order to permit the Selling Stockholders to offer the shares for resale from time to time. The Selling Stockholders may sell some, all or none of their shares of Common Stock. We do not know how long the Selling Stockholders will hold the Warrants, whether any will exercise the Warrants, and upon such exercise, how long such Selling Stockholders will hold the shares of Common Stock before selling them, and we currently have no agreements, arrangements or understandings with the Selling Stockholders regarding the sale of any of the shares.

Neither the Selling Securityholders, nor any persons having control over the Selling Securityholders, have held any position or office with us or our affiliates within the last three years or have had a material relationship with us or any of our predecessors or affiliates within the past three years, other than as a result of the ownership of our shares or other securities; *provided, however*, each of Michael Vasinkevich, Noam Rubinstein, Craig Schwabe and Charles Worthman are associated persons of Wainwright, which served as our placement agent in connection with the registered direct offering we consummated on November 11, 2020, our placement agent in connection with the public offering we consummated on January 4, 2021 and our placement agent in connection with the registered direct offering we consummated on June 7, 2021 for each of which Wainwright received compensation.

The table below lists the Selling Stockholders and other information regarding the beneficial ownership of the shares of Common Stock by each of the Selling Stockholder based on information supplied to us by the Selling Stockholders. The second column lists the number of shares of Common Stock beneficially owned by each Selling Stockholder, based on its ownership of shares of Common Stock and warrants, as of the date such information was provided to us, assuming exercise of the warrants held by the selling shareholders on that date, without regard to any limitations on exercises. The third column lists the number shares of Common Stock, including shares of Common Stock issuable upon exercise of the Warrants, being offered by this prospectus by the Selling Stockholders.

In accordance with the terms of a registration rights agreement with the Selling Stockholders, this prospectus generally covers the resale of the sum of (i) the number of shares of Common Stock issued to the Selling Stockholders pursuant to the Purchase Agreement and (ii) the maximum number of shares of Common Stock issuable upon exercise of the Warrants, determined as if the outstanding Warrants were exercised in full as of the trading day immediately preceding the date this registration statement was initially filed with the SEC, each as of the trading day immediately preceding the applicable date of determination and all subject to adjustment as provided in the registration rights agreement, without regard to any limitations on the exercise of the Warrants. The fourth and fifth columns assume the sale of all of the shares of Common Stock offered by the Selling Stockholders pursuant to this prospectus. The percentage of shares beneficially owned after the offering is based on 49,950,212 shares of our Common Stock actually outstanding as of December 21, 2021 (excluding all Warrants and other warrants outstanding as of December 21, 2021); *provided, however*, for the calculation of the percentage of shares beneficially owned after the offering the shares of our Common Stock outstanding includes such individual Selling Stockholder's warrants beneficially owned after the offering by such Selling Stockholder. Except as noted herein, beneficial ownership is determined in accordance with Section 13(d) of the Exchange Act and Rule 13d-3 thereunder.

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Under the terms of the Warrants and other warrants held by the Selling Stockholders, a Selling Stockholder may not exercise such securities to the extent such exercise would cause such Selling Stockholder, together with its affiliates and attribution parties, to beneficially own a number of shares of Common Stock which would exceed 4.99% or 9.99%, as applicable, of our then outstanding Common Stock following such exercise, excluding for purposes of such determination shares of common stock issuable upon exercise of the warrants which have not been exercised. The number of shares in the table below do not reflect this limitation and therefore, the ownership percentages may appear more significant than otherwise if such beneficial ownership were calculated in accordance with Section 13(d) of the Exchange Act and Rule 13d-3 thereunder. The Selling Stockholders may sell all, some or none of their shares in this offering. See “Plan of Distribution.”

Selling Securityholders	Number of Shares Beneficially Owned Prior to this Offering	Maximum Number of Shares to be Sold Pursuant in this Offering	Number of Shares Beneficially Owned After Offering	Percentage of Shares Owned After Offering
Armistice Capital Master Fund Ltd.(1)	13,897,162	9,882,356	4,014,806	7.44%
Intracoastal Capital, LLC(2)	7,160,436	4,705,884	2,454,552	4.68%
Bigger Capital Fund, LP(3)	2,382,354	1,882,354	500,000	*
Michael Vasinkevich(4)	536,578	264,044	272,534	*
Noam Rubinstein(4)	484,082	129,706	354,376	*
Craig Schwabe(4)	28,241	13,897	14,344	*
Charles Worthman(4)	15,368	4,118	11,250	*

* Represents beneficial ownership of less than one percent.

