Filed pursuant to Rule 424(b)(3)
Registration No. 333-266366

PROSPECTUS

HISTOGEN INC.

5,647,870 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 5,647,870 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. 5,322,927 shares of Common Stock offered for resale hereby were deemed acquired by Armistice Capital Master Fund Ltd. ("Armistice") pursuant to a securities purchase agreement by and among the Company and Armistice, dated July 12, 2022 (the "Purchase Agreement"), of which 1,774,309 shares are issuable upon the exercise of a pre-funded warrant (the "Pre-Funded Warrant"), 1,774,309 shares are issuable upon the exercise of a Series A warrant (the "Series A Warrant"), and 1,774,309 shares are issuable upon the exercise of a Series B warrant (the "Series B Warrant," and together with the Pre-Funded Warrant and the Series A Warrant, the "Common Warrants") held by Armistice and issued pursuant to the Purchase Agreement. 124,202 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"). 52,558 shares of Common Stock are issuable upon the exercise of warrants (the "November 2020 Warrants") held by Armistice and issued pursuant to a securities purchase agreement by and among the Company and several institutional and accredited investors, including Armistice, dated November 11, 2020 (the "November 2020 Purchase Agreement), as amended by a warrant amendment agreement entered into by the Company and Armistice in connection with the Purchase Agreement (the "Warrant Amendment"). 148,183 shares of Common Stock are issuable upon the exercise of warrants (the "June 2021 Warrants," and collectively with the November 2020 Warrants, the "Existing Warrants"; the Existing Warrants collectively with the Common Warrants and the Placement Agent Warrants, the "Warrants") held by Armistice and issued pursuant to a securities purchase agreement by and among the Company and several institutional and accredited investors, including Armistice, dated June 7, 2021 (the "June 2021 Purchase Agreement"), as amended by the Warrant Amendment. 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 underlying the (i) Common Warrants covered by this prospectus as required by the Purchase Agreement and registration rights agreement; and (ii) Placement Agent Warrants and Existing Warrants covered by this prospectus based on our election to include such Common Stock in this registrations statement.

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 15. 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 August 2, 2022, the last reported sale price for our common stock was $2.535 per share.

Investing in our securities involves risks. See "Risk Factors" beginning on page 8 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 August 3, 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 8 of this prospectus. These and other factors could cause our future performance to differ materially from our assumptions and estimates.

On June 2, 2022, the Company's Board of Directors approved a one-for-twenty reverse stock split of its then outstanding common stock (the "Reverse Stock Split") with any fractional shares resulting from the Reserve Stock Split rounded down to the next whole share of common stock. The par value and the authorized shares of the common stock were not adjusted as a result of the Reverse Stock Split. All references to share and per share amounts for all periods presented in this prospectus have been retrospectively restated to reflect this Reverse Stock Split.

"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 8 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.

We are a clinical-stage therapeutics company focused on developing our proprietary hypoxia-generated growth factor technology platform and stem cell-free biologic products as potential first-in-class restorative therapeutics that ignite the body's natural process to repair and maintain healthy biological function. Our proprietary hypoxia-generated growth factor technology is based on the discovery that growing fibroblast cells under simulated embryonic conditions induces them to become multipotent with stem cell-like properties. The environment created by our proprietary process mimics the conditions within the womb — very low oxygen and suspension culture. When incubated 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. Our proprietary manufacturing process provides targeted solutions that harness the body's inherent regenerative power across a broad range of therapeutic indications including joint cartilage regeneration and spinal disc repair.

