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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2022

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 001-36003

Histogen Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**20-3183915**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
10655 Sorrento Valley Road, Suite 200, San Diego CA	**92121**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (858) 526-3100

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value	HSTO	The Nasdaq Capital Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES ☒ NO ☐

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

Large accelerated filer	☐	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. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

As of June 30, 2022, the last day of the Registrant's most recently completed second quarter, the aggregate market value of the common stock held by non-affiliates of the Registrant was approximately $5.4 million, based on the closing price of the shares of common stock on The NASDAQ Global Market on June 30, 2022 of $2.28 per share.

The number of shares of Registrant's Common Stock outstanding as of March 8, 2023 was 4,271,759.

DOCUMENTS INCORPORATED BY REFERENCE

The following documents are incorporated by reference into the following parts of the Annual Report on Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the Registrant's Proxy Statement for the 2023 Annual Meeting of Stockholders.

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PART I

Cautionary Note Regarding Forward-Looking Statements

This Annual Report contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical facts contained in this Annual Report are forward-looking statements, including statements regarding:

- *the sufficiency of our cash and cash equivalents and our ability to obtain funding for our operations, including funding necessary to complete further development and any commercialization of our product candidates;*
- *our ability to continue as a going concern;*
- *our expectations regarding the potential benefits of our strategy and technology and our ability to successfully develop product candidates using our technology;*
- *our expectations regarding the operation of our product candidates, future collaborations and related benefits;*
- *our beliefs regarding the success, cost and timing of our product candidate development and current and future clinical trials and studies;*
- *our beliefs regarding the potential markets for our product candidates;*
- *any impact of the COVID-19 pandemic, or responses to the pandemic, on our business, future collaborations, clinical trials or personnel;*
- *our beliefs regarding our industry;*
- *our ability to attract and retain key personnel; and*
- *regulatory developments in the United States and foreign countries, with respect to our product candidates.*

These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance and achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "could," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology. These forward-looking statements are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of risks, uncertainties and assumptions, including those described in Part I, Item 1A, "Risk Factors." The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

We have common law trademark rights in the unregistered marks "Histogen Inc.," "Histogen Therapeutics Inc.," "Histogen," and the Histogen logo in certain jurisdictions. Solely for convenience, trademarks and tradenames referred to in this Annual Report appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

Item 1. Business.

Overview

We are clinical-stage therapeutics company focused on developing potential first-in-class clinical and preclinical small molecule pan-caspase and caspase selective inhibitors that protect the body's natural process to restore immune function. Our product candidates include emricasan, CTS-2090 and CTS-2096. Currently, we are developing emricasan for acute bacterial skin and skin structure infections (ABSSSI) as well evaluating its use for other infectious diseases. Our pipeline also includes novel preclinical product candidates including CTS-2090 and CTS-2096, which are highly selective small molecule inhibitors of caspase-1 designed for the treatment of certain inflammatory diseases.

Our Product Candidates

Small Molecule Pipeline

- **Emricasan** is an orally available pan-caspase inhibitor designed to reduce the activities of human caspases, which are enzymes that mediate inflammation and apoptosis. Emricasan has completed extensive toxicology testing including chronic toxicology and clean carcinogenicity testing. The drug candidate has previously been shown to be well tolerated in multiple clinical studies involving approximately 1000 subjects employing multiple doses ranging from 1 mg to 500 mg orally with dosing for up to two years, including a Phase 1 study in mild symptomatic COVID-19 patients to assess safety, tolerability, and preliminary efficacy. Additionally, in the fourth quarter of 2021, we completed our pre-clinical evaluation of emricasan for the potential treatment of acute bacterial skin infections, including those related to MRSA, and anticipate initiating clinical development activities for the treatment of ABSSSI in the first half of 2023.

  In June 2021, we 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.

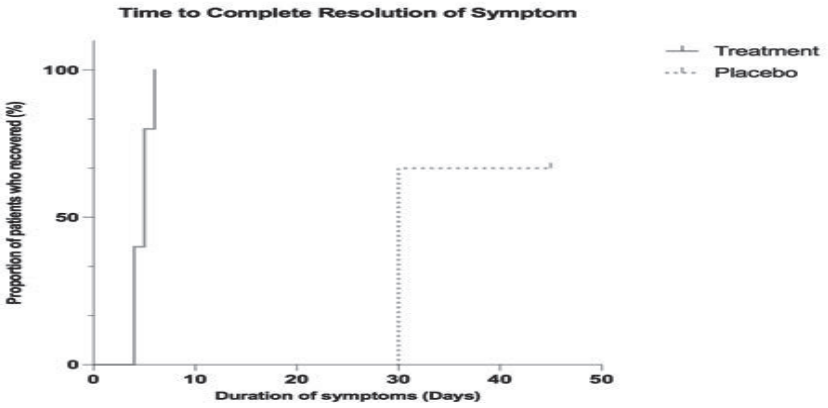

Figure 1. Per-protocol analysis of time to complete resolution of symptoms. Symptoms were defined by the 14-point questionnaire recommended by the FDA for outpatient COVID-19 studies. For the first 14 days, patients had daily tele-visits. In-person follow up visits were conducted on days 14, 30 and 45. 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).

At present, the Company has decided to pause development of emricasan as a treatment for COVID-19 in favor of development activities related to emricasan as a treatment for ABSSSI.

Additionally within our small molecule pipeline, we have assembled a proprietary portfolio of orally active molecules that inhibit inflammasome pathways and thus the activation of the potent inflammatory cytokine interleukin-1β, or IL-1β. Inhibition of IL-1β 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-1β. 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-1β has been linked to a variety of diseases including rare genetic inflammatory diseases, neurological diseases, cancer, liver and other gastrointestinal diseases, and cardiovascular diseases.

CTS-2090 and CTS-2096 are selective caspase-1 inhibitors targeting inflammasome activation and have potential to treat a variety of inflammation mediated diseases. Inflammasomes are a collection of large multiprotein structures responsible for the activation of inflammatory responses. There are six known inflammasome subtypes - NLRP1, NLRP3, NLRC4, NLRP6, AIM2 and IFI 16 - that respond to different stimuli. A primary function of the inflammasomes is to generate active caspase-1 from procaspase 1 in response to various pathogens and other stimuli. The ultimate products produced by the activation of caspase 1 are highly pro-inflammatory cytokines, IL-1ß and IL-18. In addition, caspase 1 initiates pyroptosis, a highly inflammatory form of cell death, through the cleavage of gasdermin D. 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.

Technology and Product Licensing Opportunities

Previously, our focus was 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. In December 2022, we announced termination of our HST-003 study for futility related to patient recruitment and due to pipeline reprioritization, in the third quarter of 2022, we suspended all IND enabling activities on our HST-004 program.

While we are actively seeking collaboration partners or acquirors for our Human Multipotent Cell Conditioned Media, or CCM and our Human Extracellular Matrix, or hECM, there are no assurances that we will find a collaboration partner or acquirer for CCM or hECM or that the terms and timing of any such arrangements would be acceptable to us.

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 CCM and 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.*

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 Orthopaedic 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 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 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. The Company added three additional clinical sites in the first quarter of 2022 in an attempt to help address the recruitment challenges. In the second quarter of 2022, the Company expanded its efforts in addressing the recruiting challenges, which included engaging a clinical research organization, or CRO, to evaluate both protocol changes and the potential of adding more clinical sites. In the third quarter of 2022, the Company implemented the protocol changes which the Company believes addressed the study inclusion criteria which should have improved the ability of the clinical sites to enroll patients. Despite these efforts, the clinical sites continue to be unsuccessful in recruiting and enrolling additional patients. Therefore, the Company made the decision in December of 2022 to terminate the study for futility regarding patient recruitment and redirect efforts and funding away from HST-003 to other product candidates.

- **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. In the third quarter of 2022, the Company suspended all IND enabling activities for the HST-004 program due to pipeline reprioritization.

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.

Market and Commercial Opportunity

Our small molecule pipeline of clinical and preclinical candidates, emricasan, CTS-2090 and CTS-2096, address what we believe to be underserved, multibillion-dollar global markets for the treatments for infectious and inflammatory diseases. We are currently developing emricasan for ABSSSI.

Material Contracts

Pfizer Inc.

In July 2010, we entered into a Stock Purchase Agreement with Pfizer pursuant to which it acquired all of the outstanding capital stock of Idun Pharmaceuticals, Inc. ("Idun"), a wholly-owned subsidiary of Pfizer at the time. Pursuant to the Stock Purchase Agreement, we will be required to make additional payments to Pfizer totaling $18.0 million upon the achievement of specified regulatory milestones relating to emricasan.

Prior to the termination of the Collaboration Agreement with Amerimmune on November 28, 2022, the obligations pursuant to the Stock Purchase Agreement were the responsibility of our former collaboration partner, Amerimmune. In accordance with authoritative guidance, amounts for the milestone payments will be recognized when it is probable that the related contingent liability has been incurred and the amount owed is reasonably estimated. No amounts for the milestone payments have been recorded during the year ended December 31, 2022.

Idun Distribution Agreement

In January 2013, the Company conducted a spin-off of its subsidiary Idun, which the Company had acquired from Pfizer in the transaction described above, to stockholders at that time. Immediately prior to the spin-off, all rights relating to emricasan were distributed to the Company pursuant to a distribution agreement.

PUR

In April 2019, Private Histogen entered into a Settlement, Release and Termination Agreement ("PUR Settlement") with PUR Biologics, LLC and its members which terminated the License, Supply and Operating Agreements between Private Histogen and PUR, eliminated Private Histogen's membership interest in PUR and returned all in-process research and development assets to Private Histogen (the "Development Assets"). The agreement also provided indemnifications and complete releases by and among the parties. The acquisition of the Development Assets was accounted for as an asset acquisition in accordance with ASC 805-50-50, Acquisition of Assets Rather than a Business.

As consideration for the reacquisition of the Development Assets, Private Histogen compensated PUR with both equity and cash components, including 8,366 shares of Series D convertible preferred stock with a fair value of $1.75 million and a potential cash payout of up to $6.25 million (the "Cap Amount"). Private Histogen paid PUR $0.5 million in upfront cash, forgave approximately $22 thousand of accounts receivable owed by PUR to Private Histogen, and settled an outstanding payable of PUR of approximately $23 thousand owed to a third party. The Company is also obligated to make milestone and royalty payments, including (a) a $0.4 million payment upon the unconditional acceptance and approval of a New Drug Application or Pre-Market Approval Application by the FDA related to the Development Assets, (b) a $0.4 million commercialization milestone upon reaching gross sales (by the Company or licensee) of the $0.5 million of products incorporating the Development Assets, and (c) a five percent (5%) royalty on net revenues collected by Histogen from commercial sales (by the Company or licensee) of products incorporating the Development Assets. The aforementioned cash payments, along with any future milestone and royalty payments, are all applied against the Cap Amount. In accordance with authoritative guidance, amounts for the milestone and royalty payments will be recognized when it is probable that the related contingent liability has been incurred and the amount owed is reasonably estimated. No amounts for the milestone and royalty payments have been recorded as a contingent liability at December 31, 2022 and 2021.

Governmental Regulation

FDA Regulation and Marketing Approval

In the U.S., the FDA regulates active pharmaceutical ingredients (API), drug products, biological products, and medical devices under the Federal Food, Drug, and Cosmetic Act (FDCA), the Public Health Service (PHS) Act, and other federal regulations. These FDA-regulated products are also subject to state and local statutes and regulations, as well as applicable laws or regulations in foreign countries, as applicable. The FDA, and comparable regulatory agencies in state and local jurisdictions and in foreign countries, impose substantial requirements on the research, development, testing, manufacture, quality control, labeling, packaging, storage, distribution, record-keeping, approval, post-approval monitoring, advertising, promotion, marketing, sampling and import and export of FDA-regulated products. Failure to comply with the applicable requirements at any time during the drug development process, approval process or after approval may subject an applicant to administrative or judicial sanctions or non-approval of product candidates. These sanctions could include a clinical hold on clinical trials, FDA's refusal to approve pending applications or related supplements, withdrawal of an approval, untitled or warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, restitution, disgorgement, civil penalties or criminal prosecution. Such actions by government agencies could also require us to expend a large number of resources to respond to the actions. Any agency or judicial enforcement action could have a material adverse effect on us.

IND and Clinical Trials of Drug

Prior to commencing a human clinical trial of a drug or biological product, an IND application, which contains the results of preclinical studies along with other information, such as information about product chemistry, manufacturing and controls and a proposed protocol, must be submitted to the FDA. An IND is a request for authorization from the

FDA to administer an investigational drug or biological product to humans. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA within the 30-day time period raises concerns or questions about the conduct of the clinical trial. In such a case, the IND sponsor must resolve any outstanding concerns with the FDA before the clinical trial may begin. A separate submission to the existing IND must be made for each successive clinical trial to be conducted during drug development.

An independent Institutional Review Board (IRB) for each site proposing to conduct the clinical trial must review and approve the investigational plan for the trial before it commences at that site. Informed written consent must be obtained from each trial subject.

Human clinical trials for drug and biological products typically are conducted in sequential phases that may overlap:

- Phase I—the investigational drug/biologic is given initially to healthy human subjects or patients with the target disease or condition in order to determine metabolism and pharmacologic actions of the drug in humans, side effects and, if possible, to gain early evidence on effectiveness. During Phase I clinical trials, sufficient information about the investigational drug/biologic's pharmacokinetics and pharmacologic effects may be obtained to permit the design of well-controlled and scientifically valid Phase II clinical trials.
- Phase II—clinical trials are conducted to evaluate the effectiveness of the drug/biologic for a particular indication or in a limited number of patients in the target population to identify possible adverse effects and safety risks, to determine the efficacy of the drug/biologic for specific targeted diseases and to determine dosage tolerance and optimal dosage. Multiple Phase II clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase III clinical trials.
- Phase III—when Phase II clinical trials demonstrate that a dosage range of the drug/biologic appears effective and has an acceptable safety profile, and provide sufficient information for the design of Phase III clinical trials, Phase III clinical trials in an expanded patient population at multiple clinical sites may begin. They are intended to further evaluate dosage, effectiveness and safety, to establish the overall benefit-risk relationship of the investigational drug/biologic and to provide an adequate basis for product labeling and approval by the FDA. In most cases, the FDA requires two adequate and well-controlled Phase III clinical trials to demonstrate the efficacy of the drug in an expanded patient population at multiple clinical trial sites.

All clinical trials must be conducted in accordance with FDA regulations, including good clinical practice (GCP) requirements, which are intended to protect the rights, safety and well-being of trial participants, define the roles of clinical trial sponsors, administrators and monitors and ensure clinical trial data integrity. Regulatory authorities, including the FDA, an IRB, a data safety monitoring board or the sponsor, may suspend or terminate a clinical trial at any time on various grounds, including a finding that the participants are being exposed to an unacceptable health risk or that the clinical trial is not being conducted in accordance with FDA requirements.

During the development of a new drug or biologic, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND (pre-IND), at the end of Phase II clinical trials (End-of-Phase (EOP) II), and before an NDA (pre-NDA) is submitted. Meetings at other times may be requested (Type A or C meetings). These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the EOP II meeting(s) to discuss their Phase II clinical trials results and present their plans for the pivotal Phase III registration trial that they believe will support approval of the new drug/biologic.

An investigational drug product that is a combination of two different drugs in the same dosage form or a combination of a drug/biologic with a device must comply with an additional rule that requires that each component make a contribution to the claimed effects of the drug product/combination device. This typically requires larger studies that test the drug against each of its components.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, biologics, and devices, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of

investigation, study sites and investigators, and other aspects of the clinical trial, is made public as part of the registration. Sponsors also are obligated to discuss the results of their clinical trials after completion. Disclosure of the clinical trial results can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

The New Drug Application (NDA) Approval Process

Our drug products must be approved by the FDA through the NDA approval process before they may be legally marketed in the U.S. The process required by the FDA before drugs may be marketed in the U.S. generally involves the following:

- completion of non-clinical laboratory tests, animal studies and formulation studies conducted according to good laboratory practice or other applicable regulations;
- submission of an IND application;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use or uses conducted in accordance with GCP;
- submission to the FDA of an NDA after completion of all pivotal clinical trials;
- FDA pre-approval inspection of manufacturing facilities and audit of clinical trial sites; and
- FDA approval of an NDA.

In order to obtain approval to market a drug in the U.S., a marketing application must be submitted to the FDA that provides data establishing to the FDA's satisfaction the safety and effectiveness of the investigational drug for the proposed indication. Each NDA submission requires a substantial user fee payment unless a waiver or exemption applies. The application includes all relevant data available from pertinent non-clinical studies, or preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other information. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators that meet GCP requirements.

Companies also must develop additional information about the chemistry and physical characteristics of the drug and finalize a process for the NDA sponsor's manufacturing the product in compliance with current good manufacturing practice (CGMP) requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate, and the manufacturer must develop and validate methods for testing the identity, strength, quality and purity of the API and drug product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf-life.

The results of drug development, non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product.

The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. The FDA has 60 days from its receipt of an NDA to conduct an initial review to determine whether the application will be accepted for filing.

If the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with CGMPs to ensure the product's identity, strength, quality and purity. The FDA has agreed to specific performance goals on the review of NDAs and seeks to review standard NDAs within 12 months from submission. The review process may be extended by the FDA for three additional months to consider certain late submitted information or information intended to clarify information already provided in the submission.

After the FDA evaluates the NDA, it will issue either an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional pivotal clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA may refer applications for novel drug products or drug products that present difficult questions of safety or effectiveness to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and, if so, under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facilities where the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with CGMP requirements and adequate to assure consistent production of the product within required specifications. We currently have manufacturing facilities at our corporate headquarters; however, we intend to facilitate a technology transfer of such functions and obligations to a third-party contract development manufacturing organization, for its clinical materials, and certain of its commercial partners for their commercial supply. Until such time as we no longer manufacture any clinical or commercial supply of product, we must ensure that our facilities satisfy FDA manufacturing requirements. Additionally, before approving an NDA, the FDA may inspect one or more clinical sites for compliance with GCP regulations.

If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies and often will request additional testing or information. This may significantly delay further review of the application. If the FDA finds that a clinical site did not conduct the clinical trial in accordance with GCP regulations, the FDA may determine the data generated by the clinical site should be excluded from the primary efficacy analyses provided in the NDA. Additionally, notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

As a condition of approval, the FDA may require, additional clinical trials after a product is approved. These so-called Phase IV or post-approval clinical trials may be a condition for continuing drug approval. The results of Phase IV clinical trials can confirm the effectiveness of a product candidate and can provide important safety information. In addition, the FDA now has express statutory authority to require sponsors to conduct post-marketing trials to specifically address safety issues identified by the agency.

The FDA also has authority to require a Risk Evaluation and Mitigation Strategy ("REMS") to ensure that the benefits of a drug outweigh its risks. A sponsor may also voluntarily propose a REMS as part of the NDA submission. The need for a REMS is determined as part of the review of the NDA. Elements of a REMS may include "dear doctor letters," a medication guide, more elaborate targeted educational programs, and in some cases elements to assure safe use ("ETASU"), which is the most restrictive REMS. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. These elements are negotiated as part of the NDA approval, and in some cases the approval date may be delayed. Once implemented, REMS are subject to periodic assessment and modification.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, manufacturing processes or facilities, may require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing original NDAs.

Even if a product candidate receives regulatory approval, the approval may be limited to specific disease states, patient populations and dosages, or might contain significant limitations on use in the form of warnings, precautions or contraindications, or in the form of onerous risk management plans, restrictions on distribution or post-marketing trial requirements. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Delay in obtaining, or failure to obtain, regulatory approval for our products, or obtaining approval but for significantly limited use, would harm our business. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products in development. In addition, we cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

The Hatch-Waxman Amendments

Under the Drug Price Competition and Patent Term Restoration Act of 1984, as amended, commonly known as the Hatch-Waxman Amendments, a portion of a product's U.S. patent term that was lost during clinical development and regulatory review by the FDA may be restored. The Hatch-Waxman Amendments also provide a process for listing patents pertaining to approved products in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book) and for a competitor seeking approval of an application that references a product with listed patents to make certifications pertaining to such patents. In addition, the Hatch-Waxman Amendments provide for a statutory protection, known as non-patent exclusivity, against the FDA's acceptance or approval of certain competitor applications.

Patent Term Restoration

Patent term restoration can compensate for time lost during drug development and the regulatory review process by returning up to five years of patent life for a patent that covers a new product or its use. This period is generally one-half the time between the effective date of an IND (falling after issuance of the patent) and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, provided the sponsor acted with diligence. Patent term restorations, however, cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended and the extension must be applied for prior to expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed by the NDA holder in the drug's application or otherwise are published in the FDA's Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application (ANDA). An ANDA permits marketing of a drug product that has the same active ingredient(s) in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical studies or clinical trials to prove the safety or effectiveness of their drug product. Drugs approved under and ANDA are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug.

Section 505(b)(2) of the FDCA provides an alternate regulatory pathway to FDA approval for new or improved formulations or new uses of previously approved drug products. Specifically, Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference.

Any applicant who files an ANDA seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must certify to the FDA that (i) no patent information on the drug product that is the subject of the application has been submitted to the FDA; (ii) such patent has expired; (iii) the date on which such patent expires; or (iv) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. This last certification is known

as a paragraph IV certification. A notice of the paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA or 505(b)(2) application refers. The applicant also may elect to submit a "section viii" statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the reference NDA holder and patent owners assert a patent challenge directed to one of the Orange Book listed patents within 45 days of the receipt of the paragraph IV certification notice, the FDA is prohibited from approving the application until the earlier of 30 months from the receipt of the paragraph IV certification expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired.

Market Exclusivity

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain drug applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a Paragraph IV certification.

The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, were conducted or sponsored by the applicant deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active ingredient. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA is required to conduct or obtain a right of reference to all of the non-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Post-Marketing Requirements for FDA Regulated Products

Following approval of a new product, the Company and the approved products are subject to continuing regulation by the FDA, state and foreign regulatory authorities including, among other things, monitoring and record-keeping activities, reporting adverse experiences to the applicable regulatory authorities, providing regulatory authorities with updated safety and efficacy information, manufacturing products in accordance with CGMP requirements, product sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising and restrictions on promoting products for uses or in patient populations that are not consistent with the drug's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet, including social media. Although physicians may prescribe products for off-label uses, manufacturers may not market or promote such off-label uses. Modifications or enhancements to the product or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, who may or may not grant approval, or may include in a lengthy review process.

The FDA, state and foreign regulatory authorities have broad enforcement powers. Failure to comply with applicable regulatory requirements could result in enforcement action by the FDA, state or foreign regulatory authorities (as applicable), which may include the following:

- untitled letters or warning letters;
- fines, disgorgement, restitution or civil penalties;
- injunctions (e.g., total or partial suspension of production) or consent decrees;
- product recalls, administrative detention, or seizure;

- customer notifications or repair, replacement or refunds;
- operating restrictions or partial suspension or total shutdown of production;
- delays in or refusal to grant requests for future product approvals or foreign regulatory approvals of new products, new intended uses, or modifications to existing products;
- withdrawals or suspensions of FDA product marketing approvals or foreign regulatory approvals, resulting in prohibitions on product sales;
- clinical holds on clinical trials;
- FDA refusal to issue certificates to foreign governments needed to export products for sale in other countries; and
- criminal prosecution.

Any of these sanctions could result in higher than anticipated costs or lower than anticipated sales and have a material adverse effect on our reputation, business, financial condition and results of operations. Such actions by government agencies could also require us to expend a large amount of resources to respond to the actions. Any agency or judicial enforcement action could have a material adverse effect on us.

In the U.S., after a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in registered facilities and in accordance with CGMP. We expect to rely on third parties for the production of clinical and commercial quantities of our products in accordance with CGMP regulations. CGMP regulations require, among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct deviations from CGMP. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. Manufacturers and other entities involved in the manufacture and distribution of approved drugs, biologics and medical devices are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and state agencies for compliance with CGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain CGMP compliance.

NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms and, in certain circumstances, suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to CGMP, could result in enforcement actions that can interrupt the operation of any such firm or result in restrictions on product supply, including, among other things, recall or withdrawal of the product from the market.

Newly-discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures.

Healthcare Laws and Regulations

Sales of our product candidates, if approved, or any other future product candidate will be subject to healthcare regulation and enforcement by the federal government and the states and foreign governments in which we might conduct our business. The healthcare laws and regulations that may affect our ability to operate include the following:

- The federal Anti-Kickback Statute makes it illegal for any person or entity to knowingly and willfully, directly or indirectly, solicit, receive, offer, or pay any remuneration that is in exchange for or to induce the referral of business, including the purchase, order, lease of any good, facility, item or service for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. The term "remuneration" has been broadly interpreted to include anything of value untitled letters or warning letters;

- Federal false claims and false statement laws, including the federal civil False Claims Act, prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, for payment to, or approval by, federal programs, including Medicare and Medicaid, claims for items or services, including drugs, that are false or fraudulent;
- Health Insurance Portability and Accountability Act of 1996 ("HIPAA") created additional federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors or making any false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services;
- Health Insurance Portability and Accountability Act of 1996 ("HIPAA") created additional federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors or making any false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and their implementing regulations, impose obligations on certain types of individuals and entities regarding the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information;
- The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services information related to payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

Also, many states have similar laws and regulations, such as anti-kickback and false claims laws that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, we may be subject to state laws that require pharmaceutical companies to comply with the federal government's and/or pharmaceutical industry's voluntary compliance guidelines, state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, as well as state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA.

Additionally, to the extent that our product is sold in a foreign country, we may be subject to similar foreign laws.

Chemistry, Manufacturing, and Controls

For our small molecule pipeline product candidates, we have successfully developed production processes that are scalable and economically viable. We have used contract manufacturing organizations for our own preclinical and clinical supply. Currently, we are not a party to any manufacturing agreements.

For our biologics technology platform licensing opportunities, we had established in-house research development and manufacturing capabilities in our corporate headquarters.

Intellectual Property

The proprietary nature of, and protection for, the Company's product candidates and discovery programs and know-how are important to its business. We have sought patent protection in the United States and internationally for emricasan and crystalline forms of emricasan. In addition, the Company has patent protection covering certain other preclinical stage compounds. The Company's policy is to pursue, maintain and defend patent rights whether developed internally or licensed from third parties and to protect the technology, inventions and improvements that are commercially important to the development of its business.

As of February 1, 2023, we hold or control 9 issued U.S. patents, 6 pending U.S. patent applications, and 62 patents in various jurisdictions outside the United States related to our small molecule product candidates and biologics technology. Additionally, we are pursuing 24 corresponding patent applications that are pending in various foreign jurisdictions. Further advancement of our intellectual property portfolio will require the filing of patent applications related to our small molecule compounds and product candidates. We have patents extending into the late 2020s, and early 2040 related to our small molecule product candidates, and late 2020s, and 2030 related to our biologics technology platform product candidates, as well as trade secrets protecting our intellectual property. Our patent prosecution strategy includes exploration of opportunities to expand our patent life in order to broaden our existing patent portfolio.

The following is a further description of certain of our key issued patents and pending applications related to our small molecule product candidates, including composition of matter coverage, method of protection, expiration date, number of related patents issued/pending in the US and foreign jurisdictions and the product candidates to which each patent/application relates. We currently hold or control:

- one patent issued in the United States (U.S. Patent No. 7,692,038) and twenty patents issued in foreign jurisdictions directed to the crystalline forms of emricasan. We expect that the crystalline forms and methods of use patent, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, will expire in July 2028 (United States) and December 2027 (international). It is possible that the term of a crystalline forms patent in the United States could be extended up to five additional years under the provisions of the Hatch-Waxman Act. Patent term extension may be available in certain foreign countries upon regulatory approval;
- one patent issued in the United States (U.S. Patent No. 11,447,497) and two patent applications pending in foreign jurisdictions directed to (S)-3-(2-(4-(benzyl)-3-oxopiperazin-1-yl)acetamido)-4-oxo-5-(2,3,5,6-tetrafluoro phenoxy) pentanoic acid derivatives and related compounds as caspase inhibitors for treating cardiovascular diseases. We expect that the patents granted in this family, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, will expire in June 2039; and
- two patent applications pending in the United States (U.S. Patent Application Nos. 16/812,063 and 18/104,691) and fourteen patent applications pending in foreign jurisdictions directed to caspase inhibitors, including CTS-2090 and CTS-2096, for treating autoimmune diseases, inflammatory diseases, CNS diseases liver diseases, respiratory diseases, cardiovascular diseases, dermatological diseases, rheumatological diseases, kidney diseases, and cancers. We expect that the patents granted in this family, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, will expire in March 2040.

In addition, below is a further description of certain of our key issued patents related to our biologics technology platform, including the method of protection, expiration date, number of related patents issued in the US and foreign jurisdictions and the product candidates to which each patent relates. We currently hold or control:

- three patents issued in the United States (U.S. Patent Nos. 10,538,736, 8,257,947 and 8,524,494) and forty-two patents issued in foreign jurisdictions directed to the production and use of extracellular matrix compositions and more specifically to proteins obtained by culturing cells under hypoxic conditions on a microcarrier beads or a three-dimensional surface in a suitable growth medium. The culturing method produces both soluble and non-soluble fractions, which may be used separately or in combination to obtain physiologically acceptable compositions useful in a variety of medical and therapeutic applications. These U.S. patents relate to HST-001, HST-002, HST-003, HST-004 and HST-005 and are expected to expire between January 2029 and 2030, while patents issued in foreign jurisdictions are expected to expire between January 2029 and July 2030, and three pending applications in foreign jurisdictions with one pending US application;
- one patent issued in the United States (U.S. Patent Nos. 8,535,913) and four issued patents in foreign jurisdictions which are also directed to the production and use of extracellular matrix compositions and more specifically to proteins obtained by culturing cells under hypoxic conditions on a surface in a suitable growth medium useful for promoting hair growth. This U.S. patent relates to HST-001 and it is expected to expire in January 30, 2029. The issued patents in foreign jurisdictions are expected to expire in January 2029; and four pending applications in foreign jurisdictions with two U.S. applications pending;

- three patents issued in the United States (U.S. Patent Nos. 8,530,415, 9,512,403, and 11,274,276) and three issued patents in foreign jurisdictions which are also directed to the production of a tissue patch for the repair and regeneration of cells and methods of use using of extracellular matrix compositions and more specifically to proteins obtained by culturing cells under hypoxic conditions on microcarrier beads or a three-dimensional a surface in a suitable growth medium. These U.S. patents relate to HST-003, HST-004 and HST-005 and are expected to expire January to March 2029. The issued patents in foreign jurisdictions are expected to expire in January 2029, and four pending applications in foreign jurisdictions with two US applications pending; and
- four patents issued in the United States (U.S. Patent Nos. 9,034,312, 9,506,038, 10,675,303, 11,191,780) and four patents issued in foreign jurisdictions related to extracellular matrix compositions for the treatment of cancer, which are scheduled to expire between January 2029 and November 2030, while patents issued in foreign jurisdictions are expected to expire in January 2029; and four pending applications in foreign jurisdictions with two US applications pending, and one further pending U.S. application related to skin care.

Wherever possible, we seek to protect our inventions by filing U.S. patents as well as foreign counterpart applications in select other countries. Because patent applications in the U.S. are maintained in secrecy for at least eighteen months after the applications are filed, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain that we were the first to make the inventions covered by each of our issued or pending patent applications, or that we were the first to file for protection of inventions set forth in such patent applications. Our planned or potential products may be covered by third-party patents or other intellectual property rights, in which case continued development and marketing of its products would require a license. Required licenses may not be available to us on commercially acceptable terms, if at all. If we do not obtain these licenses, we could encounter delays in product introductions while we attempt to design around the patents, or we could find that the development, manufacture or sale of products requiring such licenses are not possible.

In addition to patent protection, we also rely on know-how, trade secrets and the careful monitoring of proprietary information, all of which can be difficult to protect. We seek to protect some of our proprietary technology and processes by entering into confidentiality agreements with our employees, consultants, and contractors. These agreements may be breached, we may not have adequate remedies for any breach and our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our employees or our consultants or contractors use intellectual property owned by others in their work for us, disputes may also arise as to the rights in related or resulting know-how and inventions.

Competition

The biopharmaceutical industry is highly competitive, and many of our competitors have substantially greater financial resources and experience in research and development, manufacturing, conducting clinical trials, obtaining regulatory approvals and marketing products.

While we believe our small molecule pipeline focus on addressing underserved, multibillion-dollar global markets, in-house research and development, knowledge, experience, and scientific resources offer competitive advantages, we face competition in the biopharmaceutical industry. The key competitive factors affecting the success of emricasan and our other product candidates are successful completion of clinical trials and timely regulatory approval in markets worldwide.

Emricasan (ABSSSI)

Currently there is no direct competition in the pharmaceutical market for the treatment of ABSSSI ("Acute bacterial skin and skin structure infections") using a pan-caspase inhibitor:

- ABSSSI is a hard to treat hospital and community acquired bacterial skin infection that can result in extended hospital stays and in significant instances lead to death, often due to bacteremia.
- Last line antibiotics provide current treatment options that are eclipsed by bacterial strains causing ABSSSI developing antibiotic resistance against these antibiotics.

- ABSSSI is characterized by a pathogenic modulation of the human immune system, leading to cell death of immune cells and an aberrant cytokine storm.
- A recent published pre-clinical study establishes that modulating the host immune system with systemic administration of pan-caspase inhibitors, such as emricasan, can lead to a reduction of ABSSSI lesions caused by organisms such as MRSA.
- Currently, the commonly used antibiotic treatments for ABSSSI include dalbavancin, oritavancin, tedizolid, vancomycin, doxycycline and delafloxacin. However, there are no FDA approved treatments for ABSSSI that target this novel mechanism of action.

Emricasan (COVID-19)

Currently there are no approved treatments in the pharmaceutical market for the treatment of COVID-19 using a commercially available, or available under Emergency Use Authorization (EUA), pan-caspase inhibitor:

- COVID-19 is a multiple system disease that affects the lungs, circulatory system, the brain, kidney and other organs. Patients show a widespread of severity, some which remain asymptomatic, and others that progress all the way to rapid health deterioration, including death due to organ failure.
- While vaccination can prevent or diminish infection, or in case of break-through infection diminish mortality when compared to unvaccinated individuals, the constantly evolving virus may evade immunosurveillance and cause more serious disease, thus warranting the development of treatments that directly combat the viral life cycle.
- Patients that show greater morbidity and mortality are typically characterized by lymphopenia, a rapid decline in white blood cells. Preliminary studies indicate that lymphopenia is associated with more severe disease and outcomes. Emricasan targets multiple caspases including caspase-1 which is believed to be a key enzyme that when activated leads to lymphopenia.
- Physicians, and their patients, are seeking treatment options that will shorten recovery periods and prevent progression of the disease and its severity.
- Current non-vaccine treatment options fall into several therapeutic categories geared toward interfering with different aspects of the disease, including RNA polymerase inhibitors to prevent replication of the virus, general anti-inflammatory drugs, and monoclonal antibodies to interfere with cellular receptors to prevent uptake of the virus.
- Currently, there are no caspase inhibitors on the market that are targeting the same mechanism of action, such as prevention of lymphopenia.

Other treatments which aim to interfere with different aspects of the disease that are currently on the market as FDA approved drugs, under a FDA EUA or in active clinical development include: Remdesivir/Veklury (approved RNApol inhibitor), Dexamethasone (corticosteroid, anti-inflammatory), Bamlanivimab (Lilly, anti-COVID mAbs), and Casirivmab/Imdevimab (Regeneron, anti-COVID mAbs), Bamlaniviman/etesevimab combination (Lilly, anti-COVID mAbs combination), baricitinib/remdesivir combination (Lilly; combination treatment of remdesivir with a janus kinase inhibitor). More recently, molnupiravir (Merck), a viral RNA-dependent RNA polymerase inhibitor, and the PAXLOVID (nirmatrelvir ritonavir® combination treatment; Pfizer), a potent inhibitor of the virus poly-protein processing protease, and Evusheld (viral spike-protein binding monoclonal antibody combination; AstraZeneca) have been approved by the FDA under an EUA and have demonstrated moderate to significantly effective reductions in hospitalizations if taken early. Others are Sotrovimab (viral spike-protein binding; GSK), Actemra (IL-6 receptor binding; Genentech).

Human Capital

As of December 31, 2022, we had 7 full-time employees and 3 of our employees are engaged in research and development activities. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good notwithstanding the claims brought by two former employees. See Item 3. Legal Proceedings.

We recognize that attracting, motivating and retaining talent at all levels is vital to our continued success. Our employees are a significant asset and we aim to create an equitable, inclusive and empowering environment in which our employees can grow and advance their careers, with the overall goal of developing, expanding and retaining our workforce to support our current pipeline of product candidates and future business goals. By focusing on employee retention and engagement, we also improve our ability to support our clinical trials, our product candidate pipeline, our platform technologies, business and operations, and also protect the long-term interests of our security holders. Our success also depends on our ability to attract, engage and retain a diverse group of employees. Our efforts to recruit and retain a diverse and passionate workforce include providing competitive compensation and benefits packages and ensuring we listen to our employees.

We value innovation, passion, data-driven decision making, persistence and honesty, and are building a diverse environment where our employees can thrive and be inspired to make exceptional contributions to bring novel and more effective therapies to patients.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, motivating and integrating our existing and future employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through grants of stock-based compensation awards and payments of cash-based performance bonus awards, in order to increase stockholder value and the success of our company by motivating our employees to perform to the best of their abilities and achieve our objectives. We are committed to providing a competitive and comprehensive benefits package to our employees. Our benefits package provides a balance of protection along with the flexibility to meet the individual health and wellness needs of our employees. We plan to continue to refine our efforts related to optimizing our use of human capital as we grow, including improvements in the way we hire, develop, motivate and retain employees.

Corporate History and Reorganization

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 Annual Report, and you should not consider information on our website to be part of this Annual Report on Form 10-K. We have included our website address as an inactive textual reference only.

Item 1A. Risk Factors.

Summary of Risk Factors

We are providing the following summary of the risk factors contained in this Annual Report on Form 10-K to enhance the readability and accessibility of our risk factor disclosures. This summary does not address all of the risks that we face. We encourage you to carefully review the full risk factors contained in this Annual Report on Form 10-K in their entirety for additional information regarding the material factors that make an investment in our securities speculative or risky. The primary categories by which we classify risks include those related to: (i) our business and FDA Regulation, (ii) our intellectual property, and (iii) owning our common stock. Set forth below within each of these categories is a summary of the principal factors that make an investment in our common stock speculative or risky.

General Risks

- We must raise additional funds to finance our operations to remain a going concern.
- Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern, which may hinder our ability to obtain future financing.
- We will need to raise additional capital; however, it may be unavailable to us or, even if capital is obtained, may cause dilution or place significant restrictions on our ability to operate our business, including progressing development of our pipeline candidates.
- If we fail to retain current members of our senior management and scientific personnel, or to attract and keep additional key personnel, we may be unable to successfully develop or commercialize our product candidates.
- Our common stock may be delisted from Nasdaq if we fail to comply with Nasdaq's continued listing requirements, which could lead to the delisting of our common stock from Nasdaq and our common stock trading, if at all, only on the over-the-counter market, or OTC market.
- We will need to increase the size of our organization and may not successfully manage our growth.

Risks Related to Our Business, Industry, and FDA Regulation

- We are a clinical-stage development company, have a very limited operating history, are not currently profitable, do not expect to become profitable in the near future and may never become profitable.
- We are dependent on the success of one or more of our current product candidates, which are in early stages of clinical development, and we cannot be certain that any of them will receive regulatory approval or be commercialized.
- Any further development of product candidates will require significant resources from us or another collaboration partner, and in the event that we do not find a collaboration partner, development could be significantly delayed or result in the discontinuation of development of our product candidates.
- Employee litigation and unfavorable publicity could negatively affect our future business.
- Clinical drug development involves uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results.
- If development of our product candidates does not produce favorable results, we, and our future collaborators, may be unable to commercialize these products.

- We expect to continue to incur significant research and development expenses, which may make it difficult for us to attain profitability.

- We will need to raise additional capital; however, it may be unavailable to us or, even if capital is obtained, may cause dilution or place significant restrictions on our ability to operate our business, including progressing development of our pipeline candidates.

- Our product candidates are subject to extensive regulation under the FDA or comparable foreign authorities, which can be costly and time consuming, cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

Risks Related to Our Intellectual Property

- We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.
- We may not be able to protect our proprietary or licensed technology in the marketplace.
- Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection for licensed patents, pending patent applications and potential future patent applications and patents could be reduced or eliminated for non-compliance with these requirements.
- We may infringe the intellectual property rights of others, which may prevent or delay our drug development efforts and prevent us from commercializing or increase the costs of commercializing our products, if approved.

Risks Related to Owning Our Common Stock

- The market price of our common stock has been and may continue to be volatile, which could significantly worsen if we are delisted from Nasdaq and begin to trade on the OTC market.
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidate.
- Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our management.
- Our pre and post-Merger net operating loss carryforwards and certain other tax attributes may be subject to limitations. The pre and post-Merger net operating loss carryforwards and certain other tax attributes of us may also be subject to limitations as a result of ownership changes resulting from the Merger and subsequent financings.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should consider carefully the following risks factors, together with all of the other information included or incorporated by reference in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations." The risks described below are material risks currently known, expected or reasonably foreseeable by us. However, the risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business, operating results, prospects or financial condition. If any of these risks actually materialize, our business, prospects, financial condition, and results of operations could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

General Risks

We must raise additional funds to finance our operations to remain a going concern.

As of December 31, 2022, the Company has an accumulated deficit of $88.3 million and expects to incur operating losses and generate negative cash flows from operations for the foreseeable future. As of December 31, 2022, we had approximately $12.1 million in cash and cash equivalents. Based on our current business plan and related operating budget, there is substantial doubt about the Company's ability to continue as a going concern within one year from the date the consolidated financial statements are issued.

We have not yet established ongoing sources of revenues sufficient to cover our ongoing operating costs and will need to continue efforts to raise additional capital to support our future operating activities, including progression of our development programs, preparation for commercialization, and other operating costs. Management's plans with regard to these matters include entering into a combination of debt or additional equity financing arrangements, strategic partnerships, collaboration and licensing arrangements, or other similar arrangements. There can be no assurance that we will be able to obtain additional financing on terms acceptable to us, on a timely basis or at all. In addition, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate.

The consolidated financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. Based on the current business plan and operating budget, there is substantial doubt about the Company's ability to continue as a going concern within one year from the date the consolidated financial statements are issued. The consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

Our ability to continue as a going concern requires that we obtain sufficient funding to finance our operations in the near term. If we are unable to obtain sufficient funding, our business, prospects, financial condition and results of operations will be materially and adversely affected, and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding to us on commercially reasonable terms or at all.

We will require additional capital for the further development and, if approved, commercialization of our product candidates. Additional capital may not be available when we need it, on terms acceptable to us or at all. If adequate capital is not available to us on a timely basis, we may be required to significantly delay, scale back or discontinue our research and development programs or the commercialization of any product candidates, if approved, or be unable to continue or expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, results of operations, growth prospects and cause the price of our common stock to decline.

Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern, which may hinder our ability to obtain future financing.

Our consolidated financial statements as of December 31, 2022, were prepared under the assumption that we will continue as a going concern for the next twelve months. Due to our recurring losses from operations, we concluded that there is substantial doubt in our ability to continue as a going concern within one year after the financial statements are issued without additional capital becoming available. Our independent registered public accounting firm has issued an audit opinion that included an explanatory paragraph expressing substantial doubt in our ability to continue as a going concern without additional capital becoming available. Our ability to continue as a going concern is dependent upon our ability to obtain additional equity or debt financing, attain further operating efficiencies, reduce expenditures, and, ultimately, to generate revenue. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

We will need to raise additional capital; however, it may be unavailable to us or, even if capital is obtained, may cause dilution or place significant restrictions on our ability to operate our business.

Our operations have required substantial amounts of cash since inception. To date, we have funded our operations primarily through the sale of our preferred and common stock. We are currently advancing one product candidate through clinical development, and have other product candidates in preclinical development, as well as early-stage research projects. Developing our product candidates is expensive, and we expect to continue to spend substantial amounts as we fund our early-stage research projects and continue to advance our programs through preclinical and clinical development. Even if we are successful in developing our product candidates, obtaining regulatory approvals and potentially launching and commercializing any product candidate will require substantial additional funding. Since we will be unable to generate sufficient, if any, cash flow to fund our operations for the foreseeable future, we will need to seek additional equity or debt financing to provide the capital required to maintain or expand our operations.

There can be no assurance that we will be able to raise sufficient additional capital on acceptable terms or at all. If such additional financing is not available on satisfactory terms, or is not available in sufficient amounts, we may be required to significantly delay, scale back or discontinue our research and development programs or the commercialization of any product candidates, if approved, or be unable to continue or expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, results of operations, growth prospects and cause the price of our common stock to decline. In addition, we may be required to grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our inability to fund our business could lead to the loss of your investment.

Our future capital requirements will depend on many factors, including, but not limited to:

- the scope, rate of progress, results and cost of our clinical trials, preclinical studies and other related activities;
- our ability to establish and maintain strategic licensing or other arrangements and the financial terms of such arrangements;
- the timing of, and the costs involved in, obtaining regulatory approvals for any of our current or future product candidates;
- the number and characteristics of the product candidates we seek to develop or commercialize;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates;
- the cost of commercialization activities if any of our current or future product candidates are approved for sale, including marketing, sales and distribution costs;
- the expenses needed to attract and retain skilled personnel;
- the costs associated with being a public company;

- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing possible patent claims, including litigation costs and the outcome of any such litigation; and
- the impact of any natural disasters or public health crises, such as the COVID-19 pandemic, including on our ability to conduct clinical trials and further product candidate development.

If we raise additional capital by issuing common stock, or any other equity securities or securities convertible into equity, the percentage ownership of our existing stockholders may be reduced, and accordingly these stockholders may experience substantial dilution. We may also issue equity securities that provide for rights, preferences and privileges senior to those of our common stock. Given our need for cash and that equity issuances are the most common type of fundraising for similarly situated companies, the risk of dilution is particularly significant for our stockholders.

Further, SEC regulations limit the amount of funds we can raise during any 12-month period pursuant to our shelf registration statement on Form S-3. We are currently subject to General Instruction I.B.6 to Form S-3, or the Baby Shelf Rule, and the amount of funds we can raise through primary public offerings of securities in any 12-month period using our registration statement on Form S-3 is limited to one-third of the aggregate market value of the voting and non-voting common equity held by non-affiliates. We are currently limited by the Baby Shelf Rule as of the filing of this Annual Report on Form 10-K, until such time as our public float exceeds $75 million. If we are required to file a new registration statement on another form, we may incur additional costs and be subject to delays due to review by SEC staff.

If we fail to retain current members of our senior management and scientific personnel, or to attract and keep additional key personnel, we may be unable to successfully develop or commercialize our product candidates.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends on our continued ability to attract, retain, and motivate highly qualified management and scientific personnel. Competition for qualified personnel is intense. We may not be successful in attracting qualified personnel to fulfill our current or future needs and there is no guarantee that any of these individuals will join us on a full-time employment basis, or at all. Additionally, if we are unable to raise capital, this may further harm our ability to attract and retain key personnel. In the event we are unable to fill critical open employment positions, we may need to delay our operational activities and goals, including the development of our product candidates, and may have difficulty in meeting our obligations as a public company. We do not maintain "key person" insurance on any of our employees.

In addition, competitors and others are likely in the future to attempt to recruit our employees. The loss of the services of any of our key personnel, the inability to attract or retain highly qualified personnel in the future or delays in hiring such personnel, particularly senior management, and other technical personnel, could materially and adversely affect our business, financial condition, and results of operations. In addition, the replacement of key personnel likely would involve significant time and costs, and may significantly delay or prevent the achievement of our business objectives.