- (1) The shares are directly held by Armistice Capital Master Fund Ltd., a Cayman Islands exempted company (the “Master Fund”), and may be deemed to be indirectly beneficially owned by: (i) Armistice Capital, LLC (“Armistice Capital”), as the investment manager of the Master Fund; and (ii) Steven Boyd, as the Managing Member of Armistice Capital. The number of shares includes 8,955,984 shares of common stock issuable upon exercise of warrants held by the Master Fund, which, in each case, is subject to certain beneficial ownership limitations of 4.99% that prohibit the Master Fund from exercising any portion of a warrant if such exercise would result in the Master Fund owning a percentage of our outstanding common stock exceeding the 4.99% ownership limitation after giving effect to the issuance of common stock in connection with the Master Fund’s exercise of any portion of a warrant. The number of shares includes 8,955,984 shares of common stock issuable upon the exercise of certain warrants, all of which are subject to beneficial ownership limitations of 4.99% that prohibit the Master Fund from exercising any portion of a warrant if such exercise would result in the Master Fund owning a percentage of our outstanding common stock exceeding the 4.99% ownership limitation after giving effect to the issuance of common stock in connection with the Master Fund’s exercise of any portion of a warrant. The percentage of shares owned after offering assumes the exercise of all warrants held by the Master Fund, notwithstanding the existence of beneficial ownership limitations described above. Armistice Capital and Steven Boyd disclaim beneficial ownership of the securities except to the extent of their respective pecuniary interests therein. The business address of the Master Fund is c/o Armistice Capital, LLC, 510 Madison Ave, 7th Floor, New York, NY 10022.
- (2) Mitchell P. Kopin (“Mr. Kopin”) and Daniel B. Asher (“Mr. Asher”), each of whom are managers of Intracoastal Capital LLC (“Intracoastal”), have shared voting control and investment discretion over the securities reported herein that are held by Intracoastal. As a result, each of Mr. Kopin and Mr. Asher may be deemed to have beneficial ownership (as determined under Section 13(d) of the Exchange Act) of the securities reported herein that are held by Intracoastal. The number of shares includes 2,352,942 shares of common stock issuable upon exercise of a Warrant, which is subject to certain beneficial ownership limitations. The business address of Intracoastal is 245 Palm Trail, Delray Beach, FL 33483.
- (3) Michael Bigger is a managing member of Bigger Capital Fund, LP and has sole voting and dispositive power over the securities held by Bigger Capital Fund, LP. The number of shares includes 941,177 shares of

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common stock issuable upon exercise of a Warrant, which is subject to certain beneficial ownership limitations. The number of shares beneficially owned prior to this offering excludes 500,000 shares of common stock issuable upon exercise of a Warrant held by District 2 Capital Fund LP which Mr. Bigger is the managing member. The business address of Bigger Capital Fund, LP is 11700 West Charleston Blvd., #170-659, Las Vegas, NV 89135.

- (4) Each of the Selling Stockholders is affiliated with Wainwright, a registered broker dealer and has a registered address of c/o H.C. Wainwright & Co. 430 Park Ave, 3rd Floor, New York, NY 10022, and has sole voting and dispositive power over the securities held. The Selling Stockholder purchased the Warrants in the ordinary course of business and, at the time of purchase of the securities that are registered for resale, the selling shareholders had no agreements or understanding, directly or indirectly with any person to distribute securities.

PLAN OF DISTRIBUTION

Each Selling Stockholder of the securities and any of their pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their securities covered hereby on the principal Trading Market or any other stock exchange, market or trading facility on which the securities are traded or in private transactions. These sales may be at fixed or negotiated prices. A Selling Stockholder may use any one or more of the following methods when selling securities:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the securities as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales;
- in transactions through broker-dealers that agree with the Selling Stockholders to sell a specified number of such securities at a stipulated price per security;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The Selling Stockholders may also sell securities under Rule 144 or any other exemption from registration under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the Selling Stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the Selling Stockholders (or, if any broker-dealer acts as agent for the purchaser of securities, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this Prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with FINRA Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2440.