Our manufacturing process yields multiple biologic products 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 secreted into the liquid media. 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, protease inhibitors to prevent the turn-over of ECM, and other vital proteins which support the stem cells that renew cells 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 and crosslinked material. It is most ECM present in 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 this structural microenvironment and have shown potential as therapeutics in vivo.*

Under our biologics technology platform, our product candidates in development are HST-003, a treatment for joint cartilage repair, and HST-004, a treatment for spinal disc repair. In addition, within our small molecule pipeline, our product candidates include emricasan, CTS-2090 and CTS-2096. Currently, emricasan is being developed both jointly with our collaboration partner, Amerimmune, for the treatment of COVID-19, and we are evaluating the use of emricasan for other infectious diseases, including for the treatment of methicillin-resistant staphylococcus aureus ("MRSA"). We also have preclinical product candidates, CTS-2090 and CTS-2096, novel,

potent, orally bioavailable, and highly selective small molecule inhibitors of caspase-1 designed for the treatment of certain inflammatory diseases.

Biologics Technology Platform

- **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, DoD, 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. In June 2021, we initiated the trial and to date have had significant challenges with patient recruitment due to the specific nature of the study inclusion criteria and the impact of COVID-19 on the elective surgery environment. We have added additional qualified clinical sites to help supplement recruitment. We are currently evaluating the overall feasibility of the ongoing HST-003 trial including, implementing protocol modifications and adding more sites and other study resources. We expect to complete our feasibility evaluation in the fourth quarter of 2022.
- **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. However, due to pipeline program prioritization, the earliest we would anticipate filing an IND for HST-004 is the second half of 2023.

CCM Skin Care Ingredient

- 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"), who formulates the ingredient into their skin care product lines.

Small Molecule Pipeline

- Emricasan is an orally available pan-caspase inhibitor currently being developed both in collaboration with Amerimmune, for the treatment of COVID-19, and we are evaluating the use of emricasan for other infectious diseases, including for the treatment of MRSA. In October 2020, we entered into the Collaborative Agreement with Amerimmune. Under the Collaborative Agreement, during the agreed upon

research term, Amerimmune, at its own expense and in collaboration with us, is required to use commercially reasonable efforts to lead the development activities for emricasan, limited to the treatment of COVID-19. We believe that, for numerous reasons set forth in our demand for arbitration ("Arbitration Demand"), Amerimmune has failed to undertake commercially reasonable efforts towards the development of emricasan as required by the Collaborative Agreement. Therefore, we are currently seeking, amongst other remedies, a declaratory judgment that Amerimmune has materially breached the Collaborative Agreement. In which case, we would be entitled to terminate the Collaborative Agreement thereby terminating all rights and licenses granted to Amerimmune by us, and we would then have the rights to independently proceed with the development of emricasan for the treatment of infectious and inflammatory diseases at our discretion.

In July 2022, Amerimmune filed a complaint against us in the United States District Court for the Southern District of California, and a second, separate complaint against us in the Superior Court for the County of San Diego, in each case seeking injunctive and declaratory relief relating to Amerimmune's purported exercise of an option for additional license rights to develop additional products under the Collaborative Agreement. However, we have rejected Amerimmune's election of the option and believe that Amerimmune no longer has the right to exercise the option based on, among other reasons, our belief that the Collaborative Agreement was properly terminated as set forth in the Arbitration Demand. While we have not yet been served with either complaint, we believe any claims related to the Collaborative Agreement are subject to the arbitration proceeding and therefore, that both complaints were filed improperly and are subject to dismissal for this and additional reasons. Moreover, we deny the allegations set forth in both complaints, and intend to vigorously defend against the litigations.

Prior to initiating the Arbitration Demand, 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 June 2021, we along with 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. No patients in the placebo arm who completed the study experienced COVID-19 associated symptom resolution at any time point out to day 14. Some of the placebo patients did have COVID-19 symptom resolution at day 30 while others experienced symptoms that persisted at day 45. A total of 13 subjects were consented and randomized to receive either placebo or 25 mg emricasan orally, BID for 14 days. PK samples, taken at day 14 of the study to check for compliance, revealed that one patient in the treatment arm did not show any indications of emricasan or its known metabolites in plasma, leading to a reclassification of the patient for the subsequent analysis shown in Figure 1. Additionally, there were no serious adverse events reported, and the emricasan group had fewer adverse events compared to placebo; 33 vs 66%, respectively. As compared with placebo, the proportional odds of having a worse score on an eight-level ordinal scale (persistence of a score of 3) with emricasan was 0.1 (95% CI, 0.006 to 1.544) at day 14 and 0.12 (95% CI, 0 to 3.41) at days 30 and 45. The time to complete resolution of symptoms was shorter in the emricasan group compared to placebo (hazard ratio, 5.3, 95% CI, 1.005 to 27.9) (Figure 1).