On November 8, 2021, Richard Pascoe stepped down from his position as our President and Chief Executive Officer and as a member of our Board. The Board appointed Steven J. Mento, Ph.D., a current member of the Company's Board of Directors, as Executive Chairman and Interim President and Chief Executive Officer as of November 8, 2021. On February 22, 2022, we announced the Board's decision to postpone any search for a permanent President and Chief Executive Officer at this time. We may also have to take additional measures to retain existing executives and other personnel.

From time to time, our management seeks the advice and guidance of certain scientific advisors and consultants regarding clinical and regulatory development programs and other customary matters. These scientific advisors and consultants are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, our scientific advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

Our common stock may be delisted from Nasdaq if we fail to comply with Nasdaq's continued listing requirements, the failure of which could lead to the delisting of our common stock from Nasdaq and our common stock trading, if at all, only on the over-the-counter market, or OTC market.

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 Nasdaq, which we have in the past. Nasdaq may take steps to delist our common stock. While we currently are in compliance with the Nasdaq listing rules, if we fail in the future to comply with Nasdaq listing rules, it could lead to the delisting of our common stock from Nasdaq and our common stock trading, if at all, only on the over-the-counter market, or OTC market.

If we fail to maintain our listing on Nasdaq, it 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. 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. If our common stock is delisted by Nasdaq, our common stock may be eligible to trade on an over-the-counter quotation system, such as the OTCQB market, where an investor may find it more difficult to sell our common stock or obtain accurate quotations as to the market value of our common stock. We cannot assure you that our common stock, if delisted from Nasdaq, will be listed on another national securities exchange or quoted on an over-the counter quotation system. If our common stock is delisted, it may come within the definition of "penny stock" as defined in the Exchange Act, and would be covered by Rule 15g-9 of the Exchange Act. That Rule imposes additional sales practice requirements on broker-dealers who sell securities to persons other than established customers and accredited investors. For transactions covered by Rule 15g-9, the broker-dealer must make a special suitability determination for the purchaser and receive the purchaser's written agreement to the transaction prior to the sale. Consequently, Rule 15g-9, if it were to become applicable, would affect the ability or willingness of broker-dealers to sell our securities, and accordingly would affect the ability of stockholders to sell their securities in the public market. These additional procedures could also limit our ability to raise additional capital in the future.

We will need to increase the size of our organization and may not successfully manage our growth.

We are a clinical-stage biopharmaceutical company with a small number of employees, and our management systems currently in place are not likely to be adequate to support our future growth plans. Our ability to grow and to manage our growth effectively will require us to hire, train, retain, manage and motivate additional employees and to implement and improve our operational, financial and management systems. These demands also may require the hiring of additional senior management personnel or the development of additional expertise by our senior management personnel. Hiring a significant number of additional employees, particularly those at the management level, would increase our expenses significantly. Moreover, if we fail to expand and enhance our operational, financial and management systems in conjunction with our potential future growth, it could have a material adverse effect on our business, financial condition and results of operations.

Risks Related to Our Business, Industry and FDA Regulation

We are involved, and may become involved in the future, in disputes and other legal or regulatory proceedings that, if adversely decided or settled, could materially and adversely affect our business, financial condition and results of operations.

We are, and may in the future become, party to litigation, arbitration, regulatory proceedings or other disputes. In general, claims made by or against us in disputes and other legal or regulatory proceedings can be expensive and time consuming to bring or defend against, requiring us to expend significant resources and divert the efforts and attention of our management and other personnel from our business operations. These potential claims include, but are not limited to, personal injury claims, class action lawsuits, intellectual property claims, employment litigation and regulatory investigations and causes of action relating to the advertising and promotional claims about our products.

On January 19, 2022, we provided a notice of material breach in connection with Amerimmune's non-performance under the Collaboration Agreement and, on March 3, 2022, we filed the Arbitration Demand. On March 11, 2022, JAMS issued a Notice of Commencement of Arbitration letter, confirming the commencement of the arbitration as of that date. As part of our Arbitration Demand, we sought a declaratory judgment that Amerimmune had materially breached the Collaboration Agreement, and we are therefore entitled to terminate the Collaboration Agreement. On November 28, 2022, the arbitrator issued an interim award in favor of the Company, granting the Company's request for declaratory relief and specific performance terminating the Collaboration Agreement and denying each of Amerimmune's counterclaims. On January 2, 2023, the arbitrator issued a final award affirming the arbitration outcome set forth in the interim award and further awarding the Company its costs in pursuing the arbitration. On February 9, 2023, the Company filed a petition in the Superior Court of California, County of San Diego, seeking to confirm the arbitration award. A hearing on the petition is currently scheduled for May 26, 2023. While we expect the court to confirm the arbitration award, there cannot be absolute certainty that such arbitration award will be confirmed by the Superior Court of California.

Two former employees of the Company filed a complaint in the Superior Court of California, County of San Diego, alleging certain employment-related claims, described in more depth in the following risk factor titled "Employee litigation and unfavorable publicity could negatively affect our future business.".

Any adverse determination against us in these proceedings, or even the allegations contained in the claims, regardless of whether they are ultimately found to be without merit, may also result in settlements, injunctions or damages that could have a material adverse effect on our business, financial condition and results of operations.

We are a clinical-stage development company, have a very limited operating history, are not currently profitable, do not expect to become profitable in the near future and may never become profitable.

We are a clinical-stage biopharmaceutical company, have no approved products and have generated minimal revenues from the sale of products. We are focused on developing potential first-in-class clinical and preclinical small molecule pan-caspase and caspase selective inhibitors that protect the body's natural process to restore immune function. Our product candidates include emricasan, CTS-2090 and CTS-2096. Currently, we are developing emricasan for acute bacterial skin and skin structure infections (ABSSSI) as well evaluating its use for other infectious diseases. We also have novel preclinical product candidates including CTS-2090 and CTS-2096, which are highly selective small molecule inhibitors of caspase-1 designed for the treatment of certain inflammatory diseases.

Our operations to date have been limited to organizing, staffing, and financing our company, applying for patent rights, manufacturing on a clinical scale, undertaking clinical trials of our product candidates, and engaging in research and development. As a result, we have limited historical operations upon which to evaluate our business and prospects and have not yet demonstrated an ability to obtain marketing approval for any of our product candidates or successfully overcome the risks and uncertainties frequently encountered by companies in the biopharmaceutical industry. We also have generated limited revenues from licensing agreements or product sales to date and continue to incur significant research and development and other expenses. As a result, we have not been profitable and have incurred significant operating losses in every reporting period since our inception, except for the year ended December 31, 2017. For the years ended December 31, 2022 and 2021, we reported net losses of $10.6 million and $15.0 million, respectively, and had an accumulated deficit of $88.3 million as of December 31, 2022.

For the foreseeable future, we expect to continue to incur losses, which will increase significantly from historical levels as we expand our drug development activities, seek regulatory approvals for our product candidates and begin to commercialize them if they are approved by the U.S. Food and Drug Administration (the "FDA") or comparable foreign regulatory authorities. Even if we succeed in developing and commercializing one or more product candidates, we may never become profitable.

We are dependent on the success of one or more of our current product candidates, which are in early stages of clinical development, and we cannot be certain that any of them will receive regulatory approval or be commercialized.

We currently have one product candidate in development, emricasan, for acute bacterial skin and skin structure infections (ABSSSI) as well evaluating its use for other infectious diseases. We had also previously been focused on developing HST-003 for the treatment of articular cartilage defects in the knee and HST-004 for the spine, and stopped development activities following our strategic pipeline review in late 2022. To date, we have spent significant time, money, and effort on the development of our product candidates, emricasan, HST-003, HST-004, and other pre-clinical assets. To date, no pivotal clinical trials designed to provide clinically and statistically significant proof of efficacy, or to provide sufficient evidence of safety to justify approval, have been completed with any of our product candidates. Success in preclinical studies and early clinical trials does not ensure that later clinical trials will generate adequate data to demonstrate the efficacy and safety of a therapeutic candidate.

There is no guarantee that any future clinical trials will be started or completed in a timely fashion or succeed. Further, we have experienced delays in enrollment of patients in our clinical trials due to the COVID-19 pandemic, which could result in material delays and complications with respect to our research and development programs and clinical trials. Our ability ultimately to reach profitability is critically dependent on our future success in obtaining regulatory approval and/or commercialization for our product candidates. However, there can be no guarantee that any future clinical trials will be timely commenced, successful, or that regulators will approve our product candidates in a timely manner, or at all. None of our product candidates have been approved for marketing or are being marketed or commercialized at this time.

We do not anticipate that any of our current product candidates will be eligible to receive regulatory approval from the FDA or comparable foreign authorities and begin commercialization for a number of years, if ever. Even if we ultimately receive regulatory approval for any of these product candidates, we or our current or potential future partners, if any, may be unable to commercialize them successfully for a variety of reasons. These include, for example, the availability of alternative treatments, lack of cost-effectiveness, the cost of manufacturing the product on a commercial scale and competition with other drugs or therapies. The success of our product candidates may also be limited by the prevalence and severity of any adverse side effects. If we fail to commercialize one or more of our current product candidates, we may be unable to generate sufficient revenues to attain or maintain profitability, and our financial condition and stock price may decline.

The termination of our Collaboration Agreement with Amerimmune resulted in all rights to emricasan being returned to us. Any further development of emricasan will require significant resources from us or another collaboration partner, and in the event that we do not find a collaboration partner, the development of emricasan could be significantly delayed or result in the discontinuation of the development of emricasan.

In late 2022, in accordance with an arbitration award, we terminated the Amerimmune Collaboration Agreement and all rights to emricasan, CTS-2090, and CTS-2096 were returned to us. Further development of emricasan will require significant resources from us or another collaboration partner. We or a new collaboration partner will be responsible for funding any new emricasan development and clinical trial activities undertaken after the termination. Any such further development will require significant resources to develop and commercialize emricasan, and such further development may not be possible in the near term without a new collaboration partner. There are no assurances that we will have access to additional capital or find a new collaboration partner or that the terms and timing of any such arrangements would be acceptable to us. As a result, we could experience a significant delay in the emricasan development process. If we determine instead to discontinue the development of emricasan, we will not receive any future return on our investment from that product candidate.

Employee litigation and unfavorable publicity could negatively affect our future business.

From time to time, companies become involved in employment related litigation, including claims of age discrimination, sexual harassment, gender discrimination, creating a hostile workplace, retaliation, wrongful termination, immigration violations, or other local, state, and federal labor law violations. In recent years, there has been an increase in the number of discrimination and harassment claims generally. Coupled with the expansion of social media platforms and similar devices that allow individuals access to a broad audience, these claims have had a

significant negative impact on some businesses. Certain companies that have faced employment or harassment related lawsuits have had to terminate management or other key personnel, and have suffered reputational harm that has negatively impacted their business. Any employment-related claim could negatively affect our business.

On or about February 17, 2022, two former employees, each of whom separately resigned and terminated their employment with Histogen, filed a complaint in the Superior Court of California, County of San Diego against us, our Board of Directors and certain other of our current and prior employees. The former non-executive employees of the Company have asserted causes of action for whistleblower status, retaliation, discrimination, unfair business practices, wrongful termination, violation of civil rights, and other California state law claims. The Company objects to the naming of each of the defendants in this matter and denies each of the plaintiffs' claims. The plaintiffs agreed to pre-arbitration mediation, which was conducted on May 4, 2022, as was required by the arbitration agreement executed by each of the plaintiffs. Considering that the parties did not resolve the matter through this mediation, we petitioned the San Diego Superior Court for an order that the matter be submitted to arbitration consistent with each of the plaintiff's arbitration agreements. The hearing for the motion to compel arbitration was held on August 12, 2022 and the San Diego Superior Court issued a ruling to uphold the binding arbitration agreements signed by both plaintiff's. The matter is expected to proceed to arbitration but is the responsibility of the plaintiffs to initiate the arbitration proceeding. We believe that our defense costs, settlement monies, damages or any other awards would be covered by our liability insurance; provided, however, insurance may not cover all claims or could exceed our insurance coverage. We also believe that there are substantial defenses to this lawsuit, and we intend to vigorously defend against each of these claims. While this litigation matter is in the early stages, we believe the action is without merit.

However, because of the uncertain nature of litigation, the outcome of these claims or any other such employment related actions and proceedings cannot be predicted with certainty and an unfavorable resolution of one or more of them could have a material adverse effect on our business, financial condition, results of operations, cash flows, reputation, brand identity and the trading price of our securities. Any such litigation, with or without merit, could also result in substantial expenditures of time and money, and divert attention of our management team from other tasks important to the success of our business.

Clinical drug development involves uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials relating to our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or safety profiles, notwithstanding promising results in earlier trials. We cannot be certain that any of our current or future clinical trials will be successful and support regulatory approval in any jurisdiction. Failure in one indication may have negative consequences for the development of our product candidates for other indications. Any such failure may harm our business, prospects, and financial condition.

If development of our product candidates does not produce favorable results, we, and any future collaborators, may be unable to commercialize these products.

To receive regulatory approval for the commercialization of our product candidate emricasan, being developed for ABSSSI, and our other preclinical product candidates, CTS-2090 and CTS-2096, or any other product candidates that we may develop, adequate and well-controlled clinical trials must be conducted to demonstrate safety and efficacy in humans to the satisfaction of the FDA and comparable foreign regulatory authorities. In order to support marketing approval, these agencies typically require successful results in one or more Phase 3 clinical trials, which our current product candidates have not yet reached and may never reach. In addition to the risks described above under "Clinical drug development involves uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results," we may experience numerous unforeseen events during, or as a result of, the development process that could delay or prevent commercialization of our current or future product candidates, including the following:

- clinical trials may produce negative or inconclusive results;
- preclinical studies conducted with product candidates during clinical development to, among other things, evaluate their toxicology, carcinogenicity and pharmacokinetics and optimize their formulation may produce unfavorable results;
- patient recruitment and enrollment in clinical trials may be slower than we anticipate, particularly for subjects who are at a higher risk of severe illness or death from COVID-19;
- costs of development may be greater than we anticipate;
- our product candidates may cause undesirable side effects that delay or preclude regulatory approval or limit their commercial use or market acceptance, if approved;
- licensees who may be responsible for the development of our product candidates may not devote sufficient resources to these clinical trials or other preclinical studies of these candidates or conduct them in a timely manner; or
- we may face delays in obtaining regulatory approvals to commence one or more clinical trials.

In the future, we or any future collaborators will be responsible for establishing the targeted endpoints and goals for development of our product candidates. These targeted endpoints and goals may be inadequate to demonstrate the safety and efficacy levels required for regulatory approvals. Even if we believe data collected during the development of our product candidates are promising, such data may not be sufficient to support marketing approval by the FDA or comparable foreign authorities. Further, data generated during development can be interpreted in different ways, and the FDA or comparable foreign authorities may interpret such data in different ways than us or our collaborators. Our failure to adequately demonstrate the safety and efficacy of our product candidates would prevent our receipt of regulatory approval, and ultimately the potential commercialization of these product candidates.

In addition, since we do not currently possess the resources necessary to complete development and commercialize our product candidates or any other product candidates that we may develop, we have entered into and may seek to enter into license agreements to assist in the development and potential future commercialization of some or all of our product candidates as a component of our strategic plan. See *"Risk Factor – "We expect to depend on collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates"*.

We may fail to select or capitalize on the most scientifically, clinically or commercially promising or profitable product candidates.

We continue to evaluate our business strategy and, as a result, may modify our strategy in the future. In this regard, we may, from time to time, focus our product development efforts on different product candidates or may delay, suspend or terminate the future development of a product candidate at any time for strategic, business, financial or other reasons. For example, in late 2022, we decided to pause development activities on our CCM and our hECM lines of product candidates and focus development efforts elsewhere within the product portfolio while we continue to seek potential strategic partners for such assets. As a result of changes in our strategy, we have and may in the

future change or refocus our existing product development, commercialization and manufacturing activities. This could require changes in our facilities and our personnel. Any product development changes that we implement may not be successful. In particular, we may fail to select or capitalize on the most scientifically, clinically or commercially promising or profitable product candidates. Our decisions to allocate our research and development, management and financial resources toward particular product candidates may not lead to the development of viable commercial products and may divert resources from better opportunities. Similarly, our decisions to delay or terminate product development programs may also prove to be incorrect and could cause us to miss valuable opportunities.

We expect to continue to incur significant research and development expenses, which may make it difficult for us to attain profitability.

We expect to expend substantial funds in research and development, including preclinical studies and clinical trials of our product candidates, and to manufacture and market any product candidates in the event they are approved for commercial sale. We also may need additional funding to develop or acquire complementary companies, technologies and assets, as well as for working capital requirements and other operating and general corporate purposes. Moreover, our planned increases in staffing will dramatically increase our costs in the near and long-term. Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA, or foreign regulatory agencies, to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our or our future collaborators' clinical trials or the development of any of our product candidates. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate and ongoing compliance efforts.

However, our spending on current and future research and development programs and product candidates for therapeutic indications may not yield any commercially viable products. Due to our limited financial and managerial resources, we must focus on a limited number of research programs and product candidates and on specific therapeutic indications. Our resource allocation decisions may cause us to fail to capitalize on viable product candidates or profitable market opportunities.

Because the successful development of our product candidates is uncertain, we are unable to precisely estimate the actual funds we will require to develop and potentially commercialize them. In addition, we may not be able to generate sufficient revenue, even if we are able to commercialize any of our product candidates, to become profitable.

We expect to depend on collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.

We anticipate seeking third-party collaborators for the research, development, and commercialization of certain of the product candidates we may develop. For example, we previously entered into an agreement with Amerimmune under which we and Amerimmune were jointly developing emricasan for the treatment of COVID-19. As a result of the termination of the Collaboration Agreement with Amerimmune in late 2022, we will need to invest or find a collaboration partner to invest significant resources in the further development of emricasan.

The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty, such as:

- a collaboration partner may shift its priorities and resources away from our product candidates due to a change in business strategies, or a merger, acquisition, sale or downsizing;
- a collaboration partner may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- a collaboration partner may cease development in therapeutic areas which are the subject of our strategic collaboration;

- a collaboration partner may not devote sufficient capital or resources towards our product candidates;
- a collaboration partner may change the success criteria for a product candidate thereby delaying or ceasing development of such candidate;
- a significant delay in initiation of certain development activities by a collaboration partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- a collaboration partner could develop a product that competes, either directly or indirectly, with our product candidate;
- a collaboration partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- a collaboration partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- a collaboration partner may terminate a strategic alliance;
- a dispute may arise between us and a partner concerning the research, development or commercialization of a product candidate resulting in a delay in milestones, royalty payments or termination of an alliance and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and
- a partner may use our products or technology in such a way as to make us subject to litigation with a third party.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing or commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of capital.

For any such arrangements with third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

In addition, we may face significant competition in seeking appropriate collaborations and the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

Our product candidates may cause undesirable side effects that could delay or prevent their regulatory approval or commercialization or have other significant adverse implications on our business, financial condition and results of operations.

Undesirable side effects observed in clinical trials or in supportive preclinical studies with our product candidates could interrupt, delay or halt their development and could result in the denial of regulatory approval by the FDA or comparable foreign authorities for any or all targeted indications or adversely affect the marketability of any such product candidates that receive regulatory approval. In turn, this could eliminate or limit our ability to commercialize our product candidates.

Our product candidates may exhibit adverse effects in preclinical toxicology studies and adverse interactions with other drugs. There are also risks associated with additional requirements the FDA or comparable foreign authorities may impose for marketing approval with regard to a particular disease.

Our product candidates may require a risk management program that could include patient and healthcare provider education, usage guidelines, appropriate promotional activities, a post-marketing observational study, and ongoing safety and reporting mechanisms, among other requirements. Prescribing could be limited to physician specialists or physicians trained in the use of the drug, or could be limited to a more restricted patient population. Any risk management program required for approval of our product candidates could potentially have an adverse effect on our business, financial condition and results of operations.

Undesirable side effects involving our product candidates may have other significant adverse implications on our business, financial condition and results of operations. For example:

- we may be unable to obtain additional financing on acceptable terms, if at all;
- our collaborators may terminate any license agreements covering these product candidates;
- if any license agreements are terminated, we may determine not to further develop the affected product candidates due to resource constraints and may not be able to establish additional license agreements for their further development on acceptable terms, if at all;
- if we were to later continue the development of these product candidates and receive regulatory approval, earlier findings may significantly limit their marketability and thus significantly lower our potential future revenues from their commercialization;
- we may be subject to product liability or stockholder litigation; and
- we may be unable to attract and retain key employees.

In addition, if any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the product:

- regulatory authorities may withdraw their approval of the product, or us or our partners may decide to cease marketing and sale of the product voluntarily;
- we may be required to change the way the product is administered, conduct additional clinical trials or preclinical studies regarding the product, change the labeling of the product, or change the product's manufacturing facilities; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, financial condition, results of operations, and growth prospects. We cannot predict whether our product candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on nonclinical studies or early-stage clinical trials.

Delays in the commencement or completion of clinical trials could result in increased costs to us and delay our ability to establish strategic license agreements.

Delays in the commencement or completion of clinical trials could significantly impact our drug development costs. We do not know whether planned clinical trials will begin on time or be completed on schedule, if at all.

The commencement of clinical trials can be delayed for a variety of reasons, including, but not limited to, delays related to:

- obtaining regulatory approval to commence one or more clinical trials;
- reaching agreement on acceptable terms with prospective third-party contract research organizations ("CROs") and clinical trial sites;
- manufacturing sufficient quantities of a product candidate or other materials necessary to conduct clinical trials;
- obtaining institutional review board approval to conduct one or more clinical trials at a prospective site;
- recruiting and enrolling patients to participate in our clinical trials; and
- the failure of our licensees to adequately resource our product candidates due to their focus on other programs or as a result of general market conditions.

In addition, once a clinical trial has begun, it may be suspended or terminated by us, our licensees, the institutional review boards or data safety monitoring boards charged with overseeing our clinical trials, the FDA or comparable foreign authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols;
- inspection of the clinical trial operations or clinical trial site by the FDA or comparable foreign authorities resulting in the imposition of a clinical hold;
- unforeseen safety issues; or
- lack of adequate funding to continue the clinical trial.

The progress of clinical trials and clinical studies also may be affected by significant global public health matters such as the current novel coronavirus outbreak. Factors related to the novel coronavirus outbreak that may impact the timing and conduct of our clinical trials and clinical studies include:

- the diversion of healthcare resources away from the conduct of clinical trial and clinical study matters to focus on pandemic-related concerns, including the attention of physicians serving as clinical trial investigators, hospitals and clinics serving as clinical trial sites, and medical staff supporting the conduct of clinical trials;
- limitations on travel and distancing requirements that interrupt key trial or study activities, such as site initiations and monitoring, or that limit the ability of a patient to participate in a clinical trial or study or delay access to drug dosing or assessments;
- interruption in global shipping affecting the transport of clinical trial materials, such as investigational drug product; and
- employee furlough days that delay necessary interactions with local regulators, ethics committees and other important agencies and contractors.

In addition, if patients or subjects participating in our clinical trials or studies were to contract COVID-19, there could be an adverse impact on the trials or studies. For example, such patients may be unable to participate further or may need to limit participation in a clinical trial or study; the results and data recorded for such patients may differ from those that would have been recorded if the patients had not been affected by COVID-19; or such patients could experience adverse events that could be attributed to the drug product under investigation.

If we experience delays in the completion or termination of any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to commence product sales and generate product revenues from any of our product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs and slow down our product candidate development and approval process. Delays in completing our clinical trials could also allow our competitors to obtain marketing approval before we do or shorten the patent protection period during which we may have the exclusive right to commercialize our product candidates. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

Results of earlier clinical trials may not be predictive of the results of later-stage clinical trials.

The results of preclinical studies and early clinical trials of product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy results despite having progressed through preclinical studies and initial clinical trials. Many companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to adverse safety profiles or lack of efficacy, notwithstanding promising results in earlier studies. Similarly, our future clinical trial results may not be successful for these or other reasons.