In connection with the sale of the securities or interests therein, the Selling Stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the securities in the course of hedging the positions they assume. The Selling Stockholders may also sell securities short and deliver these securities to close out their short positions, or loan or pledge the securities to broker-dealers that in turn may sell these securities. The Selling Stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities which require the delivery to such broker-dealer or other financial institution of securities offered by this prospectus, which securities such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The Selling Stockholders and any broker-dealers or agents that are involved in selling the securities may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the securities purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each Selling Stockholder has informed the Company that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the securities.

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The Company is required to pay certain fees and expenses incurred by the Company incident to the registration of the securities. The Company has agreed to indemnify the Selling Stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

We agreed to keep this prospectus effective until the earlier of (i) the date on which the securities may be resold by the Selling Stockholders without registration and without regard to any volume or manner-of-sale limitations by reason of Rule 144, without the requirement for the Company to be in compliance with the current public information under Rule 144 under the Securities Act or any other rule of similar effect or (ii) all of the securities have been sold pursuant to this prospectus or Rule 144 under the Securities Act or any other rule of similar effect. The resale securities will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the resale securities covered hereby may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale securities may not simultaneously engage in market making activities with respect to the common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the Selling Stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of the common stock by the Selling Stockholders or any other person. We will make copies of this prospectus available to the Selling Stockholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

Our common stock is quoted on The NASDAQ Capital Market under the symbol "HSTO."

LEGAL MATTERS

DLA Piper LLP (US), San Diego, California will pass for us upon the validity of the securities being offered by this prospectus and applicable prospectus supplement, and counsel named in the applicable prospectus supplement will pass upon legal matters for any underwriters, dealers or agents.

EXPERTS

The consolidated financial statements as of and for the years ended December 31, 2020 and 2019, included in our Annual Report on Form 10-K for the year ended December 31, 2020, have been audited by Mayer Hoffman McCann P.C., independent registered public accounting firm, as set forth in their report, and have been incorporated herein by reference in reliance on the report of Mayer Hoffman McCann P.C., given on the authority of such firm as experts in auditing and accounting in giving said reports.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We are subject to the informational requirements of the Exchange Act and in accordance therewith file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission. The Securities and Exchange Commission maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the Securities and Exchange Commission. The address of the Securities and Exchange Commission's website is www.sec.gov.

We make available free of charge on or through our website at www.histogen.com, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with or otherwise furnish it to the Securities and Exchange Commission.

We have filed with the Securities and Exchange Commission a registration statement under the Securities Act of 1933, as amended, relating to the offering of these securities. The registration statement, including the attached exhibits, contains additional relevant information about us and the securities. This prospectus does not contain all of the information set forth in the registration statement. You can obtain a copy of the registration statement for free at www.sec.gov. The registration statement and the documents referred to below under "Incorporation of Certain Information By Reference" are also available on our website, www.histogen.com.

We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with it into this prospectus, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this registration statement and prospectus the following documents, and any future filings we will make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the initial registration statement but prior to effectiveness of the registration statement and after

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the date of this prospectus but prior to the termination of the offering of the securities covered by this prospectus (other than current reports or portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K):

- Our Annual Report on Form 10-K for the year ended December 31, 2020, filed on [March 11, 2021](#);
- Our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2021, June 30, 2021, and September 30, 2021 filed on [May 13, 2021](#), [August 11, 2021](#), and [November 10, 2021](#), respectively;
- Our Current Reports on Form 8-K filed on [March 25, 2021](#), [May 27, 2021](#), [June 3, 2021](#), [June 8, 2021](#), [June 9, 2021](#), [June 25, 2021](#), [August 20, 2021](#), [November 8, 2021](#), [November 10, 2021](#) and [December 16, 2021](#); and
- the description of our common stock contained in our Registration Statement on [Form 8-A](#) (File No. 001-36003) filed with the SEC on July 12, 2013, pursuant to Section 12(b) of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

We will provide each person, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the information that has been incorporated by reference into this prospectus but not delivered with this prospectus upon written or oral request at no cost to the requester. Requests should be directed to:

Histogen Inc.
10655 Sorrento Valley Road, Suite 200
San Diego, CA 92121
(858) 526-3100
Attention: Investor Relations

We also maintain a website at www.histogen.com where incorporated reports or other documents filed with the SEC may be accessed. We have not incorporated by reference into this prospectus the information contained in, or that can be accessed through, our website, and you should not consider it to be part of this prospectus.