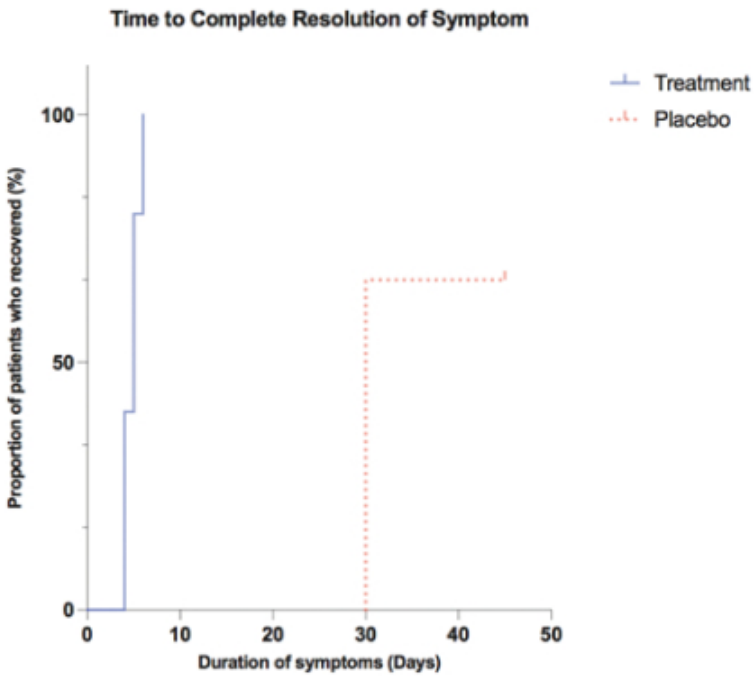

Figure 1. Per-protocol analysis of time to complete resolution of symptoms. Symptoms were defined by the 14-point questionnaire recommended by the FDA for outpatient COVID-19 studies. For the first 14 days, patients had daily tele-visits. In-person follow up visits were conducted on days 14, 30 and 45. The Kaplan-Meier plots for time-to-recovery show faster recovery in patients treated with emricasan, with a median of 5 (interquartile range 4-6 days) vs 37 days (interquartile range of 30-45) for participants randomized to the placebo group. The mean number of days to recovery for patients was 4.8 days with a SD=0.83 in the emricasan arm and 37.5 days, SD=8.2 in the placebo arm (p=0.001).

We believe that Amerimmune has failed to undertake commercially reasonable efforts toward conducting and completing the Phase 2 study as required by the Collaborative Agreement. As part of our Arbitration Demand, we have asked the arbitrator to terminate the Collaborative Agreement so that we can choose to conduct and complete the Phase 2 study independently. There can be no assurances that the Arbitration Demand will result in our favor and terminate the Collaborative Agreement. The ultimate outcome of this Arbitration is unknown at this time.

Independently, we are exploring the feasibility of testing emricasan in animal studies of other infectious diseases, initially focused on MRSA. We anticipate completing the feasibility assessment in the third quarter of 2022.