This product candidate development risk is heightened by any changes in the planned clinical trials compared to the completed clinical trials. As product candidates are developed through preclinical and early-stage to late-stage clinical trials towards approval and commercialization, it is customary that various aspects of the development program, such as manufacturing and methods of administration, are altered along the way in an effort to optimize processes and results. While these types of changes are common and are intended to optimize the product candidates for late-stage clinical trials, approval and commercialization, such changes carry the risk that they will not achieve these intended objectives.

Any of these changes could make the results of our planned clinical trials or other future clinical trials we may initiate less predictable and could cause our product candidates to perform differently, including causing toxicities, which could delay completion of our clinical trials, delay approval of our product candidates, and/or jeopardize our ability to commence product sales and generate revenues.

If we experience delays in the enrollment of patients in our clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or other regulatory authorities. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating, as well as the impact of the COVID-19 pandemic.

If we fail to enroll and maintain the number of patients for which the clinical trial was designed, the statistical power of that clinical trial may be reduced, which would make it harder to demonstrate that the product candidate being tested in such clinical trial is safe and effective. Additionally, enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause our value to decline and limit our ability to obtain additional financing. Our inability to enroll a sufficient number of patients for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

A pandemic, epidemic or outbreak of an infectious disease, such as COVID-19, or the perception of their effects, may materially and adversely affect our business, operations and financial condition.

Outbreaks of epidemic, pandemic or contagious diseases, such as COVID-19, have and may continue to significantly disrupt our business. Such outbreaks pose the risk that we or our employees, contractors, suppliers, and other partners may be prevented from conducting business activities for an indefinite period of time due to spread of the disease, or due to shutdowns that may be requested or mandated by federal, state and local governmental authorities both within and outside the United States. Business disruptions could include disruptions or restrictions on our ability to travel, as well as temporary closures of our facilities and the facilities of clinical trial sites, service providers, suppliers or contract manufacturers. While it is not possible at this time to estimate the overall impact that the COVID-19 pandemic could have on our business, the continued rapid spread of COVID-19, both across the United States and through much of the world, and the measures taken by the governments of countries and local authorities has disrupted and could delay advancing our product pipeline, could delay our clinical trials, and could delay our overall development activities. Any of these effects could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses and have a material adverse effect on our business, prospects and financial condition.

We continue to evaluate the impact COVID-19 may have on our ability to effectively conduct our business operations as planned while taking into account regulatory, institutional, and government guidance and policies, but there can be no assurance that we will be able to avoid part or all of any impact from the spread of COVID-19 or its consequences. Any shutdowns or other business interruptions could result in material and negative effects to our ability to conduct our business in the manner and on the timelines presently planned, which could have a material adverse effect on our business, prospects and financial condition.

We intend to rely on third parties to conduct our preclinical studies and clinical trials and perform other tasks. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business, financial condition and results of operations could be substantially harmed.

We intend to rely upon third-party CROs, medical institutions, clinical investigators and contract laboratories to monitor and manage data for our ongoing preclinical and clinical programs. Nevertheless, we maintain responsibility for ensuring that each of our clinical trials and preclinical studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with current requirements on good manufacturing practices ("CGMP"), good clinical practices ("GCP") and good laboratory practice ("GLP") which are a collection of laws and regulations enforced by the FDA, and comparable foreign authorities for all of our product candidates in clinical development. Regulatory authorities enforce these regulations through periodic inspections of preclinical study and clinical trial sponsors, principal investigators, preclinical study and clinical trial sites, and other contractors. If we or any of our CROs or vendors fails to comply with applicable regulations, the data generated in our preclinical studies and clinical trials may be deemed unreliable and the FDA, or comparable foreign authorities may require us to perform additional preclinical studies and clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with products produced consistent with CGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the development and regulatory approval processes.

We may not be able to enter into arrangements with CROs on commercially reasonable terms, or at all. In addition, our CROs will not be our employees, and except for remedies available to us under our agreements with such CROs, we will not be able to control whether or not they devote sufficient time and resources to our ongoing preclinical and clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the data, they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements, or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. CROs may also generate higher costs than anticipated. As a result, our business, financial condition and results of operations and the commercial prospects for our product candidates could be materially and adversely affected, our costs could increase, and our ability to generate revenue could be delayed.

Switching or adding additional CROs, medical institutions, clinical investigators or contract laboratories involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work replacing a previous CRO. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. There can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse effect on our business, financial condition or results of operations.

The FDA regulatory approval process is lengthy and time-consuming and we could experience significant delays in the clinical development and regulatory approval of our product candidates.

We may experience delays in commencing and completing clinical trials of our product candidates. We do not know whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Any of our future clinical trials may be delayed for a variety of reasons, including delays related to:

- the availability of financial resources for us to commence and complete our planned clinical trials;
- reaching an agreement on acceptable terms with prospective contract research organizations ("CROs"), and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining IRB approval at each clinical trial site;
- obtaining regulatory approval for clinical trials in each country;
- recruiting suitable patients to participate in clinical trials;
- having patients complete a clinical trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- adding new clinical trial sites;
- developing one or more new formulations or routes of administration; or
- manufacturing sufficient quantities of our product candidate for use in clinical trials.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the clinical trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. In addition, significant numbers of patients who enroll in our clinical trials may drop out during the clinical trials for various reasons. We believe it appropriately accounts for such increased risk of dropout rates in our trials when determining expected clinical trial timelines, but we cannot assure you that our assumptions are correct, or that it will not experience higher numbers of dropouts than anticipated, which would result in the delay of completion of such trials beyond our expected timelines.

We could encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, the IRBs in the institutions in which such trials are being conducted, the data monitoring committee for such trial, or by the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or

delays in the completion of, any clinical trial of our product candidates, the commercial prospects for such product candidate will be harmed, and our ability to generate product revenues will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, prospects, financial condition and results of operations significantly. Furthermore, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate.

In connection with clinical trials, we face risks that:

- IRBs may delay approval of, or fail to approve, a clinical trial at a prospective site;
- there may be a limited number of, and significant competition for, suitable patients for enrollment in the clinical trials;
- there may be slower than expected rates of patient recruitment and enrollment;
- patients may fail to complete the clinical trials;
- there may be an inability or unwillingness of patients or medical investigators to follow our clinical trial protocols;
- there may be an inability to monitor patients adequately during or after treatment;
- there may be termination of the clinical trials by one or more clinical trial sites;
- unforeseen ethical or safety issues may arise;
- conditions of patients may deteriorate rapidly or unexpectedly, which may cause the patients to become ineligible for a clinical trial or may prevent our product candidates from demonstrating efficacy or safety;
- patients may die or suffer other adverse effects for reasons that may or may not be related to our product candidate being tested;
- we may not be able to sufficiently standardize certain of the tests and procedures that are part of our clinical trials because such tests and procedures are highly specialized and involve a high degree of expertise;
- a product candidate may not prove to be efficacious in all or some patient populations;
- the results of the clinical trials may not confirm the results of earlier trials;
- the results of the clinical trials may not meet the level of statistical significance required by the FDA or other regulatory agencies; and
- a product candidate may not have a favorable risk/benefit assessment in the disease areas studied.

We cannot assure you that any future clinical trial for our product candidates will be started or completed on schedule, or at all. Any failure or significant delay in completing clinical trials for our product candidates would harm the commercial prospects for such product candidate and adversely affect our financial results. Difficulties and failures can occur at any stage of clinical development, and we cannot assure you that it will be able to successfully complete the development and commercialization of any product candidate in any indication.

Changes in funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including (i) government budget and funding levels, (ii) the ability to hire and retain key personnel and accept the payment of user fees and (iii) statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect its business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We are subject to a multitude of manufacturing risks, any of which could substantially increase our costs and limit supply of our product candidates.

The process of manufacturing our product candidates is complex, highly regulated, and subject to several risks. For example, the process of manufacturing our product candidates is extremely susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing processes for any of our product candidates could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. In addition, the manufacturing facilities in which our product candidates are made could be adversely affected by equipment failures, labor shortages, natural disasters, public health crises, pandemics and epidemics, such as the ongoing COVID-19 pandemic, power failures and numerous other factors.

In addition, any adverse developments affecting manufacturing operations for our product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of our product candidates. We also may need to take inventory write-offs and incur other charges and expenses for product candidates that fail to meet specifications, undertake costly remediation efforts, or seek costlier manufacturing alternatives.

We intend to rely primarily on third parties to manufacture our preclinical and clinical drug supplies, and our business, financial condition and results of operations could be harmed if those third parties fail to provide us with sufficient quantities of drug product or fail to do so at acceptable quality levels or prices.

We currently have the infrastructure or capability internally to manufacture certain of our preclinical and clinical drug supplies for use in our clinical trials, but we have engaged a contract manufacturing organization and once the technology transfer process is complete, we will rely completely on third parties for such manufacturing. We lack the resources and the capability to manufacture any of our product candidates on a late-stage clinical or commercial scale. We will rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical trials. There are a limited number of suppliers for raw materials that we use to manufacture our product candidates, and there may be a need to identify alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product candidates for our clinical trials, and, if approved, ultimately for commercial sale. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete such clinical trial, any significant delay or discontinuity in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates, which could harm our business, financial condition and results of operations.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements.

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with CGMP. These regulations govern manufacturing processes and procedures and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of an NDA on a timely basis and must adhere to GLP and CGMP regulations enforced by the FDA or comparable foreign authorities through their facilities inspection program. Some of our contract manufacturers may not have produced a commercially approved pharmaceutical product and therefore may not have obtained the requisite regulatory authority approvals to do so. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or any of our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Although we plan to oversee the contract manufacturers, we cannot control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever.

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly or time consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business, financial condition and results of operations.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or comparable foreign authorities can impose regulatory sanctions including, among other things, refusal to approve a pending application for a product candidate, withdrawal of an approval, or suspension of production. As a result, our business, financial condition and results of operations may be materially and adversely affected.

Additionally, if supply from one manufacturer is interrupted, an alternative manufacturer would need to be qualified through an NDA supplement, or equivalent foreign regulatory filing, which could result in further delay. The regulatory agencies may also require additional studies or trials if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us to incur higher costs and could cause the delay or termination of clinical trials, regulatory submissions, required approvals, or commercialization of our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed, or we could lose potential revenue.

Any license agreement that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our current and potential future product candidates.

We may seek license agreements with biopharmaceutical companies for the development or commercialization of our current and potential future product candidates. To the extent that we decide to enter into license agreements, we will face significant competition in seeking appropriate licensees. Moreover, license agreements are complex and time consuming to negotiate, execute and implement. We may not be successful in our efforts to establish and implement

license agreements or other alternative arrangements should we choose to enter into such arrangements, and the terms of the arrangements may not be favorable to us. If and when we enter into additional license agreements with a third party for development and commercialization of a product candidate, we can expect to relinquish some or all of the control over the future success of that product candidate to the third party. The success of our license agreements will depend heavily on the efforts and activities of our licensees. Licensees generally have significant discretion in determining the efforts and resources that they will apply to the product candidate.

Disagreements between parties to a license arrangement can lead to delays in developing or commercializing the applicable product candidate and can be difficult to resolve in a mutually beneficial manner. In some cases, licenses with biopharmaceutical companies and other third parties are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect our business, financial condition and results of operations.

If we face allegations of noncompliance with the law and encounter sanctions, our reputation, revenues and liquidity may suffer, and any of our product candidates that are ultimately approved for commercialization could be subject to restrictions or withdrawal from the market.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to generate revenues from any of our product candidates that are ultimately approved for commercialization. If regulatory sanctions are applied or if regulatory approval is withdrawn, our business, financial condition and results of operations will be adversely affected. Additionally, if we are unable to generate revenues from product sales, our potential for achieving profitability will be diminished and our need to raise capital to fund our operations will increase.

We are exposed to product liability, non-clinical and clinical liability risks, which could place a substantial financial burden upon us, should lawsuits be filed against us.

Our business exposes us to potential product liability and other liability risks that are inherent in the testing, manufacturing and marketing of pharmaceutical formulations and products. In addition, the use in our clinical trials of pharmaceutical products and the subsequent sale of these products by us or our potential licensees may cause us to bear a portion of or all product liability risks. A successful liability claim or series of claims brought against us could have a material adverse effect on our business, financial condition and results of operations.

Our research and development activities involve the use of hazardous materials, which subject us to regulation, related costs and delays and potential liabilities.

Our research and development activities involve the controlled use of hazardous materials, chemicals and various radioactive compounds. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of biohazardous materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate any of these laws or regulations.

We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our operations and could result in a material disruption of our drug development and clinical activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of drug development or clinical trial data could result in delays in our

regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and our development programs and the development of our product candidates could be delayed.

Our employees and consultants may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee or consultant fraud or other misconduct. Misconduct by our employees or consultants could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commissions, customer incentive programs and other business arrangements. Employee and consultant misconduct also could involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter such misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending itself or asserting our rights, those actions could have a material adverse effect on our business, financial condition and results of operations, and result in the imposition of significant fines or other sanctions against us.

Business disruptions such as natural disasters could seriously harm our future revenues and financial condition and increase our costs and expenses.

We and our suppliers may experience a disruption in their business as a result of natural disasters. A significant natural disaster, such as an earthquake, hurricane, flood or fire, could severely damage or destroy our headquarters or facilities or the facilities of our manufacturers or suppliers, which could have a material and adverse effect on our business, financial condition and results of operations. In addition, terrorist acts or acts of war targeted at the U.S., could cause damage or disruption to us, our employees, facilities, partners and suppliers, which could have a material adverse effect on our business, financial condition and results of operations.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of products, product candidates or technologies. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near- and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our business, financial condition and results of operations. For example, these transactions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention in order to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for any of these transactions;
- higher-than-expected transaction and integration costs;
- write-downs of assets or goodwill or impairment charges;

- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses or product lines with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses or product lines due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and could have a material adverse effect on our business, financial condition and results of operations.

Risks Relating to Our Intellectual Property

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

One or more of our programs may require the use of proprietary rights held by third parties. We may need to acquire or in-license additional intellectual property in the future with respect to other product candidates. Moreover, we may be unable to acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our product candidates. We face competition with regard to acquiring and in-licensing third-party intellectual property rights, including from a number of more established companies. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license intellectual property rights to us. We also may be unable to acquire or in-license third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We may enter into license agreements with U.S. and foreign academic institutions to accelerate development of our current or future preclinical product candidates. Typically, these agreements include an option for the company to negotiate a license to the institution's resulting intellectual property rights. Even with such an option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to license rights from the institution, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our desired program.

If we are unable to successfully obtain required third-party intellectual property rights or maintain our existing intellectual property rights, we may need to abandon development of the related program and our business, financial condition and results of operations could be materially and adversely affected.

We may not be able to protect our proprietary or licensed technology in the marketplace.

We depend on our ability to protect our proprietary or licensed technology. We rely on trade secret, patent, copyright and trademark laws, and confidentiality, licensing, and other agreements with employees and third parties, all of which offer only limited protection. Our success depends in large part on our ability and any licensor's or licensee's ability to obtain and maintain patent protection in the U.S. and other countries with respect to our proprietary or licensed technology and products. We currently in-license some of our intellectual property rights to develop our product candidates and may in-license additional intellectual property rights in the future. We cannot be certain that patent enforcement activities by our current or future licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights. We also cannot be certain that our current or future licensors will allocate sufficient resources or prioritize their or our enforcement of such patents. Even if we are not a party to these legal actions, an adverse outcome could prevent us from continuing to license intellectual property that we may need to operate our business, which would have a material adverse effect on our business, financial condition, and results of operations.

We believe we will be able to obtain, through prosecution of patent applications covering our owned technology and technology licensed from others, adequate patent protection for our proprietary drug technology, including those related to our in-licensed intellectual property. If we are compelled to spend significant time and money protecting or enforcing our licensed patents and future patents we may own, designing around patents held by others or licensing or acquiring, potentially for large fees, patents or other proprietary rights held by others, our business, financial condition and results of operations may be materially and adversely affected. If we are unable to effectively protect the intellectual property that we own or in-license, other companies may be able to offer the same or similar products for sale, which could materially adversely affect our business, financial condition and results of operations.

The patents of others from whom we may license technology, and any future patents we may own, may be challenged, narrowed, invalidated or circumvented, which could limit our ability to stop competitors from marketing the same or similar products or limit the length of term of patent protection that we may have for our products.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection for licensed patents, pending patent applications and potential future patent applications and patents could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or patent applications will be due to be paid to the U.S. Patent and Trademark Office ("USPTO") and various governmental patent agencies outside of the U.S. in several stages over the lifetime of the applicable patent and/or patent application. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If this occurs with respect to our in-licensed patents or patent applications we may file in the future, our competitors might be able to use our technologies, which would have a material adverse effect on our business, financial condition, and results of operations.

The patent positions of pharmaceutical products are often complex and uncertain. The breadth of claims allowed in pharmaceutical patents in the U.S. and many jurisdictions outside of the U.S. is not consistent. For example, in many jurisdictions, the support standards for pharmaceutical patents are becoming increasingly strict. Some countries prohibit method of treatment claims in patents. Changes in either the patent laws or interpretations of patent laws in the U.S. and other countries may diminish the value of our licensed or owned intellectual property or create uncertainty. In addition, publication of information related to our current product candidates and potential products may prevent us from obtaining or enforcing patents relating to these product candidates and potential products, including without limitation composition-of-matter patents, which are generally believed to offer the strongest patent protection.

Patents that we currently license and patents that we may own or license in the future do not necessarily ensure the protection of our licensed or owned intellectual property for a number of reasons, including, without limitation, the following:

- the patents may not be broad or strong enough to prevent competition from other products that are identical or similar to our product candidates;
- there can be no assurance that the term of a patent can be extended under the provisions of patent term extensions afforded by U.S. law or similar provisions in foreign countries, where available;
- the issued patents and patents that we may obtain or license in the future may not prevent generic entry into the market for our product candidates;
- we, or third parties from whom we in-license or may license patents, may be required to disclaim part of the term of one or more patents;

- there may be prior art of which we are aware, which we do not believe affects the validity or enforceability of a patent claim, but which, nonetheless, ultimately may be found to affect the validity or enforceability of a patent claim;
- there may be other patents issued to others that will affect our freedom to operate;
- if the patents are challenged, a court could determine that they are invalid or unenforceable;
- there might be a significant change in the law that governs patentability, validity and infringement of our licensed patents or any future patents we may own that adversely affects the scope of our patent rights;
- a court could determine that a competitor's technology or product does not infringe our licensed patents or any future patents we may own; and
- the patents could irretrievably lapse due to failure to pay fees or otherwise comply with regulations or could be subject to compulsory licensing. If we encounter delays in our development or clinical trials, the period of time during which we could market our potential products under patent protection would be reduced.

Our competitors may be able to circumvent our licensed patents or future patents we may own by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may seek to market generic versions of any approved products by submitting abbreviated new drug applications to the FDA in which our competitors claim that our licensed patents or any future patents we may own are invalid, unenforceable, or not infringed. Alternatively, our competitors may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend or assert our licensed patents or any future patents we may own, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our licensed patents or any future patents we may own invalid or unenforceable. We may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection. Even if we own or in-license valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

The issuance of a patent is not conclusive as to our inventorship, scope, ownership, priority, validity, or enforceability. In this regard, third parties may challenge our licensed patents or any future patents we may own in the courts or patent offices in the U.S. and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated, or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products or limit the duration of the patent protection of our technology and potential products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized.

We may infringe the intellectual property rights of others, which may prevent or delay our drug development efforts and prevent us from commercializing or increase the costs of commercializing our products, if approved.

Our commercial success depends significantly on our ability to operate without infringing the patents and other intellectual property rights of third parties. For example, there could be issued patents of which we are not aware that our current or potential future product candidates infringe. There also could be patents that we believe we do not infringe, but that we may ultimately be found to infringe.

Moreover, patent applications are in some cases maintained in secrecy until patents are issued. The publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made and patent applications were filed. Because patents can take many years to issue, there may be currently pending applications of which we are unaware that may later result in issued patents that our product candidates or potential products infringe. For example, pending applications may exist that claim or can be amended to claim subject matter that our product candidates or potential products infringe. Competitors may file continuing patent applications claiming priority to already issued patents in the form of continuation, divisional, or continuation-in-part applications, in order to maintain the pendency of a patent family and attempt to cover our product candidates.

Third parties may assert that we are employing their proprietary technology without authorization and may sue us for patent or other intellectual property infringement. These lawsuits are costly and could adversely affect our business, financial condition and results of operations and divert the attention of managerial and scientific personnel. If we are sued for patent infringement, we would need to demonstrate that our product candidates, potential products, or methods either do not infringe the claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving invalidity is difficult. For example, in the U.S., proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion. If a court holds that any third-party patents are valid, enforceable and cover our products or their use, the holders of any of these patents may be able to block our ability to commercialize our products unless we acquire or obtains a license under the applicable patents or until the patents expire.

We may not be able to enter into licensing arrangements or make other arrangements at a reasonable cost or on reasonable terms. Any inability to secure licenses or alternative technology could result in delays in the introduction of our products or lead to prohibition of the manufacture or sale of products by us. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, in any such proceeding or litigation, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially and adversely affect our business, financial condition, and results of operations. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar material and adverse effect on our business, financial condition, and results of operations. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

Any claims or lawsuits relating to infringement of intellectual property rights brought by or against us will be costly and time consuming and may adversely affect our business, financial condition, and results of operations.

We may be required to initiate litigation to enforce or defend our licensed and owned intellectual property. Lawsuits to protect our intellectual property rights can be very time consuming and costly. There is a substantial amount of litigation involving patent and other intellectual property rights in the biopharmaceutical industry generally. Such litigation or proceedings could substantially increase our operating expenses and reduce the resources available for development activities or any future sales, marketing, or distribution activities.

In any infringement litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are resolved. Further, any claims we assert against a perceived infringer could provoke these parties to assert counterclaims against us alleging that we have infringed their patents. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to develop our product candidates.

In addition, our licensed patents and patent applications, and patents and patent applications that we may apply for, own or license in the future, could face other challenges, such as interference proceedings, opposition proceedings, re-examination proceedings and other forms of post-grant review. Any of these challenges, if successful, could result in the invalidation of, or in a narrowing of the scope of, any of our licensed patents and patent applications and patents and patent applications that we may apply for, own or license in the future. Any of these challenges, regardless of their success, would likely be time consuming and expensive to defend and resolve and would divert our management and scientific personnel's time and attention.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is costly, time-consuming, and inherently uncertain. For example, the U.S. previously enacted and is currently implementing wide-ranging patent reform legislation. Specifically, on September 16, 2011, the Leahy-Smith America Invents Act (the "Leahy-Smith Act") was signed into law and included a number of significant changes to U.S. patent law, and many of the provisions became effective in March 2013. However, it may take the courts years to interpret the provisions of the Leahy-Smith Act, and the implementation of the statute could increase the uncertainties and costs surrounding the prosecution of our licensed and future patent applications and the enforcement or defense of our licensed and future patents, all of which could have a material adverse effect on our business, financial condition, and results of operations.

In addition, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we might obtain in the future.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates throughout the world would be prohibitively expensive. Competitors may use our licensed and owned technologies in jurisdictions where we have not licensed or obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain or license patent protection, but where patent enforcement is not as strong as that in the U.S. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our licensed patents and future patents we may own, or marketing of competing products in violation of our proprietary rights generally. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our licensed and owned intellectual property both in the U.S. and abroad. For example, China currently affords less protection to a company's intellectual property than some other jurisdictions. As such, the lack of strong patent and other intellectual property protection in China may significantly increase our vulnerability regarding unauthorized disclosure or use of our intellectual property and undermine our competitive position. Proceedings to enforce our future patent rights, if any, in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

In order to protect our proprietary and licensed technology and processes, we rely in part on confidentiality agreements with our corporate partners, employees, consultants, manufacturers, outside scientific advisors and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of our confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. Failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties.