16,882,359 Shares of Common Stock

PROSPECTUS

, 2022

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

The following table sets forth the anticipated costs and expenses payable by Histogen Inc. (other than commissions and fees) in connection with the sale of the securities being registered. All amounts shown are estimates except for the SEC registration fee.

SEC registration fee	\$ 595
Legal fees and expenses	\$ 35,000
Accounting fees and expenses	\$ 7,500
Printing and miscellaneous expenses	\$ 6,905
Total	\$ 50,000

Item 15. Indemnification of Officers and Directors

Section 145 of the DGCL authorizes a court to award or a corporation's board of directors to grant indemnification to directors and officers in terms sufficiently broad to permit such indemnification under certain circumstances for liabilities (including reimbursement for expenses incurred) arising under the Securities Act.

Our certificate of incorporation includes a provision that, to the fullest extent permitted by the DGCL, eliminates the personal liability of our directors for monetary damages for breach of fiduciary duty as a director. In addition, together our certificate of incorporation and our bylaws require us to indemnify, to the fullest extent permitted by law, any person made or threatened to be made a party to an action, suit or proceeding (whether criminal, civil, administrative or investigative) by reason of the fact that such person is or was, or has agreed to become, a director or officer of Histogen or any predecessor of ours, or serves or served at any other enterprise as a director, officer or employee at our request or the request of any predecessor of ours, against expenses (including attorneys' fees), liabilities, losses, judgments, fines, and amounts paid in settlement actually and reasonably incurred in connection with any proceeding, if such person acted in good faith and in a manner which he or she 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 his or her conduct was unlawful. We are required to advance expenses incurred by our directors, officers, employees and agents in defending any action or proceeding for which indemnification is required or permitted, subject to certain limited exceptions. The indemnification rights conferred by our certificate of incorporation and bylaws are not exclusive.

In addition, we have entered into indemnification agreements with each of our executive officers and directors. We also maintain an officers and directors liability insurance policy.

The foregoing may reduce the likelihood of derivative litigation against our directors and executive officers and may discourage or deter stockholders or management from suing directors or executive officers for breaches of their duty of care, even though such actions, if successful, might otherwise benefit the company and our stockholders.

The underwriting agreement that we may enter into, Exhibit 1.1 to this registration statement, will provide for indemnification by any underwriters of the company, our directors, our officers who sign the registration statement and our controlling persons, if any, for some liabilities, including liabilities arising under the Securities Act.

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Item 16. Exhibits

<u>Exhibit Number</u>	<u>Description</u>
3.1	<u>Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K (File No. 001-36003) filed with the Commission on August 1, 2013).</u>
3.2	<u>Certificate of Amendment, filed May 26, 2020 (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K (File No. 001-36003) filed with the Commission on May 27, 2020).</u>
3.3	<u>Certificate of Amendment, filed May 26, 2020 (incorporated by reference to Exhibit 3.2 to the Current Report on Form 8-K (File No. 001-36003) filed with the Commission on May 27, 2020).</u>
3.4	<u>Amended and Restated Bylaws (incorporated by reference to Exhibit 3.3 to the Current Report on Form 8-K (File No. 001-36003) filed with the Commission on May 27, 2020).</u>
4.1	<u>Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q filed on August 13, 2020).</u>
4.2	<u>Form of Warrant (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form S-4 (Registration No. 333-236332) filed with the Securities and Exchange Commission on February 7, 2020).</u>
4.3	<u>Form of Warrant (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on November 12, 2020).</u>
4.4	<u>Form of placement agent's warrant (incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on November 12, 2020).</u>
4.5	<u>Form of Common Warrant (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form S-1 (Registration No. 333-251491) filed with the Securities and Exchange Commission on December 18, 2020).</u>
4.6	<u>Form of placement agent's warrant (incorporated by reference to Exhibit 4.6 to the Company's Registration Statement on Form S-1 (Registration No. 333-251491) filed with the Securities and Exchange Commission on December 18, 2020).</u>
4.7	<u>Form of pre-funded warrant (incorporated by reference to Exhibit 4.7 to the Company's Registration Statement on Form S-1 (Registration No. 333-251491) filed with the Securities and Exchange Commission on December 18, 2020).</u>
4.8	<u>Form of Warrant (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 8, 2021).</u>
4.9	<u>Form of Placement Agent Warrant (incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 8, 2021).</u>
4.10	<u>Form of Warrant (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on December 16, 2021).</u>
4.11	<u>Form of Placement Agent Warrant (incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on December 16, 2021).</u>
5.1*	<u>Opinion of DLA Piper LLP (US).</u>
23.1*	<u>Consent of Mayer Hoffman McCann P.C.</u>
23.2*	<u>Consent of DLA Piper LLP (US) (included in Exhibit 5.1).</u>
24.1	<u>Power of Attorney (included immediately following the signature page to the registration statement).</u>