- **CTS-2090 and CTS-2096** are selective caspase-1 inhibitors targeting inflammasome activation and have potential to intervene in a variety of inflammation mediated diseases. In our internal small molecule program, we have assembled a proprietary portfolio of orally active molecules that inhibit inflammasome pathways and thus the activation of the potent inflammatory cytokine interleukin-1ß, or IL-1ß. Inhibition of IL-1ß is a clinically validated approach to treating inflammatory diseases, with injectable biologic products using that mechanism of action already on the market. The NLRP3 inflammasome pathway, for example, is dependent upon caspase-1, which activates IL-1ß. As such, caspase-1 occupies a uniquely central position in the inflammasome pathway, and we have leveraged our scientific expertise in caspase research and

development to design potent, selective and orally bioavailable inhibitors of caspase-1. Excess IL-1ß has been linked to a variety of diseases including rare genetic inflammatory diseases, cancer, liver and other gastrointestinal diseases, and cardiovascular diseases.

Our caspase-1 pipeline include preclinical product candidates CTS-2090 and CTS-2096. The selection of product candidate, CTS-2090, as a lead compound is based on its preclinical profile, including high selectivity for caspase-1, and drug-like properties showing a high degree of drug exposure in the intestinal track after oral administration. Similarly, we intend to evaluate CTS-2096, as an additional caspase-1 inhibitor drug candidate, and are in the process of exploring its drug like properties.

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 5,647,870 shares of Common Stock. 5,322,927 shares of Common Stock offered for resale hereby are issuable upon exercise of Warrants acquired by Armistice pursuant to the Purchase Agreement by and among the Company and Armistice, dated July 12, 2022, of which 1,774,309 shares are issuable upon the exercise of the Pre-Funded Warrant, 1,774,309 shares are issuable upon the exercise of the Series A Warrant, and 1,774,309 shares are issuable upon the exercise of the Series B Warrant held by Armistice and issued pursuant to the Purchase Agreement. 124,202 shares of Common Stock are issuable upon the exercise of the Placement Agent Warrants issued to Wainwright, the Company's placement agent, in connection with the Purchase Agreement. 52,558 shares of Common Stock are issuable upon the exercise of the November 2020 Warrants issued to Armistice pursuant to the November 2020 Purchase Agreement, dated November 11, 2020, as amended by the Warrant Amendment. 148,183 shares of Common Stock are issuable upon the exercise of the June 2021 Warrants issued to Armistice pursuant to the June 2021 Purchase Agreement, dated June 7, 2021, as amended by the Warrant Amendment.

Common Stock to be offered by the Selling Stockholders issuable upon exercise of the Warrants	5,647,870 shares of Common Stock issuable upon the exercise of Warrants.
Common Stock outstanding prior to this offering	8,145,320 shares (assuming the exercise of all Warrants).
Common Stock to be outstanding after this offering	2,497,450 shares (assuming the exercise of all Warrants held by the Selling Stockholders and sale of shares underlying the Warrants).
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 11 of this prospectus.
Risk factors:	You should read the "Risk Factors" section beginning on page 8 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, 2021, or any updates in our Quarterly Reports on Form 10-Q or Current Reports on Form 8-K (other than, in each case, information furnished rather than filed), which are incorporated by reference herein, and those risk factors that may be included in any applicable prospectus supplement, together with all of the other information included in this prospectus, any prospectus supplement and the documents we incorporate by reference. 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

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 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 $22.20 per share and as low as $2.06 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 July 28, 2022, we have outstanding warrants to purchase an aggregate of approximately 6.85 million shares of our common stock, and options to purchase an aggregate of approximately 133 thousand 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.

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 July 28, 2022, our executive officers, directors and greater than 5% stockholders, in the aggregate, own approximately 4.7% 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:

- our ability to obtain funding for our operations, including funding necessary to complete further development and any commercialization of our product candidates;
- our expectations regarding the potential benefits of our strategy and technology;
- our expectations regarding the arbitration proceeding related to emricasan and the joint development agreement with Amerimmune for COVID-19 and other infectious and inflammatory diseases;
- our expectations regarding the operation of our product candidates, collaborations and related benefits;
- 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, collaborations and our collaborators' ability to serve those markets;
- any impact of the COVID-19 pandemic, or responses to the pandemic, on our business, collaborations, clinical trials or personnel;
- our beliefs regarding our industry;
- our ability to attract and retain key personnel;
- regulatory developments in the United States and foreign countries, with respect to our product candidates; and
- the expected impact of any arbitration and litigation proceedings on our business, cash resources and the time required by management to address such proceedings.