We employ individuals who were previously employed at other biopharmaceutical companies. Although we have no knowledge of any such claims against us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees. To date, none of our employees have been subject to such claims.

We may be subject to claims challenging the inventorship of our licensed patents, any future patents we may own and other intellectual property.

Although we are not currently experiencing any claims challenging the inventorship of our licensed patents or our licensed or owned intellectual property, we may in the future be subject to claims that former employees, licensees or other third parties have an interest in our licensed patents or other licensed or owned intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business, financial condition, and results of operations. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation extending the terms of our licensed patents and any future patents we may own, our business, financial condition and results of operations may be materially and adversely affected.

Depending upon the timing, duration, and specifics of FDA regulatory approval for our product candidates, one or more of our licensed U.S. patents or future U.S. patents that we may license or own may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during drug development and the FDA regulatory review process. This period is generally one-half the time between the effective date of an investigational new drug application ("IND") (falling after issuance of the patent), and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Patent term restorations, however, cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval by the FDA.

The application for patent term extension is subject to approval by the USPTO, in conjunction with the FDA. It takes at least six months to obtain approval of the application for patent term extension. We may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than our requests. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than our requests, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain earlier approval of competing products, and our ability to generate revenues could be materially adversely affected.

Risks Related Owning Our Common Stock

The market price of our common stock has been and may continue to be volatile.

The market price of our common stock has been and may continue to be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- results from, and any delays in, planned clinical trials for our product candidates, or any other future product candidates, and the results of trials of competitors or those of other companies in our market sector;
- any delay in filing an Investigational New Drug Application, or NDA, for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND or NDA;
- significant lawsuits, including patent or stockholder litigation;
- inability to obtain additional funding;
- failure to successfully develop and commercialize our product candidates;
- changes in laws or regulations applicable to our product candidates;
- inability to obtain adequate product supply for our product candidates, or the inability to do so at acceptable prices;
- unanticipated serious safety concerns related to any of our product candidates;
- adverse regulatory decisions;
- introduction of new products or technologies by our competitors;
- failure to meet or exceed drug development or financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- the perception of the biopharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our licensed and owned technologies;
- additions or departures of key scientific or management personnel;
- changes in the market valuations of similar companies;
- general economic and market conditions and overall fluctuations in the U.S. equity market;
- public health crises, pandemics and epidemics, such as the ongoing COVID-19 pandemic;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, the stock market, in general, and small biopharmaceutical companies, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. Further, a decline in the financial markets and related factors beyond our control may cause our stock price to decline rapidly and unexpectedly.

If we were to be delisted from Nasdaq and begin to be quoted on the OTC market, the quotation of our common stock on the OTC market does not assure that a meaningful, consistent and liquid trading market currently exists, and in

recent years such market has experienced extreme price and volume fluctuations that have particularly affected the market prices of many smaller companies like us. Our common stock would be subject to this volatility. Sales of substantial amounts of common stock, or the perception that such sales might occur, could adversely affect prevailing market prices of our common stock and our stock price may decline substantially in a short time and our stockholders could suffer losses or be unable to liquidate their holdings.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations, or require us to relinquish rights to our technologies or product candidate.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidate, or grant licenses on terms unfavorable to us.

Our board of directors has in the past issued and may in the future issue one or more series of preferred stock without stockholder approval with the effect of diluting existing stockholders and impairing their voting and other rights.

Our amended and restated certificate of incorporation authorizes the issuance of up to 10,000,000 shares of "blank check" preferred stock, with designations, rights and preferences as may be determined from time to time by our board of directors without stockholder approval. In March 2022, we entered into a securities purchase agreement with certain investors, pursuant to which we issued and sold 2,500 shares of our newly designated Series A Convertible Redeemable Preferred Stock and 2,500 shares of our newly designated Series B Convertible Redeemable Preferred Stock (collectively the Preferred Stock) in a private placement transaction. In June 2022, all shares of Preferred Stock were redeemed and no shares of Preferred Stock are currently outstanding. If our board of directors without stockholder approval, issues one or more additional series of preferred stock with dividend, liquidation, conversion, supermajority voting, redemption or other rights, it could dilute the interest of, or impair the voting power of, our common stockholders.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our management.

Provisions in our certificate of incorporation and bylaws may delay or prevent an acquisition or a change in management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of the board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law ("DGCL"), which prohibits stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. Although we believe these provisions collectively will provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove then current management by making it more difficult for stockholders to replace members of the board of directors, which is responsible for appointing the members of management.

If our common stock is not listed on a national securities exchange, compliance with applicable state securities laws may be required for subsequent offers, transfers and sales of the shares of common stock offered hereby.

The securities offered hereby are being offered pursuant to one or more exemptions from registration and qualification under applicable state securities laws. Because our common stock is listed on Nasdaq, we are not required to register or qualify in any state the subsequent offer, transfer or sale of the common stock. If our common stock is delisted from

Nasdaq and is not eligible to be listed on another national securities exchange, subsequent transfers of the shares of our common stock offered hereby by U.S. holders may not be exempt from state securities laws. In such event, it will be the responsibility of the holder of shares or warrants to register or qualify the shares for any subsequent offer, transfer or sale in the United States or to determine that any such offer, transfer or sale is exempt under applicable state securities laws.

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 31, 2022, we have outstanding warrants to purchase an aggregate of approximately 4.9 million shares of our common stock, and options to purchase an aggregate of approximately 118 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 reviews, 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, 2022, our executive officers, directors and greater than 5% stockholders, in the aggregate, own approximately 8.1% 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.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We lease one floor of a two-story building containing our research and development, manufacturing and office space located at 10655 Sorrento Valley Road, Suite 200, San Diego, California, which we believe will accommodate our anticipated workforce and near-term growth needs. In January 2020, we entered into a new long-term lease agreement with San Diego Sycamore, LLC for office and laboratory space. The new lease commenced on March 1, 2020 and expires on August 31, 2031, with no options to renew or extend. Base rent is equal to $59,775 per month at commencement and increases at a fixed rate over the term of the lease. In addition to monthly base rent, we are obligated to pay certain customary amounts for our share of operating expenses and utilities. The lease agreement includes six months of rent abatement and a tenant improvement allowance for renovations.

Item 3. Legal Proceedings.

Employee Litigation

On or about February 17, 2022, two former employees, each of whom separately resigned and terminated their employment with Histogen, filed a complaint in the Superior Court of California, County of San Diego against us, our Board of Directors, our former Chief Executive Officer, as well as three individuals that are currently employed by the Company. Although the complaint lists the "Histogen Board of Directors, a business entity form unknown" as a defendant, the complaint does not specifically list the names of the board members. The plaintiffs allege whistleblower status, retaliation, discrimination, unfair business practices, wrongful termination, violation of civil rights, and other California state law claims. We have tendered the complaint to our liability insurer and engaged outside litigation counsel, as approved by our carrier, to defend Histogen, the Board of Directors and the individuals in this matter. We object to the naming of each of the defendants in this matter and deny each of the plaintiffs' claims. The plaintiffs agreed to pre-arbitration mediation, which was conducted on May 4, 2022, as was required by the arbitration agreement executed by each of the plaintiffs. Considering that the parties did not resolve the matter through this mediation, the Company petitioned the San Diego Superior Court for an order that the matter be submitted to arbitration consistent with each of the plaintiff's arbitration agreements. The hearing for the motion to compel arbitration was held on August 12, 2022 and the San Diego Superior Court issued a ruling to uphold the binding arbitration agreements signed by both plaintiff's. The matter is expected to now proceed to arbitration but is the responsibility of the plaintiffs to initiate the arbitration proceeding. We believe that our defense costs, settlement monies, damages or any other awards would be covered by our liability insurance; provided, however, insurance may not cover all claims or could exceed our insurance coverage. We believe that there are substantial defenses to this lawsuit, and we intend to vigorously defend against each of these claims. While this litigation matter is in the early stages, we believe the action is without merit. Nonetheless, the ultimate outcome is unknown at this time.

Amerimmune Collaborative Development and Commercialization Agreement Arbitration

On March 3, 2022, we filed a demand for arbitration ("Arbitration Demand") with JAMS in the county of San Diego, against Amerimmune LLC ("Amerimmune") seeking a declaratory judgment that Amerimmune had materially breached the Collaboration Agreement entered into by and between us and Amerimmune on October 26, 2020, and that the we are therefore entitled to terminate the Collaboration Agreement in accordance with its terms. On November 28, 2022, the arbitrator issued an interim award in favor of the Company, granting the Company's request for declaratory relief and specific performance terminating the Collaboration Agreement and denying each of Amerimmune's counterclaims. On January 2, 2023, the arbitrator issued a final award affirming the arbitration outcome set forth in the interim award and further awarding the Company its costs in pursuing the arbitration. On February 9, 2023, the Company filed a petition in the Superior Court of California, County of San Diego, seeking to confirm the arbitration award. A hearing on the petition is currently scheduled for May 26, 2023.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock is listed on the Nasdaq Capital Market under the ticker "HSTO".

Holders of Common Stock

On February 28, 2023, there were approximately 101 holders of record of our common stock.

Dividend Policy

We have never declared or paid any dividends on our common stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Recent Sales of Unregistered Securities.

None.

Recent Repurchases of Equity Securities.

None.

Item 6. Selected Financial Data

Not required.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our audited consolidated financial statements and related notes thereto included elsewhere in this Annual Report on Form 10-K for the period ended December 31, 2022. As further described in Note 1of the notes to our consolidated financial statements included elsewhere in this Annual Report, Private Histogen was determined to be the accounting acquirer in the Merger. In addition, references to the Company's operating results prior to the Merger will refer to the operating results of Private Histogen. Except as otherwise indicated herein or as the context otherwise requires, references in this Annual Report on Form 10-K to "Histogen" "the Company," "we," "us" and "our" refer to Histogen Inc., a Delaware corporation, on a post-Merger basis, and the term "Private Histogen" refers to the business of privately-held Histogen Inc. prior to completion of the Merger. The following discussion and analysis of our financial condition and results of operations contains forward-looking statements that involve a number of risks, uncertainties and assumptions. Actual events or results may differ materially from our expectations. Important factors that could cause actual results to differ materially from those stated or implied by our forward-looking statements include, but are not limited to, those set forth in the "Risk Factors" section of this annual report, many of which are outside of our control. All forward-looking statements included in this annual report are based on information available to us as of the time we file and, except as required by law, we undertake no obligation to update publicly or revise any forward-looking statements.

Overview

We are clinical-stage therapeutics company focused on developing potential first-in-class clinical and preclinical small molecule pan-caspase and caspase selective inhibitors that protect the body's natural process to restore immune function. Our product candidates include emricasan, CTS-2090 and CTS-2096. Currently, we are developing emricasan for acute bacterial skin and skin structure infections (ABSSSI) as well evaluating its use for other infectious diseases. Our pipeline also includes novel preclinical product candidates including CTS-2090 and CTS-2096, which are highly selective small molecule inhibitors of caspase-1 designed for the treatment of certain inflammatory diseases.

Previously, our focus was 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. In December 2022, we announced termination of our HST-003 study for futility related to patient recruitment and due to pipeline reprioritization, in the third quarter of 2022, we suspended all IND enabling activities on our HST-004 program.

While we are actively seeking collaboration partners or acquirors for our Human Multipotent Cell Conditioned Media, or CCM and our Human Extracellular Matrix, or hECM, there are no assurances that we will find a collaboration partner or acquirer for CCM or hECM or that the terms and timing of any such arrangements would be acceptable to us.

Components of Results of Operations

Revenue

Our revenues to date have been generated primarily from the sale of cosmetic ingredient products ("CCM"), license fees, professional services revenue, and a National Science Foundation grant award.

License and Product Revenue

Our license and product revenue to date has been generated primarily from payments received under the Allergan Agreements.

Grant Revenue

In March 2017, the National Science Foundation ("NSF"), a government agency, awarded us a research and development grant to develop a novel wound dressing for infection control and tissue regeneration. As of March 31, 2021, we completed all obligations under the NSF grant and, as such, no longer generate any revenue in connection with the research and development grant.

Operating Expenses

Cost of Revenues

Cost of product revenue represents direct and indirect costs incurred to bring the product to saleable condition, including write-offs of inventory.

Research and Development

Research and development expenses consist primarily of costs incurred for the preclinical and clinical development of our product candidates, which include:

- expenses under agreements with third-party contract organizations, investigative clinical trial sites that conduct research and development activities on our behalf, and consultants;
- costs related to develop and manufacture preclinical study and clinical trial material;
- salaries and employee-related costs, including stock-based compensation;
- costs incurred and reimbursed under our grant awarded by the U.S. Department of Defense ("DoD") to partially fund our Phase 1/2 clinical trial of HST-003 for regeneration of cartilage in the knee;
- costs incurred for IND enabling activities for HST-004 for spinal disc repair;
- costs incurred for completing the feasibility assessment of emricasan for the potential treatment of skin bacterial infections including those related to ABSSSI's, as well as other infectious diseases; and
- laboratory and vendor expenses related to the execution of preclinical and clinical trials.

We accrue all research and development costs in the period for which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors, collaborators and third-party service providers. Advance payments for goods or services to be received in future periods for use in research and development activities are deferred and then expensed as the related goods are delivered and as services are performed.

We expect our research and development expenses to increase substantially for the foreseeable future as we: (i) invest in additional operational personnel to support our planned product development efforts, and (ii) continue to invest in developing our product candidates as our product candidates advance into later stages of development, and as we begin to conduct larger clinical trials. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

Our direct research and development expenses are tracked by product candidate and consist primarily of external costs, such as fees paid under third-party license agreements and to outside consultants, contract research organizations ("CROs"), contract manufacturing organizations and research laboratories in connection with our preclinical development, process development, manufacturing and clinical development activities. We do not allocate employee costs and costs associated with our discovery efforts, laboratory supplies and facilities, including other indirect costs, to specific product candidates because these costs are deployed across multiple programs and, as such, are not separately classified. We use internal resources primarily to conduct our research as well as for managing our preclinical development, process development, manufacturing and clinical development activities.

These employees work across multiple programs and, therefore, we do not track our costs by product candidate unless such costs are includable as subaward costs. The following table shows our research and development expenses by type of activity (in thousands):

	Years Ended December 31,	
	2022	2021
Pre-clinical and clinical	$ 1,418	$ 2,700
Salaries and benefits	2,182	4,149
Facilities and other costs	1,421	1,624
Total research and development expenses	$ 5,021	$ 8,473

We cannot determine with certainty the timing of initiation, the duration or the completion costs of current or future preclinical studies and clinical trials of our product candidates due to the inherently unpredictable nature of preclinical and clinical development, including any potential expanded dosing beyond the original protocols based in part on ongoing clinical success. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. We anticipate that we will make determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to the results of ongoing and future preclinical studies and clinical trials, regulatory developments and our ongoing assessments of each product candidate's commercial potential. We will need to raise substantial additional capital in the future. In addition, we cannot forecast which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

General and Administrative

General and administrative expenses consist primarily of personnel-related costs, insurance costs, facility costs and professional fees for legal, patent, consulting, investor and public relations, accounting and audit services. Personnel-related costs consist of salaries, benefits, and stock-based compensation. We expect our general and administrative expenses to increase substantially as we: (i) incur additional costs associated with being a public company, including audit, legal, regulatory, and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs, (ii) hire additional personnel, and (iii) protect our intellectual property.

Other Income (Expense)

Interest Income

Interest income consists of interest earned on our cash equivalents, which consist of money market funds. Our interest income has not been significant due to low interest earned on invested balances.

Other Income

Other income primarily consists of the Paycheck Protection Program Loan forgiven by the Small Business Administration on May 21, 2021.

Results of Operations

Comparison of Years Ended December 31, 2022 and 2021

The following table sets forth our selected statements of operations data for the years ended December 31, 2022 and 2021 (in thousands):

	Years Ended December 31,		
	2022	2021	Change
Revenues			
Product revenue	$ —	$ 892	$ (892)
License revenue	3,769	27	3,742
Grant revenue	—	113	(113)
Total revenues	3,769	1,032	2,737
Operating expenses			
Cost of product revenue	—	220	(220)
Research and development	5,021	8,473	(3,452)
General and administrative	9,391	7,796	1,595
Total operating expenses	14,412	16,489	(2,077)
Loss from operations	(10,643)	(15,457)	4,814
Total other income (expense), net	(1)	448	(449)
Net loss	$ (10,644)	$ (15,009)	$ 4,365

Revenues

For the years ended December 31, 2022 and 2021, we recognized license revenues of $3.8 million and $27 thousand, respectively. The increase in the current period is due to a one-time payment of $3.75 million received in March 2022 as consideration for execution of the Allergan Letter Agreement.

For the years ended December 31, 2022 and 2021, we recognized product revenues of $0 and $0.9 million, respectively. The product revenue for the year ended December 31, 2021 was due to a one-time unanticipated sale of CCM to Allergan, unrelated to the Allergan Agreements. As of March 31, 2021, all obligations of the Company related to the additional supply of CCM to Allergan under the Allergan Agreements had been completed.

For the years ended December 31, 2022 and 2021, we recognized grant revenue of $0 and $0.1 million, respectively. The grant revenue for 2021 is associated with a research and development grant awarded to the Company from the NSF. As of March 31, 2021, all work required by the Company under the grant has been completed.

Total Operating Expenses

Cost of Revenues

For the years ended December 31, 2022 and 2021, we recognized $0 and $0.2 million, respectively, for cost of product sold to Allergan under the Allergan Agreements.

Research and Development Expenses

Research and development expenses for the years ended December 31, 2022 and 2021 were $5.0 million and $8.5 million, respectively. The decrease of $3.5 million was primarily due to decreases in personnel related expenses, the number of clinical and preclinical candidates in development and corresponding reduction of costs, partially offset by facility rent increases.

General and Administrative Expenses

General and administrative expenses for the years ended December 31, 2022 and 2021 were $9.4 million and $7.8 million, respectively. The increase of $1.6 million was primarily due to increases in royalty expenses, legal fees, outside services, rent expenses and personnel expenses, partially offset by reductions in insurance and other administrative expenses.

Liquidity and Capital Resources

From inception through December 31, 2022, we have an accumulated deficit of $88.3 million and expect to incur operating losses and generate negative cash flows from operations for the foreseeable future. As of December 31, 2022, we had approximately $12.1 million in cash and cash equivalents.

We have not yet established ongoing sources of revenues sufficient to cover our operating costs and will need to continue to raise additional capital to support our future operating activities, including progression of our development programs, preparation for potential commercialization, and other operating costs. Our plans with regard to these matters include entering into a combination of additional debt or equity financing arrangements, strategic partnerships, collaboration and licensing arrangements, or other similar arrangements. There can be no assurance that we will be able to obtain additional financing on terms acceptable to us, on a timely basis or at all. The aforementioned factors raise substantial doubt about our ability to continue as a going concern.

The consolidated financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. Based on the current business plan and operating budget, there is substantial doubt about the Company's ability to continue as a going concern within one year from the date the consolidated financial statements are issued. The consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

Redeemable Convertible Preferred Stock

March 2022 Offering of Preferred Stock

As described in Note 7 to the consolidated financial statements, in March 2022, the Company completed a private placement offering (the "March 2022 Offering") of Series A Preferred Stock and Series B Preferred Stock. The proceeds of $4.76 million were held in escrow and were only permitted to be disbursed to the Company upon conversion of the Series A and Series B Preferred Stock.

Between June 2, 2022, and June 29, 2022, the Company redeemed for cash proceeds totaling $5,250,500, 2,500 outstanding shares of Series A Preferred Stock and 2,500 outstanding shares of Series B Preferred Stock based on the receipt of the Redemption Notices (the "Preferred Redemption") at a price equal to 105% of the $1,000 stated value per share.

As of December 31, 2022, all shares of the Series A and B Preferred Stock are no longer outstanding and the Company's only class of outstanding stock is its common stock. No proceeds were received from the March 2022 Offering.

Common Stock

January 2021 Offering of Common Stock

In January 2021, the Company completed an S-1 offering (the "January 2021 Offering") of an aggregate of 580,000 shares of common stock, pre-funded warrants to purchase up to 120,000 shares of its common stock, and common stock warrants to purchase up to an aggregate of 700,000 shares of common stock. To the extent that an investor determines, at their sole discretion, that they would beneficially own in excess of the Beneficial Ownership Limitations (or as such investor may otherwise choose), in lieu of purchasing shares of Common Stock and Common Warrants, such investor could have elected to purchase Pre-Funded Warrants and Common Warrants at the Pre-Funded Purchase Price in lieu of the shares of Common Stock and Common Warrants in such a manner to result in the same aggregate purchase price being paid by such investor to the Company. The combined purchase price of one share of common stock and the accompanying common stock warrant was $20.00, and the combined purchase price of one pre-funded warrant and accompanying common stock warrant was $19.998. The common stock warrants are exercisable for five (5) years at an exercise price of $20.00 per share. The pre-funded warrants are immediately exercisable at an exercise price of $0.002 per share and may be exercised at any time until all of the pre-funded warrants are exercised in full. Placement agent warrants were issued to purchase up to 35,000 shares of common stock, are immediately exercisable for an exercise price of $25.00, and are exercisable for five (5) years following the date of issuance. The Company received gross proceeds of $14.0 million and incurred placement agent's fees and other offering expenses of approximately $1.9 million.

As of December 31, 2022, a total of 336,060 warrants issued in the January 2021 Offering to purchase shares of common stock have been exercised and the Company issued 336,060 shares of its common stock. The Company received gross proceeds of approximately $6.8 million.

As of December 31, 2022, the Company had 387,565 shares and 11,375 shares of common stock reserved for issuance pursuant to the warrants and placement agent's warrants, respectively, issued by the Company in the January 2021 Offering, at an exercise price of $20.00 per share and $25.00 per share, respectively.

June 2021 Offering of Common Stock

In June 2021, the Company completed a registered direct offering (the "June 2021 Offering") of an aggregate of 298,865 shares of common stock, together with accompanying warrants to purchase up to an aggregate of 239,093 shares of common stock, at a public offering price of $22.00 per share. The accompanying warrants permit the investor to purchase additional shares equal to 80% of the number of shares of the Company's common stock purchased by the investor. The warrants have an exercise price of $20.00 per share, are immediately exercisable, and expire five and a half (5.5) years following the date of issuance. In addition, the Company's placement agent was issued compensatory warrants equal to 5.0%, or 14,946 shares, of the aggregate number of common stock sold in the offering, which are immediately exercisable for an exercise price of $27.50 and expire five (5) years following the date of issuance on June 7, 2026. The Company received gross proceeds of $6.6 million and incurred cash-based placement agent fees and other offering expenses of approximately $0.9 million.

As of December 31, 2022, no warrants associated with the June 2021 Offering have been exercised.

As of December 31, 2022, the Company had 90,910 shares and 14,946 shares of common stock reserved for issuance pursuant to the warrants and placement agent's warrants, respectively, issued by the Company in the June 2021 Offering, at an exercise price of $20.00 per share and $27.50 per share, respectively. In connection with the July 2022 Offering, the Company agreed to amend warrants, by reducing the exercise price and extending the expiration date, to purchase up to an aggregate of 148,183 shares of common stock of the Company that were originally issued to the investor in the June 2021 Offering.

December 2021 Offering of Common Stock

In December 2021, the Company completed a registered direct offering (the "December 2021 Offering") of an aggregate of 411,764 shares of common stock and 411,766 warrants to purchase up to 411,766 shares of common stock, at a public offering price of $8.50 per share. The accompanying warrants permit the investor to purchase

additional shares equal to approximately the same number of shares of the Company's common stock purchased by the investor. The warrants have an exercise price of $8.50 per share, may be exercised any time on or after 6 months and one (1) day after the issuance date, and expire five and a half (5.5) years following the date of issuance. In addition, the Company's placement agent was issued compensatory warrants equal to 5.0%, or 20,590 shares, of the aggregate number of shares of common stock sold in the offering, which are immediately exercisable for an exercise price of $10.626 and expire five and a half (5.5) years following the date of issuance on June 21, 2027. The Company received gross proceeds of $3.5 million and incurred cash-based placement agent fees and other offering expenses of approximately $0.5 million.