* Filed herewith

Item 17. Undertakings

The undersigned registrant hereby undertakes:

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 the 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 the 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 Securities and Exchange Commission (the "Commission"), pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent 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 the registration statement or any material change to such information in the registration statement;

Provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the registration statement is on Form S-3 or Form F-3 and the information required to be included in a post-effective amendment by those paragraphs 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 (the "Exchange Act"), that are incorporated by reference in the 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 to any purchaser:

i. 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

ii. 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 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 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 the 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

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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 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 an undersigned registrant; and
- iv. Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

6) That, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to section 13(a) or section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Exchange Act) that is incorporated by reference in the 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.

7) 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 Commission under Section 305(b)(2) of the Trust Indenture Act.

Insofar as indemnification for liabilities arising under the Securities Act 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 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 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 registration statement to be signed on its behalf by the undersigned thereunto duly authorized in the City of San Diego, State of California, on December 22, 2021.

HISTOGEN INC.

By: /s/ Steven J. Mento, Ph.D.
Steven J. Mento, Ph.D.
Executive Chairman and Interim
Chief Executive Officer and President

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Steven J. Mento, Ph.D. and Susan A. Knudson, and each of them acting individually, as his true and lawful attorneys-in-fact and agent, with full power of each to act alone, with full powers of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this registration statement (including post-effective amendments and any related registration statements filed pursuant to Rule 462 and otherwise), and to file the same with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents, or any of them or their substitute or resubstitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Steven J. Mento, Ph.D.</u> Steven J. Mento, Ph.D.	Executive Chairman, Interim Chief Executive Officer and President <i>(Principal Executive Officer)</i>	December 22, 2021
<u>/s/ Susan A. Knudson</u> Susan A. Knudson	Executive Vice President and Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i>	December 22, 2021
<u>/s/ Susan Windham-Bannister, Ph.D.</u> Susan Windham-Bannister, Ph.D.	Director	December 22, 2021
<u>/s/ Daniel L. Kisner, M.D.</u> Daniel L. Kisner, M.D.	Director	December 22, 2021
<u>/s/ Rochelle Fuhrmann</u> Rochelle Fuhrmann	Director	December 22, 2021

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<u>/s/ David H. Crean, Ph.D.</u> David H. Crean, Ph.D.	Director	December 22, 2021
<u>/s/ Jonathan Jackson</u> Jonathan Jackson	Director	December 22, 2021
<u>/s/ Brian M. Satz</u> Brian M. Satz	Director	December 22, 2021



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San Diego, California 92121-2133
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T 858.677.1400
F 858.677.1401

December 22, 2021

Histogen Inc.
10655 Sorrento Valley Road, Suite 200
San Diego, CA 92121

Ladies and Gentlemen:

We have acted as counsel to Histogen Inc. (the "**Company**") in connection with the preparation and filing of a Registration Statement on Form S-3 (the "**Registration Statement**") filed with the Securities and Exchange Commission (the "**Commission**") pursuant to the rules and regulations of the Securities Act of 1933, as amended (the "**Act**") relating to resale from time to time by the selling stockholders listed in the Registration Statement under "Selling Stockholders" of up to 16,882,359 shares of the Company's common stock, par value \$0.0001 per share (the "**Common Stock**"), consisting of: (i) 8,235,297 issued and outstanding shares of Common Stock (the "**Selling Stockholder Shares**"), and (ii) 8,647,062 shares of Common Stock (the "**Warrant Shares**" and collectively with the Selling Stockholder Shares, the "**Shares**") issuable upon the exercise of (a) 8,235,297 shares of Common Stock that are issuable upon the exercise of certain warrants that were acquired by the Selling Stockholders in a private placement transaction (the "**Purchaser Warrants**"), and (b) 411,765 shares of Common Stock that are issuable upon exercise of certain warrants issued to certain Selling Stockholders as the designees of H.C., Wainwright & Co., LLC, the placement agent ("**Wainwright**") as part of Wainwright's compensation pursuant to an engagement letter in connection with such private placement transaction (the "**Placement Agent Warrants**", and together with the Purchaser Warrants, the "**Warrants**").