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 July 12, 2022, we entered into the Purchase Agreement with Armistice pursuant to which we sold in a private placement (i) the Pre-Funded Warrant to purchase up to an aggregate of 1,774,309 shares of Common Stock, (ii) the Series A Warrant to purchase up to an aggregate of 1,774,309 shares of Common Stock, and (iii) the Series B Warrant to purchase up to an aggregate of 1,774,309 shares of Common Stock. The combined purchase price of one Pre-Funded Warrant and accompanying Series A Warrant and accompanying Series B Warrant was $2.818. We also issued Placement Agent Warrants to purchase up to an aggregate of 124,202 shares of Common Stock.

In connection with the Purchase Agreement, we also entered into the Warrant Amendment, pursuant to which we agreed to amend Armistice's Existing Warrants to purchase up (i) 52,558 shares of Common Stock issued pursuant to the November 2020 Purchase Agreement and (ii) 148,183 shares of Common Stock issued pursuant to the June 2021 Purchase Agreement, by reducing the Exercise Price (as defined therein) of the Existing Warrants to $2.568 per share.

The Common Stock being offered by the Selling Stockholders are those issuable to the Selling Stockholders upon exercise of the Warrants. Armistice acquired the Common Warrants pursuant to the Purchase Agreement and the Existing Warrants pursuant to the November 2020 Purchase Agreement and the June 2021 Purchase Agreement, as amended by the Warrant Amendment, and Wainwright acquired the Placement Agent Warrants in connection with an engagement letter Wainwright entered into in connection with the private place transaction. We are registering the shares of Common Stock issuable upon exercise of the Warrants 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 issuable upon exercise of the Warrants. 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 Stockholders, nor any persons having control over the Selling Stockholders, 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 5, 2021, our placement agent in connection with the registered direct offering we consummated on June 7, 2021, our placement agent in connection with the registered direct offering we consummated on December 15, 2021 and our placement agent in connection with the private placement offering we consummated on March 22, 2022, and the July 2022 Offering, 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.

This prospectus generally covers the resale of 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 2,497,450 shares of our Common Stock actually outstanding as of July 28, 2022 (excluding all Warrants and other warrants outstanding as of July 28, 2022); *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.

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 Stockholders	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)	5,770,727	5,523,668	247,059	9.89%
Michael Vasinkevich(2)	117,697	79,644	38,053	1.52%
Noam Rubinstein(2)	68,843	39,124	29,719	1.19%
Craig Schwabe(2)	6,196	4,192	2,004	*
Charles Worthman(2)	2,187	1,242	945	*

* 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 1,774,309 shares of common stock issuable upon exercise of a pre-funded warrant held by the Master Fund, which, is subject to certain beneficial ownership limitations of 9.99% that prohibit the Master Fund from exercising any portion of such pre-funded warrant if such exercise would result in the Master Fund owning a percentage of our outstanding common stock exceeding the 9.99% ownership limitation after giving effect to the issuance of common stock in connection with the Master Fund's exercise of any portion of such warrant. The number of shares includes 3,996,418 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) 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.

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, 2021 and 2020, included in our Annual Report on Form 10-K for the year ended December 31, 2021, 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

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, 2021, filed on March 10, 2022;
- the portions of our Definitive Proxy Statement on Schedule 14A (other than information furnished rather than filed) that are incorporated by reference into our Annual Report on Form 10-K, filed with the SEC on April 21, 2022;
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2022 filed on May 12, 2022;
- Our Current Reports on Form 8-K filed on February 15, 2022, February 22, 2022, March 22, 2022, March 25, 2022, April 29, 2022, June 2, 2022, June 7, 2022, June 17, 2022, June 30, 2022, and July 12, 2022; 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.

5,647,870 Shares of Common Stock

PROSPECTUS

August 3, 2022