As of December 31, 2022, no warrants associated with the December 2021 Offering have been exercised.

As of December 31, 2022, the Company had 164,707 shares and 20,590 shares of common stock reserved for issuance pursuant to the warrants and placement agent's warrants, respectively, issued by the Company in the December 2021 Offering, at an exercise price of $8.50 per share and $10.626 per share, respectively. In connection with the July 2022 Offering, the Company agreed to amend warrants, by reducing the exercise price and extending the expiration date, to purchase up to an aggregate of 247,059 shares of common stock of the Company that were originally issued to the investor in the December 2021 Offering.

July 2022 Offering of Common Stock

On July 12, 2022, the Company entered into a Securities Purchase Agreement (the "July 2022 Purchase Agreement") with a single healthcare-focused institutional investor for the sale by the Company of (i) a pre-funded warrant to purchase up to 1,774,309 shares of Common Stock (the "Pre-Funded Warrant"), (ii) a Series A warrant to purchase up to an aggregate of 1,774,309 shares of common stock (the "Series A Warrant"), and (iii) a Series B warrant to purchase up to an aggregate of 1,774,309 shares of common stock (the "Series B Warrant," and together with the Pre-Funded Warrant and the Series A Warrant, the "Warrants"), in a private placement offering (the "Offering"). The combined purchase price of one Pre-Funded Warrant and accompanying Series A Warrant and accompanying Series B Warrant was $2.818.

Subject to certain ownership limitations, the Series A Warrant is exercisable immediately after the issuance date at an exercise price equal to $2.568 per share of common stock, subject to adjustments as provided under the terms of the Series A Warrant, and has a term of five and a half (5.5) years from the issuance date. Subject to certain ownership limitations, the Series B Warrant is exercisable immediately after the issuance date at an exercise price equal to $2.568 per share of common stock, subject to adjustments as provided under the terms of the Series B Warrant, and has a term of one and a half (1.5) years from the issuance date. Subject to certain ownership limitations described in the Pre-Funded Warrant, the Pre-Funded Warrant was immediately exercisable and may be exercised at an exercise price of $0.0001 per share of common stock any time until all of the Pre-Funded Warrant is exercised in full. As of December 31, 2022, the Pre-Funded Warrant to purchase up to an aggregate of 1,774,309 shares of common stock had been fully exercised and the Company issued 1,774,309 shares of common stock.

The Company also agreed to amend certain warrants to purchase up to an aggregate of 447,800 shares of common stock of the Company that were issued to the investor in the private placement in November 2020, June 2021 and December 2021 with exercise prices ranging from $8.50 to $34.00 per share and expiration dates ranging from May 18, 2026 to June 21, 2027, so that such warrants have a reduced exercise price of $2.568 per share and expiration date of five and a half (5.5) years following the closing of the private placement, for an additional offering price of $0.0316 per amended warrant. The incremental fair value resulting from the modifications to the warrants was adjusted against the gross proceeds from the offering as an equity issuance cost.

The gross proceeds to the Company were approximately $5 million, before deducting the placement agent's fees and other offering expenses, and excluding the proceeds, if any, from the exercise of the Series A Warrant, the Series B Warrant, and amended warrants.

As of December 31, 2022, no warrants associated with the July 2022 Purchase Agreement have been exercised.

As of December 31, 2022, the Company had 3,996,418 shares and 124,202 shares of common stock reserved for issuance pursuant to the warrants and placement agent's warrants, respectively, issued by the Company in the July 2022 Purchase Agreement, at an exercise price of $2.568 per share and $3.5225 per share, respectively.

Common Stock Purchase Agreement with Lincoln Park

In July 2020, the Company entered into a common stock purchase agreement (the "2020 Purchase Agreement") with Lincoln Park which provided that, upon the terms and subject to the conditions and limitations in the 2020 Purchase Agreement, Lincoln Park was committed to purchase up to an aggregate of $10.0 million of shares of the Company's common stock at the Company's request from time to time during a 24 month period that began in July 2020 and at prices based on the market price of the Company's common stock at the time of each sale. Upon execution of the 2020 Purchase Agreement, the Company sold 16,425 shares of common stock at $60.88 per share to Lincoln Park for gross proceeds of $1.0 million. During the year ended December 31, 2020, the Company sold an additional 15,000 shares of common stock to Lincoln Park for gross proceeds of approximately $0.5 million. In addition, in consideration for entering into the 2020 Purchase Agreement and concurrently with the execution of the 2020 Purchase Agreement, the Company issued 3,348 shares of its common stock to Lincoln Park. During the year ended December 31, 2022, the Company did not sell any shares of common stock to Lincoln Park.

The 2020 Purchase Agreement expired automatically pursuant to its term on August 1, 2022, and the Company did not sell any additional shares of common stock to Lincoln Park through the date of expiration of the 2020 Purchase Agreement.

Common Stock Warrants

In 2016, Private Histogen issued warrants to purchase common stock as consideration for settlement of prior liability claims. The warrants for the purchase of up to 180 common shares at an exercise price of $461.60 per share expired on July 31, 2021.

In addition, as of December 31, 2022, warrants to purchase 68 shares of common stock with an exercise price of $1,486.00 per share remain outstanding that were issued by Conatus in connection with obtaining financing in 2016. These warrants expire on July 3, 2023.

See warrant discussion above in connection with the January 2021 Offering, the June 2021 Offering, the December 2021 Offering, and the July 2022 Offering.

Cash Flow Summary for the Years Ended December 31, 2022 and 2021

The following table shows a summary of our cash flows for the years ended December 31, 2022 and 2021 (in thousands):

	Years Ended December 31,	
	2022	2021
Net cash provided by (used in)		
Operating activities	$ (9,683)	$ (14,532)
Investing activities	(216)	(241)
Financing activities	3,323	27,085
Net increase (decrease) in cash, cash equivalents and restricted cash	$ (6,576)	$ 12,312

Operating activities

Net cash used in operating activities was $9.7 million for the year ended December 31, 2022, resulting from our net loss of $10.6 million, which included non-cash charges of $0.7 million primarily related to depreciation and amortization and stock-based compensation, coupled with a $0.2 million net increase in operating assets and liabilities.

Net cash used in operating activities was $14.5 million for the year ended December 31, 2021, resulting from our net loss of $15.0 million, which included non-cash charges of $0.4 million related to depreciation and amortization, stock-

based compensation and forgiveness of our Paycheck Protection Program Loan, coupled with a $0.1 million net increase in operating assets and liabilities.

Investing activities

Net cash used in investing activities was $0.2 million for the year ended December 31, 2022, which was related to the purchase of property and equipment.

Net cash used in investing activities was $0.2 million for the year ended December 31, 2021, all of which was related to the purchase of property and equipment.

Financing activities

Net cash provided by financing activities was $3.3 million for the year ended December 31, 2022, primarily related to $4.4 million net proceeds from a July 2022 private placement, offset by $0.6 million of issuance costs resulting from the issuance and sale of our redeemable convertible preferred stock in a March 2022 private placement offering coupled with $0.5 million related to the redemption premium paid to repurchase the redeemable convertible preferred stock.

Net cash provided by financing activities was $27.1 million for the year ended December 31, 2021, resulting from sales of our common stock in registered direct offerings and the exercise of warrants.

Funding Requirements

We are subject to a number of risks similar to those of clinical stage companies, including dependence on key individuals, uncertainty of product development and generation of revenues, dependence on outside sources of capital, risks associated with clinical trials of products, need for marketing authorization of products, risks associated with protection of intellectual property, and competition with larger, better-capitalized companies. We are closely monitoring ongoing developments in connection with the COVID-19 pandemic, which has resulted in disruptions to clinical trials and may negatively impact our ability to raise capital. To fully execute our business plan, we will need, among other things, to complete our research and development efforts and clinical and regulatory activities. These activities may take several years and will require significant operating and capital expenditures in the foreseeable future. Based on the current business plan and operating budget, there is substantial doubt about the Company's ability to continue as a going concern within one year from the date the consolidated financial statements are issued. There can be no assurance that we will be able to obtain additional financing on terms acceptable to us, on a timely basis or at all. In addition, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. Our future capital requirements will depend on many factors, including:

- the type, number, scope, progress, expansions, results, costs, and timing of our preclinical studies and clinical trials of our product candidates which we are pursuing or may choose to pursue in the future;
- the costs and timing of manufacturing for our product candidates, including commercial manufacturing if any product candidate is approved;
- the costs, timing, and outcome of regulatory review of our product candidates;
- the costs of obtaining, maintaining, and enforcing our patents and other intellectual property rights;
- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company, including enhanced internal controls over financial reporting;
- the costs associated with hiring additional personnel and consultants as our preclinical and clinical activities increase;
- the costs and timing of establishing or securing sales and marketing capabilities if any product candidate is approved;

- our ability to achieve sufficient market acceptance, adequate coverage and reimbursement from third-party payors, and adequate market share and revenue for any approved products;
- the terms and timing of establishing and maintaining collaborations, licenses, and other similar arrangements;
- the impact of any natural disasters or public health crises, such as the COVID-19 pandemic, on our operations (including clinical trials and product candidate development); and
- costs associated with any products or technologies that it may in-license or acquire.

Until such time, if ever, as we can generate substantial product revenues to support our cost structure, we expect to finance our losses from operations and capital funding needs through a combination of equity offerings, debt financings, and other sources, including potentially collaborations, licenses and other similar arrangements. To the extent we raise additional capital through the sale of convertible debt or equity securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, licenses and other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. If we are unable to raise additional funds through debt or equity financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates by ourselves. There can be no assurance that we will be able to obtain any sources of financing on acceptable terms, or at all.

We may be unable to raise additional funds on acceptable terms or at all. As a result of the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. If we are unable to raise additional funds, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

Contractual Obligations and Commitments

Pfizer Inc.

In July 2010, the Company entered into a Stock Purchase Agreement with Pfizer pursuant to which it acquired all of the outstanding capital stock of Idun Pharmaceuticals, Inc. ("Idun"), a wholly-owned subsidiary of Pfizer at the time. Pursuant to the Stock Purchase Agreement, the Company will be required to make additional payments to Pfizer totaling $18.0 million upon the achievement of specified regulatory milestones relating to emricasan.

Prior to the termination of the Collaboration Agreement with Amerimmune on November 28, 2022, the obligations pursuant to the Stock Purchase Agreement were the responsibility of our former collaboration partner, Amerimmune. In accordance with authoritative guidance, amounts for the milestone payments will be recognized when it is probable that the related contingent liability has been incurred and the amount owed is reasonably estimated. No amounts for the milestone payments have been recorded during the year ended December 31, 2022.

Idun Distribution Agreement

In January 2013, the Company conducted a spin-off of its subsidiary Idun, which the Company had acquired from Pfizer in the transaction described above, to stockholders at that time. Immediately prior to the spin-off, all rights relating to emricasan were distributed to the Company pursuant to a distribution agreement.

PUR

PUR was formed to develop and market applications along with products in the surgical/orthopedic and device markets. In April 2019, Histogen entered into a Settlement, Release and Termination Agreement with PUR and its members ("PUR Settlement") which terminated the License, Supply and Operating Agreements between Histogen and PUR, eliminated Histogen's membership interest in PUR and returned all in-process research and development assets to Histogen (the "Development Assets"). The agreement also provided indemnifications and complete releases by and among the parties. The acquisition of the Development Assets was accounted for as an asset acquisition in accordance with ASC 805-50-50, *Acquisition of Assets Rather than a Business*.

As consideration for the reacquisition of the Development Assets, Private Histogen compensated PUR with both equity and cash components, including 8,366 shares of Series D convertible preferred stock with a fair value of $1.75 million and a potential cash payout of up to $6.25 million (the "Cap Amount"). Private Histogen paid PUR $0.5 million in upfront cash, forgave approximately $22 thousand of accounts receivable owed by PUR to Private Histogen, and settled an outstanding payable of PUR of approximately $23 thousand owed to a third party. The Company is also obligated to make milestone and royalty payments, including (a) a $0.4 million payment upon the unconditional acceptance and approval of a New Drug Application or Pre-Market Approval Application by the FDA related to the Development Assets, (b) a $0.4 million commercialization milestone upon reaching gross sales (by the Company or licensee) of the $0.5 million of products incorporating the Development Assets, and (c) a five percent (5%) royalty on net revenues collected by Histogen from commercial sales (by the Company or licensee) of products incorporating the Development Assets. The aforementioned cash payments, along with any future milestone and royalty payments, are all applied against the Cap Amount. In accordance with authoritative guidance, amounts for the milestone and royalty payments will be recognized when it is probable that the related contingent liability has been incurred and the amount owed is reasonably estimated. No amounts for the milestone and royalty payments have been recorded through the year ended December 31, 2022.

Allergan License and Supply Agreements

In July 2017, the Company and Allergan entered into a letter agreement to transfer Suneva Medical, Inc.'s Amended and Restated License and Supply Agreements (collectively the "Allergan Agreements") to Allergan, which grants exclusive rights to commercialize our CCM skin care ingredient worldwide, excluding South Korea, China, and India, in exchange for royalty payments to us based on Allergan's sales of product including the licensed ingredient. Through December 31, 2020, we entered into several amendments to the Allergan Agreements to, among other things, expand Allergan's license rights, identify exclusive and non-exclusive fields of use, and clarify responsibilities related to regulatory filings. For these amendments to the Allergan Agreements, we have received cash payments of $19.5 million through December 31, 2022. The Allergan Agreements also include a potential future milestone payment of $5.5 million if Allergan's net sales of products containing our CCM skin care ingredient exceeds $60 million in any calendar year through December 31, 2027.

From time to time, we may improve our CCM skin care ingredient, and to the extent that these are within the field of use in the Allergan Agreements, we will provide the improvements to Allergan. The remaining performance obligations related to the Allergan Agreements from 2017 were our obligations to supply CCM and provide potential future improvements to Allergan, for which our obligation to supply CCM was satisfied during the fourth quarter of 2019.

On January 17, 2020, the Company and Allergan amended the Allergan Agreements, further clarifying the fields of use, the product definition, and rights to certain improvements, as well as us agreeing to supply additional CCM in 2020 and provide further technical assistance to Allergan (the cost of which was reimbursed to the Company), for a one-time payment of $1.0 million. Our obligation to supply additional CCM to Allergan was satisfied during the first quarter of 2021.

Pursuant to the 2017 Allergan Amendment, Histogen had the right to a potential milestone payment of $5.5 million if Allergan's net sales of products containing the Company's CCM skin care ingredient exceeds $60.0 million in any calendar year through December 31, 2027. In lieu of the potential payment of $5.5 million, the Company entered into a Letter Agreement on March 18, 2022 with Allegan. In consideration for the execution of the Letter Agreement, Histogen received a one-time payment equal to $3.8 million in March 2022. In exchange, among other things, the Company agreed that the final payment represents a full and final satisfaction of all money due to the Company pursuant to the Letter Agreement.

Under the Amended and Restated License Agreement, as amended, Allergan will indemnify the Company for third party claims arising from Allergan's breach of the agreement, negligence or willful misconduct, or the exploitation of products by Allergan or its sublicensees. We will indemnify Allergan for third party claims arising from our breach of the agreement, negligence or willful misconduct, or the exploitation of products by us prior to the effective date. Allergan may terminate the agreement for convenience upon one business days' notice to us.

Amerimmune Collaborative Development and Commercialization Agreement

In October 2020, we entered into a Collaborative Development and Commercialization Agreement ("the Collaboration Agreement") with Amerimmune to jointly develop emricasan for the potential treatment of COVID-19. The FDA approved an investigational new drug application (IND) to initiate a Phase 1 study of emricasan in mild COVID-19 patients to assess safety and tolerability in 2020. Under the Collaboration Agreement, during the agreed upon research term, Amerimmune, at its own expense and in collaboration with us, was required to use commercially reasonable efforts to lead the development activities for emricasan, limited to the treatment of COVID-19.

Pursuant to the terms of the Collaboration Agreement, each party retained ownership of their legacy intellectual property and was responsible for ongoing patent application prosecution and maintenance costs and jointly owned any intellectual property developed during the term of the agreement. In addition, we granted Amerimmune an exclusive option, subject to terms and conditions including completion of a Phase 2 clinical trial by Amerimmune during the research term, to obtain an exclusive license that, if granted by us, allowed Amerimmune alone, or in conjunction with one or more strategic partners, to use its commercially reasonable efforts to develop, manufacture, and commercialize emricasan and other caspase modulators, including CTS-2090 and CTS-2096, and we would share the profits equally with Amerimmune. No consideration would be transferred to the Company until profits, as defined in the Collaboration Agreement, were generated by Amerimmune from developing or commercializing products.

We identified multiple promises to deliver goods and services, which include at the inception of the agreement: (i) a license to technology and patents, information, and know-how; (ii) supply of emricasan and (iii) collaboration, including our participation in a Joint Development Committee and Joint Partnering Committee. At inception and through December 31, 2022, we identified one performance obligation for all the deliverables under the Collaboration Agreement since the delivered elements were either not capable of being distinct or are not distinct within the context of the contract. No upfront consideration was exchanged between the parties and any consideration received would have been dependent on the successful execution of a qualifying strategic partnership, as defined, on the successful commercialization of emricasan, or upon a change in control of Amerimmune, as defined. Although we would have recognized revenue upon the occurrence of one of these events, no such events have occurred as of December 31, 2022.

On January 19, 2022, we provided a notice of material breach in connection with Amerimmune's non-performance under the Collaboration Agreement and, on March 3, 2022, we filed the Arbitration Demand. As part of our Arbitration Demand, we have requested that the Collaboration Agreement be terminated. We further brought the Arbitration Demand for breach of contract, seeking an award of specific performance requiring Amerimmune to comply with the terms of the Agreement, which provide that, in the event of termination for material breach, all rights and licenses granted to Amerimmune by us shall terminate, and any and all rights granted by us to Amerimmune revert to Histogen.

On March 8, 2022, Amerimmune provided written notice to exercise an option for additional license rights to develop additional products, provided, however, we 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 Collaboration Agreement is properly terminated as set forth in our Arbitration Demand. On March 11, 2022, Judicial Arbitration and Mediation Services, Inc. ("JAMS") issued a Notice of Commencement of Arbitration letter, confirming the commencement of the arbitration as of that date.

On November 28, 2022, we received an Interim Award ("Interim Award") issued by the Arbitrator presiding over the Arbitration Demand filed by us in the County of San Diego, against Amerimmune LLC seeking a declaratory judgment that Amerimmune has materially breached the terms of the Collaboration Agreement to jointly develop emricasan for the potential treatment of COVID-19 entered into by and between the us and Amerimmune on October 26, 2020, and that we are therefore entitled to terminate the Collaboration Agreement. In the Interim Award, the Arbitrator ruled in our favor by finding that we lawfully and properly terminated the Collaboration Agreement and are entitled to declaratory relief and specific performance of the terms of the Collaboration Agreement on the finding that Amerimmune materially breached the terms of the Collaboration Agreement, and no affirmative defense excuses the breach by Amerimmune. Furthermore, the Arbitrator denied Amerimmune's request to exercise an option for additional license rights to develop additional products, as well as its claims for breach of the implied covenant of good faith and fair dealing, breach of contract, and tortious interference.

As affirmed by the Interim Award, we terminated the Collaboration Agreement and all rights and licenses granted to Amerimmune by us have been terminated, and Amerimmune shall cease any and all development, manufacture and commercialization activities under the Agreement, and any and all rights granted by us to Amerimmune reverted to us except any such rights that shall survive termination of the Collaboration Agreement.

On January 2, 2023, the parties received the Final Award affirming the arbitration outcome set forth in the Interim Award. Amerimmune will have 100 days from the date it receives the final award to petition a court to vacate or correct the Final Award. We have sought to confirm the award to judgment by filing a petition to confirm award filed.

Off Balance Sheet Arrangements

As of December 31, 2022 and 2021, we had no off-balance sheet arrangements, as defined in Item 303(a)(4)(ii) of Regulation S-K under the Exchange Act.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles ("U.S. GAAP"). The preparation of these consolidated financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities as of the date of the balance sheet and the reported amounts of expenses during the reporting period. Our estimates are based on historical trends and other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We consider our critical accounting policies and estimates to be related to accrued research and development expenses and revenue recognition. Our significant accounting policies are described in more detail in Note 2 in the notes to consolidated financial statements as of and for the years ended December 31, 2022 and 2021 appearing elsewhere in this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements and the report of our independent registered public accounting firm required pursuant to this item are incorporated by reference herein from the applicable information included in Item 15 of this Annual Report on Form 10-K and are presented beginning on page F-1.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures designed to provide reasonable assurance of achieving the objective that information in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified and pursuant to the requirements of the SEC's rules and forms and that such information is accumulated and communicated to our management, including our Interim Chief Executive Officer and Chief Financial Officer, as appropriate, to allow for timely decisions regarding required disclosures. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by SEC Rule 13a-15(b), we carried out an evaluation, with the participation of our Management, including our Interim Chief Executive Officer and Chief Financial Officer, of the effectiveness of our disclosure controls and procedures as of December 31, 2022, the end of the period covered by this report. Based upon the foregoing, our Interim Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at a reasonable assurance level as of December 31, 2022.

Management's Report on Internal Control Over Financial Reporting

Our Management is responsible for establishing and maintaining adequate internal control over our financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act as a process designed by, or under the supervision of, a company's principal executive and principal financial officers and effected by a company's board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with U.S. GAAP. Our internal control over financial reporting includes those policies and procedures that: Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our Management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in its 2013 Internal Control — Integrated Framework.

Based on our assessment, our Management has concluded that, as of December 31, 2022, our internal control over financial reporting was effective based on those criteria.

Pursuant to Regulation S-K Item 308(b), this Annual Report on Form 10-K does not include an attestation report of our company's registered public accounting firm regarding internal control over financial reporting.

Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting during the quarter ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission in connection with our 2023 Annual Meeting of Stockholders, or the Definitive Proxy Statement, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2022.

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees, which is available on our website at www.histogen.com. The Code of Business Conduct and Ethics contains general guidelines for conducting the business of our company consistent with the highest standards of business ethics and is intended to qualify as a "code of ethics" within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose (i) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

Item 11. Executive Compensation.

Information required by this item is incorporated by reference to our Proxy Statement to be filed with the Securities and Exchange Commission in connection with our 2023 Annual Meeting of Stockholders within 120 days after the end of our fiscal year ended December 31, 2022.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Information required by this item is incorporated by reference to our Proxy Statement to be filed with the Securities and Exchange Commission in connection with our 2023 Annual Meeting of Stockholders within 120 days after the end of our fiscal year ended December 31, 2022.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Information required by this item is incorporated by reference to our Proxy Statement to be filed with the Securities and Exchange Commission in connection with our 2023 Annual Meeting of Stockholders within 120 days after the end of our fiscal year ended December 31, 2022.

Item 14. Principal Accounting Fees and Services.

Information required by this item is incorporated by reference to our Proxy Statement to be filed with the Securities and Exchange Commission in connection with our 2023 Annual Meeting of Stockholders within 120 days after the end of our fiscal year ended December 31, 2022.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a)(1) The financial statements required to be filed by Items 8 and 15(c) of this Annual Report on Form 10-K, and filed herewith, are as follows:

(a)(2) Financial statement schedules required to be filed by Item 8 of this form, and by paragraph (b) below have been omitted as they are not applicable.