We are acting as counsel for the Company in connection with the sale of the Shares by the Selling Stockholders. In connection with this opinion, we have examined and relied upon the and the Registration Statement and related prospectus, the form of Purchaser Warrant, the form of Placement Agent Warrant, the Company's Amended and Restated Certificate of Incorporation, as amended, and Amended and Restated Bylaws, as amended, as currently in effect, and the originals or copies certified to our satisfaction of such other documents, records, certificates, memoranda and other instruments as in our judgment are necessary or appropriate to enable us to render the opinion expressed below.

In rendering this opinion, we have assumed the genuineness and authenticity of all signatures on original documents; the genuineness and authenticity of all documents submitted to us as originals; the conformity to originals of all documents submitted to us as copies; the accuracy, completeness and authenticity of certificates of public officials; and the due authorization, execution and delivery of all documents where due authorization, execution and delivery are prerequisites to the effectiveness of such documents (other than with respect to the Company). As to matters of fact material to the opinions expressed herein, we have relied on (a) information in public authority documents (and all opinions based on public authority documents are as of the date of such public authority documents and not as of the date of this opinion letter), and (b) factual information provided in certificates of officers of the Company. We have not independently verified the facts so relied on.

On the basis of the foregoing, and in reliance thereon, we are of the opinion that (i) the Selling Stockholder Shares to be sold by the Selling Stockholders have been duly authorized and are validly issued, fully paid and nonassessable; and (ii) the Warrant Shares, when issued upon exercise of the Warrants against payment therefor in accordance with the terms of the Warrants, will have been duly authorized and validly issued and will be fully paid and non-assessable.

The foregoing opinions are subject to the following exclusions and qualifications:

(a) Our opinions are as of the date hereof, and we have no responsibility to update this opinion for events and circumstances occurring after the date hereof or as to facts relating to prior events that are subsequently brought to our attention. This opinion is limited to the laws, including the rules and regulations, as in effect on the date hereof, and we disavow any undertaking to advise you of any changes in law.

(b) With respect to the Warrant Shares, we express no opinion to the extent that, notwithstanding the Company's current reservation of shares of Common Stock, future issuances of securities, including the Warrant Shares, of the Company and/or adjustments to outstanding securities, including the Warrants, of the Company may cause the Warrants to be exercisable for more shares of Common Stock than the number that remain authorized but unissued. Further, we have assumed the exercise price for the Warrant Shares will not be adjusted to an amount below the par value per share of the Common Stock.

(c) We do not express any opinions herein concerning any laws other than the laws in their current forms of the State of Delaware and the federal securities laws of the United States of America, and we express no opinion with respect to the laws of any other jurisdiction and expressly disclaim responsibility for advising you as to the effect, if any, that the laws of any other jurisdiction may have on the opinions set forth herein.

We consent to the reference to our firm in the prospectus and any prospectus supplements relating thereto under the caption "Legal Matters" and to the filing of this opinion as an exhibit to the Registration Statement and any amendments thereto, including any and all post-effective amendments. In giving our consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission thereunder.

Very truly yours,

/s/ DLA Piper LLP (US)

DLA PIPER LLP (US)

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in this Registration Statement on Form S-3, and related Prospectus, of our report dated March 11, 2021, with respect to the consolidated financial statements of Histogen Inc. (“Company”) as of December 31, 2020 and 2019, and for the years then ended, included in the Company’s annual report on Form 10-K for the year ended December 31, 2020, and to the reference to us under the heading “Experts” in the Prospectus which is part of this Registration Statement.

/s/ Mayer Hoffman McCann P.C.

San Diego, California
December 22, 2021