(a)(3) **Exhibits**

The following is a list of Exhibits filed as part of the Annual Report on Form 10-K:

Exhibit Number	Description of Exhibit
2.1	Distribution Agreement, dated January 10, 2013, by and between Idun Pharmaceuticals, Inc. and the Company (incorporated by reference to Exhibit 2.1 of the Company's Registration Statement on Form S-1 (Registration No. 333-189305), filed with the SEC on June 14, 2013).
2.2	Agreement and Plan of Merger and Reorganization, dated as of January 28, 2020, by and among the Company, Chinook Merger Sub, Inc. and Histogen Therapeutics Inc. (formerly Histogen Inc.) (incorporated by reference to Exhibit 2.1 of the Company's Current Report on Form 8-K filed with the SEC on January 28, 2020).
3.1	Amended and Restated Certificate of Incorporation of the Company (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on August 1, 2013).
3.2	Certificate of Amendment (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on May 27, 2020).
3.3	Certificate of Amendment (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on May 27, 2020).
3.4	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.3 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on May 27, 2020).
3.5	Certificate of Amendment, filed June 1, 2022 (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 2, 2022).
3.6	Bylaw Amendment (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 25, 2022).
3.7	Certificate of Designation of Preferences, Rights and Limitations of Series A Redeemable Convertible Preferred Stock (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 25, 2022).
3.8	Certificate of Designation of Preferences, Rights and Limitations of Series B Redeemable Convertible Preferred Stock (incorporated by reference to Exhibit 3.3 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 25, 2022).
3.9	Certificate of Elimination relating to the Certificate of Designations of Preferences, Rights and Limitations of Series A Redeemable Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 30, 2022).

3.10	Certificate of Elimination relating to the Certificate of Designations of Preferences, Rights and Limitations of Series B Redeemable Convertible Preferred Stock (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 30, 2022).
4.1	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).
4.2	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).
4.3	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.)
4.4	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.)
4.5	Form of Common Warrant (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form S-1/A (File No. 333-251491) filed with the Securities and Exchange Commission on December 29, 2020).
4.6	Form of Placement Agent Warrant (incorporated by reference to Exhibit 4.6 to the Company's Registration Statement on Form S-1/A (File No. 333-251491) filed with the Securities and Exchange Commission on December 29, 2020).
4.7	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.7 to the Company's Registration Statement on Form S-1/A (File No. 333-251491) filed with the Securities and Exchange Commission on December 29, 2020).
4.8	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).
4.9	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).
4.10	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).
4.11	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).
4.12	Form of Pre-Funded 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 July 12, 2022).
4.13	Form of Series A Warrant to Purchase Common Stock (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 July 12, 2022).
4.14	Form of Series B Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.3 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 12, 2022).
4.15	Form of Placement Agent 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 March 25, 2022).
4.16	Form of Placement Agent Warrant (incorporated by reference to Exhibit 4.4 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 12, 2022).
4.17*	Description of Securities.
10.1#	2020 Incentive Award Plan, effective May 26, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on May 27, 2020).
10.2#	Form of Stock Option Grant Notice and Option Agreement (2020 Incentive Award Plan) (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on May 28, 2020).
10.3#	2017 Stock Plan (incorporated by reference to Exhibit 10.43 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).
10.4#	Form of Stock Option Agreement (2017 Stock Plan) (incorporated by reference to Exhibit 10.44 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).

10.5# 2007 Stock Plan (incorporated by reference to Exhibit 10.45 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).

10.6# Form of Stock Option Agreement (2007 Stock Plan) (incorporated by reference to Exhibit 10.46 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).

10.7# Form of Indemnification Agreement, between the Company and its officers and directors (incorporated by reference to Exhibit 10.51 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).

10.8# Executive Employment Agreement, dated December 11, 2018, by and between the Company and Richard W. Pascoe (incorporated by reference to Exhibit 10.47 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).

10.9# Notice of Grant of Stock Option, dated January 24, 2019, by and between the Company and Richard W. Pascoe (incorporated by reference to Exhibit 10.48 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).

10.10# Amendment to Option and Employment Agreement, dated January 28, 2020, by and between the Company and Richard W. Pascoe (incorporated by reference to Exhibit 10.49 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).

10.11# Executive Employment Agreement, dated April 16, 2019, by and between the Company and Martin Latterich (incorporated by reference to Exhibit 10.50 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).

10.12 Lease, dated January 3, 2020, by and between the Company and San Diego Sycamore, LLC (incorporated by reference to Exhibit 10.57 to Amendment No. 2 to the Company's Registration Statement on Form S-4 (Registration No. 333-236332) filed with the Securities and Exchange Commission on March 30, 2020).

10.13 Irrevocable Standby Letter of Credit, dated March 13, 2020, by and between the Company and San Diego Sycamore, LLC (incorporated by reference to Exhibit 10.69 to Amendment No. 2 to the Company's Registration Statement on Form S-4 (Registration No. 333-236332) filed with the Securities and Exchange Commission on March 30, 2020).

10.14† Settlement, Release and Termination Agreement, dated April 5, 2019, by and among the Company, PUR Biologics, LLC, Wylde, LLC, Christopher Wiggins and Ryan Fernan (incorporated by reference to Exhibit 10.52 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).

10.15 Conversion, Termination and Release Agreement, dated August 26, 2016, by and among the Company, Jonathan Jackson, Lordship Ventures LLC and Lordship Ventures Histogen Holdings LLC (incorporated by reference to Exhibit 10.53 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).

10.16 Termination of Stockholder Agreements, dated January 28, 2020, by and among the Company, Lordship Ventures Histogen Holdings LLC, Pineworld Capital Limited, Gail K. Naughton, Ph.D. and certain trusts (incorporated by reference to Exhibit 10.54 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).

10.17 Second Amended and Restated Strategic Relationship Success Fee Agreement, dated January 28, 2020, by and between the Company and Lordship Ventures LLC (incorporated by reference to Exhibit 10.55 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).

10.18 Amended and Restated Release, dated January 28, 2020, by and among the Company, Jonathan Jackson, Lordship Ventures LLC, and Lordship Ventures Histogen Holdings LLC (incorporated by reference to Exhibit 10.56 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).

10.19 Exclusive License and Supply Agreement, dated September 30, 2016, by and between the Company and Pineworld Capital Limited (incorporated by reference to Exhibit 10.59 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).

10.20† Amended and Restated License Agreement, dated December 16, 2013, by and between the Company and Suneva Medical, Inc. (incorporated by reference to Exhibit 10.60 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).

10.21+ Amended and Restated Supply Agreement, dated December 16, 2013, by and between the Company and Suneva Medical, Inc. (incorporated by reference to Exhibit 10.61 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).

10.22+ Amendment No. 1 to the Amended and Restated License Agreement and Amended and Restated Supply Agreement, dated July 12, 2017, by and among the Company, Suneva Medical, Inc. and Allergan Sales, LLC (incorporated by reference to Exhibit 10.62 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).

10.23+ Amendment No. 2 to Amended and Restated License Agreement, dated October 25, 2017, by and between the Company and Allergan Sales, LLC (incorporated by reference to Exhibit 10.63 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).

10.24+ Amendment No. 3 to Amended and Restated License Agreement and Amendment No. 2 to Amended and Restated Supply Agreement, dated March 22, 2019, by and between the Company and Allergan Sales, LLC (incorporated by reference to Exhibit 10.64 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).

10.25+ Amendment No. 4 to Amended and Restated License Agreement and Amendment No. 3 to Amended and Restated Supply Agreement, dated January 17, 2020, by and between the Company and Allergan Sales, LLC (incorporated by reference to Exhibit 10.65 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).

10.26# Employment Agreement between the Company and Susan A. Knudson, dated May 27, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on May 28, 2020).

10.27 Purchase Agreement, by and between the Company and Lincoln Park, dated July 20, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 20, 2020).

10.28 Registration Rights Agreement, by and between the Company and Lincoln Park, dated July 20, 2020 (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 20, 2020).

10.29 Collaborative Development and Commercialization Agreement, by and between the Company and Amerimmune LLC, dated October 26, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on October 26, 2020).

10.30 Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on November 12, 2020.)

10.31 Engagement Letter between Histogen Inc. and H.C. Wainwright & Co., LLC, dated as of November 10, 2020 (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on November 12, 2020.)

10.32 Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.32 to the Company's Registration Statement on Form S-1/A (File No. 333-251491) filed with the Securities and Exchange Commission on December 29, 2020).

10.33 Engagement Letter between Histogen Inc. and H.C. Wainwright & Co., LLC, dated as of December 28, 2020 (incorporated by reference to Exhibit 10.33 to the Company's Registration Statement on Form S-1/A (Registration No. 333-251491) filed with the Securities and Exchange Commission on December 29, 2020).

10.34† Option, Collaboration and License Agreement, dated December 19, 2016, between the Company and Novartis Pharma AG (incorporated by reference to Exhibit 10.33 of the Company's Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on March 16, 2017).

10.35† Amendment to Option, Collaboration and License Agreement, dated September 30, 2019, by and between Novartis Pharma AG and the Company (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K, filed with the SEC on October 4, 2019).

10.36 Investment Agreement, dated December 19, 2016, between the Company and Novartis Pharma AG (incorporated by reference to Exhibit 10.34 of the Company's Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on March 16, 2017).

10.37 Convertible Promissory Note, dated February 15, 2017, issued by the Registrant to Novartis Pharma AG (incorporated by reference to Exhibit 10.35 of the Company's Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on March 16, 2017).

10.38# Confidential Severance Agreement and General Release, by and between the Company and Gail K. Naughton, Ph.D., dated May 26, 2021 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on May 27, 2021).

10.39# Consulting Agreement, by and between the Company and Gail K. Naughton, Ph.D., effective as of June 1, 2021 (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on May 27, 2021).

10.40 Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 8, 2021).

10.41 Amendment to Engagement Letter between Histogen Inc. and H.C. Wainwright & Co., LLC, dated as of June 6, 2021 (incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 8, 2021).

10.42 First Amendment to Lease, by and between Histogen Inc. and San Diego Sycamore, LLC, dated as of June 25, 2021 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on June 25, 2021).

10.43# Executive Agreement, dated November 5, 2021, by and between the Company and Steven J. Mento, Ph.D. (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on November 8, 2021).

10.44 Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on December 16, 2021).

10.45 Form of Registration Rights Agreement (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on December 16, 2021).

10.46 Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 12, 2022).

10.47 Form of Registration Rights Agreement (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 12, 2022).

10.48 Form of Warrant Amendment (incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 12, 2022).

10.49† Stock Purchase Agreement, dated July 29, 2010, by and between Pfizer Inc. and the Company (incorporated by reference to Amendment No. 3 to the Company's Registration Statement on Form S-1 (Registration No. 333-189305), filed with the Securities and Exchange Commission) on July 23, 2013.

10.50 Promissory Note, dated July 29, 2010, issued by the Company to Pfizer Inc. (incorporated by reference to the Company's Registration Statement on Form S-1 (Registration No. 333-189305), filed with the Securities and Exchange Commission on June 14, 2013).

10.51 Amendment to Promissory Note, dated July 3, 2013, by and between the Company and Pfizer Inc. (incorporated by reference to Amendment No. 2 to the Company's Registration Statement on Form S-1 (Registration No. 333-189305), filed with the Securities and Exchange Commission on July 8, 2013).

10.52 Form of Securities Purchase Agreement between Histogen Inc. and the investors therein, dated March 22, 2022 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 25, 2022).

10.53 Form of Registration Rights Agreement between Histogen Inc. and the investors therein, dated March 22, 2022 (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 25, 2022).

10.54 Engagement Letter, dated March 1, 2022, between the Company and H.C. Wainwright & Co., LLC. (incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 25, 2022).

10.55# Consulting Agreement, dated April 29, 2022, by and between the Company and Latterich Consulting Service LLC (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on April 29, 2022).

10.56#	Executive Employment Agreement, dated February 1, 2023, by and between the Company and Alfred P. Spada, Ph.D. (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on January 3, 2023).
10.57	Letter Agreement by and between Histogen, Inc. and Allergan Sales, LLC, dated March 18, 2022 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 18, 2022).
10.58	Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 12, 2022).
10.59	Form of Registration Rights Agreement (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 12, 2022).
10.60	Form of Warrant Amendment (incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on July 12, 2022).
21.1*	List of Subsidiaries.
23.1*	Consent of Mayer Hoffman McCann P.C., Independent Registered Public Accounting Firm.
24.1*	Power of Attorney (Included in the signature page hereto)
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	Inline XBRL Instance Document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document.
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

* Filed herewith.

# Indicates a management contract or compensatory plan, contract or arrangement.

† Pursuant to Item 601(b)(10) of Regulation S-K, certain confidential portions of this exhibit were omitted by means of marking such portions with an asterisk because the identified confidential portions (i) are not material and (ii) would be competitively harmful if publicly disclosed.

+ Non-material schedules and exhibits have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The Company hereby undertakes to furnish supplementally copies of any of the omitted schedules and exhibits upon request by the Securities and Exchange Commission.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 9, 2023

HISTOGEN INC.

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

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, as his or her true and lawful attorneys-in-fact and agents, each with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this report, 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 each of them, 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 to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or either of them, or their or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Steven J. Mento, Ph.D. Steven J. Mento, Ph.D.	Executive Chairman and Interim Chief Executive Officer and President *(Principal Executive Officer)*	March 9, 2023
/s/ Susan A. Knudson Susan A. Knudson	Executive Vice President and Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 9, 2023
/s/ Susan Windham-Bannister, Ph.D. Susan Windham-Bannister, Ph.D.	Director	March 9, 2023
/s/ Daniel L. Kisner, M.D. Daniel L. Kisner, M.D.	Director	March 9, 2023
/s/ Rochelle Fuhrmann Rochelle Fuhrmann	Director	March 9, 2023
/s/ David H. Crean, Ph.D. David H. Crean, Ph.D.	Director	March 9, 2023
/s/ Jonathan Jackson Jonathan Jackson	Director	March 9, 2023
/s/ Brian M. Satz Brian M. Satz	Director	March 9, 2023

HISTOGEN INC.
INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Histogen Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Histogen Inc. ("Company") as of December 31, 2022 and 2021, and the related consolidated statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

Going Concern Uncertainty

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has incurred recurring losses and negative cash flows from operations and is dependent on additional financing to fund operations. These conditions raise substantial doubt about its ability to continue as a going concern. Management's plans regarding these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

Critical audit matters are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

We have served as the Company's auditor since 2015.

/s/ Mayer Hoffman McCann P.C.

San Diego, California
March 9, 2023

HISTOGEN INC. AND SUBSIDIARIES
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)

	December 31, 2022	December 31, 2021
Assets		
Current assets		
Cash and cash equivalents	$ 12,109	$ 18,685
Restricted cash	400	400
Accounts receivable, net	99	165
Prepaid and other current assets	848	2,359
Total current assets	13,456	21,609
Property and equipment, net	436	399
Right-of-use asset	4,658	4,432
Other assets	523	805
Total assets	$ 19,073	$ 27,245
Liabilities and stockholders' equity		
Current liabilities		
Accounts payable	$ 382	$ 1,393
Accrued liabilities	595	791
Current portion of lease liabilities	238	127
Current portion of deferred revenue	19	19
Total current liabilities	1,234	2,330
Lease liabilities, non-current	4,379	4,617
Deferred revenue, non-current	79	98
Finance lease liability, non-current	5	14
Total liabilities	5,697	7,059
Commitments and contingencies (Note 9)		
Stockholders' equity		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized at December 31, 2022 and 2021; no shares issued and outstanding at December 31, 2022 and 2021	—	—
Common stock, $0.0001 par value; 200,000,000 shares authorized at December 31, 2022 and 2021; 4,271,759 and 2,497,450 shares issued and outstanding at December 31, 2022 and 2021, respectively	5	5
Additional paid-in capital	102,673	98,839
Accumulated deficit	(88,273)	(77,652)
Total Histogen Inc. stockholders' equity	14,405	21,192
Noncontrolling interest	(1,029)	(1,006)
Total equity	13,376	20,186
Total liabilities and stockholders' equity	$ 19,073	$ 27,245

The accompanying notes are an integral part of these consolidated financial statements.

HISTOGEN INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share amounts)

	Years Ended December 31,	
	2022	2021
Revenue		
Product revenue	$ —	$ 892
License revenue	3,769	27
Grant revenue	—	113
Total revenue	3,769	1,032
Operating expense		
Cost of product revenue	—	220
Research and development	5,021	8,473
General and administrative	9,391	7,796
Total operating expense	14,412	16,489
Loss from operations	(10,643)	(15,457)
Other income (expense)		
Interest expense, net	(1)	(10)
Other income, net	—	458
Net loss	(10,644)	(15,009)
Loss attributable to noncontrolling interest	23	59
Deemed dividend - accretion of discount and redemption feature of redeemable convertible preferred stock	(488)	—
Net loss available to common stockholders	$ (11,109)	$ (14,950)
Net loss per share available to common stockholders, basic and diluted	$ (3.46)	$ (7.79)
Weighted-average number of common shares outstanding used to compute net loss per share, basic and diluted	3,211,139	1,918,176

The accompanying notes are an integral part of these consolidated financial statements.

HISTOGEN INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF REDEEMABLE
CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Histogen Inc. Stockholders' Equity (Deficit)	Non-controlling Interest	Total Equity (Deficit)
	Shares	Amount	Shares	Amount					
Balance at December 31, 2020	—	$ —	751,537	$ 1	$ 70,561	$ (62,702)	$ 7,860	$ (947)	$ 6,913
Issuance of common stock, net of issuance costs	—	—	1,410,600	3	20,735	—	20,738	—	20,738
Issuance of common stock upon net exercise of warrants	—	—	336,030	1	6,839	—	6,840	—	6,840
Repurchase of common stock	—	—	(717)	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	704	—	704	—	704
Net loss	—	—	—	—	—	(14,950)	(14,950)	(59)	(15,009)
Balance at December 31, 2021	—	—	2,497,450	5	98,839	(77,652)	21,192	(1,006)	20,186
Issuance of common stock, net of issuance costs	—	—	1,774,309	—	4,405	—	4,405	—	4,405
Issuance of redeemable convertible preferred stock, net of issuance costs	5,000	4,177	—	—	—	—	—	—	—
Accretion of issuance costs, discount and redemption feature of redeemable convertible preferred stock	—	1,073	—	—	(1,073)	—	(1,073)	—	(1,073)
Redemption of redeemable convertible preferred stock	(5,000)	(5,250)	—	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	502	—	502	—	502
Net loss	—	—	—	—	—	(10,621)	(10,621)	(23)	(10,644)
Balance at December 31, 2022	—	$ —	4,271,759	$ 5	$ 102,673	$ (88,273)	$ 14,405	$ (1,029)	$ 13,376

The accompanying notes are an integral part of these consolidated financial statements.

HISTOGEN INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,	
	2022	2021
Cash flows from operating activities		
Net loss	$ (10,644)	$ (15,009)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	140	97
Stock-based compensation	502	704
Forgiveness of the Payroll Protection Program Loan	—	(467)
Loss on disposal of property and equipment	—	17
Write-off of cell bank material	61	—
Changes in operating assets and liabilities:		
Accounts receivable	66	(21)
Inventories	—	239
Prepaid expenses and other current assets	1,119	(1,176)
Other assets	221	1,187
Accounts payable	(1,011)	854
Accrued liabilities	(196)	(799)
Right-of-use asset and lease liabilities, net	78	(111)
Deferred revenue	(19)	(47)
Net cash used in operating activities	(9,683)	(14,532)
Cash flows from investing activities		
Cash paid for property and equipment	(216)	(241)
Net cash used in investing activities	(216)	(241)
Cash flows from financing activities		
Proceeds from the issuance of common stock, net of issuance costs	4,405	20,738
Repayment of finance lease obligations	(9)	(9)
Issuance costs for redeemable convertible preferred stock	(585)	—
Redemption payment for redeemable convertible preferred stock	(488)	—
Settlement of forward purchase contract	—	(290)
Payment on financing of insurance premiums	—	(193)
Proceeds from the exercise of warrants	—	6,839
Net cash provided by financing activities	3,323	27,085
Net increase (decrease) in cash, cash equivalents and restricted cash	(6,576)	12,312
Cash, cash equivalents and restricted cash, beginning of period	19,085	6,773
Cash, cash equivalents and restricted cash, end of period	$ 12,509	$ 19,085
Reconciliation of cash, cash equivalents and restricted cash to the consolidated balance sheets		
Cash and cash equivalents	$ 12,109	$ 18,685
Restricted cash	400	400
Total cash, cash equivalents and restricted cash	$ 12,509	$ 19,085
Supplemental disclosure of cash flow information		
Cash paid for interest	$ 1	$ 6
Noncash investing and financing activities		
Issuance of redeemable convertible preferred stock, proceeds were held in escrow until redemption	$ 4,762	$ —
Redemption payment of redeemable convertible preferred stock from escrow	$ (4,762)	$ —
Fair value of warrants issued to Placement Agent	$ 283	$ 590

The accompanying notes are an integral part of these consolidated financial statements.

1. Organization and Nature of Operations

Description of Business

Histogen Inc. (the "Company," "Histogen," "we," or the "combined company"), formerly known as Conatus Pharmaceuticals Inc. ("Conatus"), was incorporated in the state of Delaware on July 13, 2005. The Company is a clinical-stage therapeutics company initially focused on developing potential first-in-class clinical and preclinical small molecule pan-caspase and caspase selective inhibitors that protect the body's natural process to restore immune function.

Merger between Private Histogen and Conatus Pharmaceuticals Inc. and Name Change

On January 28, 2020, the Company, then operating as Conatus, entered into an Agreement and Plan of Merger and Reorganization, as amended (the "Merger Agreement"), with privately-held Histogen, Inc. ("Private Histogen") and Chinook Merger Sub, Inc., a wholly-owned subsidiary of the Company ("Merger Sub"). Under the Merger Agreement, Merger Sub merged with and into Private Histogen, with Private Histogen surviving as a wholly-owned subsidiary of the Company (the "Merger"). On May 26, 2020, the Merger was completed. Conatus changed its name to Histogen Inc., and Private Histogen, which remains as a wholly-owned subsidiary of the Company, changed its name to Histogen Therapeutics Inc. On May 27, 2020, the combined company's common stock began trading on The Nasdaq Capital Market under the ticker symbol "HSTO".

Reverse Stock Split

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 the consolidated financial statements have been retrospectively restated to reflect this Reverse Stock Split. Additionally, all rights to receive shares of common stock under outstanding warrants, options, and restricted stock units ("RSUs") were adjusted to give effect of the reverse stock split. Furthermore, remaining shares of common stock available for future issuance under stock-based payment award plans and employee stock purchase plans were adjusted to give effect to the Reverse Stock Split.

Liquidity and Going Concern Uncertainty

The Company has incurred operating losses and negative cash flows from operations and had an accumulated deficit of $88.3 million as of December 31, 2022. The Company expects operating losses and negative cash flows from operations to continue for the foreseeable future. As of December 31, 2022, the Company had $12.1 million in cash and cash equivalents, which will not be sufficient to sustain its operations.

The Company has not yet established ongoing sources of revenues sufficient to cover its operating costs and will need to continue to raise additional capital to support its future operating activities, including progression of its development programs, preparation for potential commercialization, and other operating costs. Management's plans with regard to these matters include entering into a combination of additional debt or equity financing arrangements, strategic partnerships, collaboration and licensing arrangements, or other similar arrangements. There can be no assurance that the Company will be able to obtain additional financing on terms acceptable to the Company, on a timely basis or at all.

The consolidated financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. Based on the current business plan and operating budget, there is substantial doubt about the Company's ability to continue as a going concern within one year from the date the consolidated financial statements

are issued. The consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its controlled subsidiaries, including Histogen Therapeutics, Inc., and have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP"). All intercompany balances and transactions have been eliminated upon consolidation.

The Company acquired Centro De Investigacion de Medicina Regenerativa, S.A. de C.V. ("CIMRESA"), a company in Mexico, during 2018 to facilitate a potential clinical development program for HST-001, or hair stimulating complex ("HSC"). This is a wholly-owned subsidiary intended to pursue registration with the COFEPRIS (Mexico equivalent to Food and Drug Administration). CIMRESA had no operational or financial activity for the years ended December 31, 2022 and 2021.

The Company holds a majority interest in Adaptive Biologix, Inc. ("AB", formerly Histogen Oncology, LLC). AB was formed to develop and market applications for the treatment of cancer. The Company consolidates AB into its consolidated financial statements.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities and the disclosure of contingent assets and liabilities and contingencies at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the periods presented. Management believes that these estimates and assumptions are reasonable, however, actual results may differ and could have a material effect on future results of operations and financial position. Though the impact of the COVID-19 pandemic to our business and operating results presents additional uncertainty, the Company continues to use the best information available to them in their significant accounting estimates.

Significant estimates and assumptions include the useful lives of property and equipment, discount rates used in recognizing contracts containing leases, unrecognized tax benefits, volatility used for stock-based compensation option pricing, and best estimate of standalone selling price of revenue deliverables. Actual results may materially differ from those estimates.

Variable Interest Entities

The Company determined that AB is a variable interest entity ("VIE") and that the Company is its primary beneficiary. The Company holds greater than 50% of the shares and has the authority to manage the business and affairs of the VIE. AB's other shareholder does not have a controlling interest.

A VIE is typically an entity for which the Company has less than a 100% equity interest but controls the decision making over the business and affairs of the entity, directs the decisions driving the economic performance of such entity and participates in the profit and losses of such an entity. The Company weighed both quantitative and qualitative information about the different risks and reward characteristics of each entity and the significance of that entity to the consolidating group in the aggregate.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker, the Interim Chief Executive Officer, in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business as one operating segment.

Cash, Cash Equivalents and Restricted Cash

The Company considers all highly liquid investments purchased with an original maturity date of ninety days or less to be cash equivalents. Cash and cash equivalents include cash in readily available checking, money market accounts and brokerage accounts.

The Company's current restricted cash consists of cash held as collateral for a letter of credit issued as a security deposit for the lease of the Company's headquarters and is required to be held throughout the lease term.

Risks and Uncertainties

Credit Risk

At certain times throughout the year, the Company may maintain deposits in federally insured financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and believes it is not exposed to significant risk on its cash balances due to the financial position of the depository institutions in which those deposits are held.

Customer Risk

During the years ended December 31, 2022 and 2021, one customer accounted for 100% and 88% of total revenues, respectively. Accounts receivable from the customer was $0 at both December 31, 2022 and 2021.

COVID-19

The cumulative effect of the COVID-19 outbreak and associated disruptions have had, and may continue to have, an adverse impact on the Company's business and its results of operations. The full impact of the COVID-19 outbreak continues to evolve as of the date these consolidated financial statements were available to be issued and will depend on future developments that are highly uncertain and unpredictable, including efficacy and adoption of vaccines, future resurgences of the virus and its variants, the imposition of governmental lockdowns, and quarantine and physical distancing requirements. As such, it is uncertain as to the full magnitude that the pandemic will have on the Company's financial condition, liquidity, and future results of operations.

Accounts Receivable

Accounts receivable are generally due within 30 days and are recorded net of the allowance for doubtful accounts, if any. Management considers all accounts receivable to be fully collectible as of December 31, 2022 and 2021, and accordingly, no provision for doubtful accounts was recorded.

Property and Equipment

Property and equipment are reported net of accumulated depreciation and amortization and are comprised of office furniture and equipment, lab and manufacturing equipment, and leasehold improvements. Ordinary maintenance and repairs are charged to expense, while expenditures that extend the physical or economic life of the assets are capitalized. Furniture and all equipment are depreciated over their estimated useful lives, or five years, using the straight-line method. Software is amortized over its estimated useful lives, or three years, using the straight-line method. Leasehold improvements are amortized over their estimated useful lives and limited by the remaining term of the building lease, using the straight-line method.

Valuation of Long-Lived Assets

Long-lived assets to be held and used, including property and equipment, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of the assets may not be recoverable. As of December 31, 2022 and 2021, the Company has not recognized any impairment to long-lived assets.

Forward Purchase Contract

In 2011, Private Histogen contracted for research services from EPS Global Research Pte. Ltd. ("EPS") to conduct clinical trials and compile data from a study that took place in 2011 and 2013. The unpaid amount due for the services was approximately $0.3 million.

In 2017, Private Histogen and EPS entered into a Debt Settlement and Conversion Agreement ("Settlement Agreement") whereby Private Histogen paid $50 thousand and issued EPS 717 shares of Series D convertible preferred stock. The Company was required to repurchase the shares at the greater of the remaining balance due of approximately $0.3 million and the market price of the shares at the time of repurchase, but in no event later than December 31, 2021. The Company had the sole option to repurchase the shares (which were converted from Series D convertible preferred stock into shares of common stock upon the Merger) at any time on or before December 31, 2021.

On December 16, 2021, the Company repurchased from EPS 717 shares of common stock in exchange for a cash payment of approximately $0.3 million. The repurchased shares were recorded as treasury stock and retired as of December 31, 2021. As of December 31, 2021, all amounts due to EPS under the Settlement Agreement have been paid.

Fair Value Measurements

ASC 820, *Fair Value Measurements*, defines fair value, establishes a framework for measuring fair value under generally accepted accounting principles and enhances disclosures about fair value measurements. Fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

- Level 1 — Observable inputs such as quoted price (unadjusted) for identical instruments in active markets.
- Level 2 — Observable inputs such as quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active, or model derived valuations whose significant inputs are observable.
- Level 3 — Unobservable inputs that reflect the reporting entity's own assumptions.

At December 31, 2022 and 2021, management believes the carrying amount of financial instruments consisting of cash, cash equivalents, restricted cash, accounts receivable, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to the short-term nature of those instruments.

Comprehensive Loss

The Company is required to report all components of comprehensive loss, including net loss, in the accompanying consolidated financial statements in the period in which they are recognized. Comprehensive loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources, including unrealized gains and losses on investments and foreign currency translation adjustments. Net loss and comprehensive loss were the same for all periods presented.

Revenue Recognition

Product and License Revenue

The Company records revenue in accordance with ASC 606, *Revenue from Contracts with Customers*, whereby revenue is recognized when a customer obtains control of promised goods or services in an amount that reflects the consideration expected to be received in exchange for those goods or services. A five-step model is used to achieve the core principle: (1) identify the customer contract, (2) identify the contract's performance obligations, (3) determine the transaction price, (4) allocate the transaction price to the performance obligations and (5) recognize revenue when or as a performance obligation is satisfied. The Company applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. Shipping charges billed to customers are included in product revenue and the related shipping costs are included in cost of product revenue. The Company applies the revenue recognition standard, including the use of any practical expedients, consistently to contracts with similar characteristics and in similar circumstances (Refer to Note 5 for further information).

Grant Awards

In March 2017, the National Science Foundation ("NSF"), a government agency, awarded the Company a research and development grant to develop a novel wound dressing for infection control and tissue regeneration. The Company has concluded this government grant is not within the scope of ASC 606, as government entities generally do not meet the definition of a "customer" as defined by ASC 606. Payments received under the grant are considered conditional, non-exchange contributions under the scope of ASC 958-605, *Not-for-Profit Entities – Revenue Recognition*, and are recorded as grant revenue in the period in which such conditions are satisfied. In reaching the determination that such payments should be recorded as revenue, management considered a number of factors, including whether the Company is a principal under the arrangement, and whether the arrangement is significant to, and part of, the Company's ongoing operations.

In September 2020, the Company was approved for a grant award from the U.S. Department of Defense ("DoD") in the amount of approximately $2.0 million to partially fund the Company's Phase 1/2 clinical trial of HST-003 for regeneration of cartilage in the knee. The Company applies International Accounting Standard ("IAS") 20, *Accounting for Government Grants and Disclosure of Government Assistance*, by analogy as there is no existing authoritative guidance under GAAP. Under the terms of the award, the DoD will reimburse the Company for certain allowable costs. The period of performance for the grant award substantially expires in September 2025 and is subject to annual and quarterly reporting requirements. As the DoD grant is a cost-type (reimbursement) grant, the Company must incur program expenses in accordance with the Statement of Work and approved budget in order to be reimbursed by the DoD. The Company will recognize funding received from the grant award as a reduction of research and development expenses in the period in which qualifying expenses have been incurred, as the Company is reasonably assured that the expenses will be reimbursed and the funding is collectible. For the years ended December 31, 2022 and 2021, qualifying expenses totaling $0.6 million and $0.7 million, respectively, were incurred with a corresponding reduction of research and development expenses related to the award. As of December 31, 2022 and 2021, $0.1 million and $0.2 million, respectively, was included within accounts receivable on the consolidated balance sheets related to the award.

Cost of Product Revenue

Cost of product revenue represents direct and indirect costs incurred to bring the product to saleable condition.

Research and Development Expenses

All research and development costs are charged to expense as incurred. Research and development expenses primarily include (i) payroll and related costs associated with research and development performed, (ii) costs related to clinical and preclinical testing of the Company's technologies under development, and (iii) other research and development costs including allocations of facility costs, net of reimbursable research and development costs incurred under the DoD grant.

General and Administrative Expenses

General and administrative expenses represent personnel costs for employees involved in general corporate functions, including finance, accounting, legal and human resources, among others. Additional costs included within general and administrative expenses consist of professional fees for legal (including patent costs), audit and other consulting services, travel and entertainment, recruiting, allocated facility and general information technology costs, depreciation and amortization, and other general corporate overhead expenses.

Patent Costs

The Company expenses all costs as incurred in connection with patent applications (including direct application fees, and the legal and consulting expenses related to making such applications) and such costs are included as a component of general and administrative expenses in the accompanying consolidated statements of operations.

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred income taxes are recorded for temporary differences between consolidated financial statement carrying amounts and the tax basis of assets and liabilities. Deferred tax assets and liabilities reflect the tax rates expected to be in effect for the years in which the differences are expected to reverse. No income tax expense or benefit was recorded for the years ended December 31, 2022 and 2021, due to the full valuation allowance on the Company's net deferred tax assets. A valuation allowance is provided if it is more likely than not that some or all the deferred tax assets will not be realized.

The Company also follows the provisions of accounting for uncertainty in income taxes which prescribes a model for the recognition and measurement of a tax position taken or expected to be taken in a tax return, and provides guidance on derecognition, classification, interest and penalties, disclosure and transition.

The Company's policy is to recognize interest or penalties related to income tax matters in income tax expense. Interest and penalties related to income tax matters were not material for the periods presented.

Net Loss Per Share

Basic net loss per share attributable to common stockholders is computed by dividing net loss attributable to common stockholders by the weighted-average common shares outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common shares and potentially dilutive securities outstanding for the period. For the years ended December 31, 2022 and 2021, diluted net loss per share attributable to common stockholders is equal to basic net loss per share attributable to common stockholders as common stock equivalent shares from stock options and warrants were anti-dilutive.

The following table sets forth outstanding potentially dilutive shares that have been excluded from the calculation of diluted net loss per share attributable to common stockholders because of their anti-dilutive effect (in common stock equivalents):

	Years Ended December 31,	
	2022	2021
Common stock options issued and outstanding	118,166	116,311
Warrants to purchase common stock	4,876,639	1,186,307
Total anti-dilutive shares	4,994,805	1,302,618

Common Stock Valuations

Prior to the Merger, Private Histogen was required to periodically estimate the fair value of common stock with the assistance of an independent third-party valuation expert when issuing stock options and computing its estimated stock-based compensation expense. The assumptions underlying these valuations represented management's best estimates, which involved inherent uncertainties and the application of significant levels of management judgment.

In order to determine the fair value, Private Histogen considered, among other things, contemporaneous valuations of its common stock, business, financial condition and results of operations, including related industry trends affecting its operations; the likelihood of achieving various liquidity events; the lack of marketability of its common stock; the market performance of comparable publicly traded companies; and U.S. and global economic and capital market conditions.

Stock-Based Compensation

Service-Based Awards

The Company recognizes stock-based compensation expense for service-based stock options and restricted stock units ("RSUs") over the requisite service period on a straight-line basis. Employee and director stock-based compensation for service-based stock options is measured based on estimated fair value as of the grant date using the Black-Scholes option pricing model. The Company estimates the fair value of RSUs based on the closing price of the Company's common stock on the date of issuance. The Company uses the following assumptions for estimating fair value of service-based option grants:

Fair Value of Common Stock – The fair value of common stock underlying the option grant is determined based on observable market prices of the Company's common stock.

Expected Volatility – Volatility is a measure of the amount by which the Company's share price has historically fluctuated or is expected to fluctuate (i.e., expected volatility) during a period. Due to the lack of an adequate history of a public market for the trading of the Company's common stock and a lack of adequate company-specific historical and implied volatility data, volatility has been estimated and based on the historical volatility of a group of similar companies that are publicly traded. For these analyses, the Company has selected companies with comparable characteristics, including enterprise value, risk profiles, and position within the industry, and with historical share price information sufficient to meet the expected term of the stock-based awards.

Expected Term – This is the period of time during which the options are expected to remain unexercised. Options have a maximum contractual term of ten years. The Company estimates the expected term of stock options using the "simplified method", whereby the expected term equals the average of the vesting term and the original contractual term of the underlying option.

Risk-Free Interest Rate – This is the observed yield on zero-coupon U.S. Treasury securities, as of the day each option is granted, with a term that most closely resembles the expected term of the option.

Expected Forfeiture Rate – Forfeitures are recognized as they occur.

Performance-Based Options

Stock-based compensation expense for performance-based options is recognized based on amortizing the fair market value as of the grant date over the periods during which the achievement of the performance is probable. Performance-based options require certain performance conditions to be achieved in order for these options to vest. These options vest on the date of achievement of the performance condition.

Market-Based Options

Stock-based compensation expense for market-based options is recognized on a straight-line basis over the derived service period, regardless of whether the market condition is satisfied. Market-based options subject to market-based performance targets require achievement of the performance target in order for these options to vest. The Company estimates the fair value of market-based options as of the grant date and expected term using a Monte Carlo simulation that incorporates option-pricing inputs covering the period from the grant date through the end of the derived service period.

Recently Adopted Accounting Pronouncements

In August 2020, the FASB issued ASU No. 2020-06, Debt – Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815-40) ("ASU 2020-06"). This new guidance is intended to simplify the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts on an entity's own equity. Entities may adopt ASU 2020-06 using either a partial retrospective or fully retrospective method of transition. This ASU is effective for public business entities for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years, with early adoption permitted. The Company adopted ASU 2020-06 on January 1, 2022, utilizing the modified retrospective method. The adoption of this standard did not result in an adjustment and did not have a material impact on the Company's consolidated financial statements or related disclosures.

In May 2021, the FASB issued ASU No. 2021-04, Earnings Per Share (Topic 260), Debt — Modifications and Extinguishments (Subtopic 470-50), Compensation — Stock Compensation (Topic 718), and Derivatives and Hedging — Contracts in Entity's Own Equity (Subtopic 815-40): Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options ("ASU 2021-04"). The amendments in ASU 2021-04 provide guidance to clarify and reduce diversity in an issuer's accounting for modifications or exchanges of freestanding equity-classified written call options (for example, warrants) that remain equity classified after modification or exchange. The accounting standard update is effective for fiscal years beginning after December 15, 2021. On January 1, 2022, the Company adopted ASU 2021-04. The adoption of this standard did not have a material impact on the Company's consolidated financial statements or related disclosures.

In November 2021, the FASB issued ASU No. 2021-10, Government Assistance (Topic 832): Disclosure by Business Entities about Government Assistance ("ASU 2021-10"), which improves the transparency of government assistance received by certain business entities by requiring the disclosure of (1) the types of government assistance received; (2) the accounting for such assistance, and (3) the effect of the assistance on the business entity's financial statements. ASU 2021-10 is effective for fiscal years beginning after December 15, 2021, with early adoption permitted. The Company adopted ASU 2021-10 on January 1, 2022. The adoption of this standard did not have a material impact on the Company's consolidated financial statements or related disclosures.

3. Property and Equipment

Property and equipment, net, consisted of the following (in thousands):

	December 31,	
	2022	2021
Lab and manufacturing equipment	$ 937	$ 943
Office furniture and equipment	225	42
Software	48	48
Total	1,210	1,033
Less: accumulated depreciation and amortization	(774)	(634)
Property and equipment, net	$ 436	$ 399

Depreciation and amortization expense was approximately $0.1 million for the years ended December 31, 2022 and 2021. During the year ended December 31, 2021, the Company disposed of approximately $1.4 million in property and equipment that had been depreciated and amortized in full and had an immaterial impact on the accompanying consolidated statements of operations.

4. Balance Sheet Details

Prepaid and other current assets consist of the following (in thousands):

	December 31,	
	2022	2021
Insurance	$ 626	$ 691
Tenant improvement reimbursement receivable	—	1,057
Prepaid rent	81	132
Pre-clinical and clinical related expenses	64	158
Prepaid materials	—	138
Other	77	183
Total	$ 848	$ 2,359

Other assets consist of the following (in thousands):

	December 31,	
	2022	2021
Insurance	$ 513	$ 732
Cell bank material	—	61
Other	10	12
Total	$ 523	$ 805

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2022	2021
Current portion of finance lease liabilities	$ 9	$ 9
Accrued compensation	160	346
Clinical study related expenses	150	103
Legal fees	44	144
Accrued franchise tax	162	18
Other	70	171
Total	$ 595	$ 791

5. Revenue

The following is a summary description of the material revenue arrangements, including arrangements that generated revenues during the years ended December 31, 2022 and 2021.

Allergan License Agreements

2017 Allergan Amendment

In 2017, the Company entered into a series of agreements (collectively, the "2017 Allergan Agreement"), which ultimately transferred Suneva Medical, Inc.'s license and supply rights of Histogen's cell conditioned medium ("CCM") skin care ingredient in the medical aesthetics market to Allergan Sales LLC ("Allergan") and granted Allergan an exclusive, royalty-free, perpetual, irrevocable, non-terminable and transferable license, including the right to sublicense to third parties, to use the Company's CCM skin care ingredient in the medical aesthetics market. The 2017 Allergan Agreement also obligated the Company to deliver CCM to Allergan (the "Supply of CCM to Allergan") in the future as well as share with Allergan any potential future improvements to the Company's CCM skin care ingredients identified through the Company's research and development efforts ("Potential Future Improvements"). In consideration for the execution of the agreements, the Company received a cash payment of $11.0 million and a potential additional payment of $5.5 million if Allergan's net sales of products containing the Company's CCM skin care ingredient exceeds $60.0 million in any calendar year through December 31, 2027.

2019 Allergan Amendment

In March 2019, the Company entered into a separate agreement with Allergan (the "2019 Allergan Amendment") to amend the 2017 Allergan Agreement in exchange for a one-time payment of $7.5 million to the Company. The agreement broadened Allergan's license rights, expanding Allergan's access to certain sales channels where its products incorporating the CCM ingredient can be sold. Specifically, the license was broadened to provide Allergan the exclusive right to sell through the "Amazon Professional" website, or any website or digital platform owned or licensed by Allergan or under the Allergan brand name, and non-exclusive rights to sell on other websites and through brick-and-mortar medical spas and wellness centers (excluding websites and brick-and-mortar stores of luxury brands).

The Company evaluated the 2019 Allergan Amendment under ASC 606 and concluded that Allergan continues to be a customer and that the expanded license is distinct from the 2017 Allergan Agreement. The Company determined the expanded license under the 2019 Allergan Amendment to be functional intellectual property as Allergan has the right to utilize the Company's CCM skin care ingredient, and that ingredient is functional to Allergan at the time the Company transferred the expanded license.

The standalone selling price of the expanded license was not readily observable since the Company has not yet established a price for this expanded license and the expanded license has not been sold on a standalone basis to any customer. The Company accounted for the 2019 Allergan Amendment as a modification to the 2017 Allergan Agreement. The contract modification was accounted for as if the 2017 Allergan Agreement had been terminated and the new contract included the expanded license as well as the remaining performance obligations that arose from the 2017 Allergan Agreement related to the Supply of CCM to Allergan and Potential Future Improvements.

The total transaction price for the new contract included the $7.5 million from the 2019 Allergan Amendment as well as the amounts deferred as of the 2019 Allergan Amendment execution date for each the Supply of CCM to Allergan and Potential Future Improvements.

The standalone selling price for the Supply of CCM to Allergan was determined based on comparable sales transactions. The standalone selling price of the Potential Future Improvements was estimated at the fully burdened rate of research and development employees cost plus a commercially reasonable markup. The amount of the total transaction price allocated to the expanded license was determined using the residual approach, as a result of not having a standalone selling price for the expanded license; that is, the total transaction price less the standalone selling prices of the Supply of CCM to Allergan and Potential Future Improvements.

Revenue related to the Supply of CCM to Allergan has been deferred and recognized at the point in time in which deliveries are completed while revenue related to the Potential Future Improvements has been deferred and amortized ratably over the remaining 9-year life of the patent. The Supply of CCM to Allergan under the 2019 Allergan Amendment was entirely fulfilled during the year ended December 31, 2019. The $7.5 million residual amount of the total transaction price allocated to the expanded license was recognized as license revenue upon transfer of the license to Allergan in March 2019.

2020 Allergan Amendment

In January 2020, the Company further amended the 2019 Allergan Amendment in exchange for a one-time payment of $1.0 million to the Company (the "2020 Allergan Amendment"). The 2020 Allergan Amendment further broadened Allergan's exclusive and non-exclusive license rights to include products used for or in connection with microdermabrasion. In addition, the Company agreed to provide Allergan with an additional 200 kilograms of CCM (the "Additional Supply of CCM to Allergan").

The Company evaluated the 2020 Allergan Amendment under ASC 606 and concluded that Allergan continues to be a customer and that the expanded license is distinct from the 2019 Allergan Amendment. The Company determined the expanded license under the 2020 Allergan Amendment to be functional intellectual property as Allergan has the right to utilize the Company's CCM skin care ingredient, and that ingredient is functional to Allergan at the time the Company transferred the expanded license.

The standalone selling price of the expanded license was not readily observable since the Company has not yet established a price for this expanded license and the expanded license has not been sold on a standalone basis to any customer. The Company accounted for the 2020 Allergan Amendment as a modification to the 2019 Allergan Amendment (which had modified the 2017 Allergan Agreement, as noted above). The contract modification was accounted for as if the 2019 Allergan Amendment had been terminated and the new contract included the expanded license and Additional Supply of CCM to Allergan, as well as the remaining performance obligation related to Potential Future Improvements.

The total transaction price for the new contract included the $1.0 million from the 2020 Allergan Amendment, the future payment for the Additional Supply of CCM to Allergan, as well as the amounts deferred as of the 2020 Allergan Amendment execution date for Potential Future Improvements.

The standalone selling price for the Additional Supply of CCM to Allergan was determined using the observable inputs of historical comparable sales transactions, including the margin from such sales. The Company also considered its reduced expected cost of satisfying this performance obligation based on the current efficiencies within its CCM manufacturing processes. Due to significant efficiencies in the Company's CCM manufacturing processes, the forecasted cost of CCM production has decreased, while the applied margin was determined by comparison to similar sales transactions in prior years. The standalone selling price of the Potential Future Improvements was estimated at the fully burdened rate of research and development employees cost plus a commercially reasonable markup. The amount of the total transaction price allocated to the expanded license was determined using the residual approach, as a result of not having a standalone selling price for the expanded license; that is, the total transaction price less the standalone selling prices of the Additional Supply of CCM to Allergan and Potential Future Improvements.

Under the Amended and Restated License Agreement, as amended, Allergan will indemnify the Company for third party claims arising from Allergan's breach of the agreement, negligence or willful misconduct, or the exploitation of products by Allergan or its sublicensees. The Company will indemnify Allergan for third party claims arising from the Company's breach of the agreement, negligence or willful misconduct, or the exploitation of products by the Company prior to the effective date. Allergan may terminate the Agreement for convenience upon one business days' notice to the Company.

Revenue related to the Additional Supply of CCM to Allergan was deferred and was recognized at the point in time in which deliveries were completed. All deliveries of Additional Supply of CCM to Allergan have been completed as of March 31, 2021. As such, there is no revenue for the year ended December 31, 2022.

Revenue of $0.2 million related to the Potential Future Improvements has been deferred and amortized ratably over the remaining 9-year life of the patent, for which $19 thousand of previously deferred revenue was recognized in revenue during each of the years ended December 31, 2022 and 2021.

The $0.9 million residual amount of the total transaction price allocated to the expanded license was recognized as license revenue upon transfer of the license to Allergan in January 2020.

In August 2021, unrelated to the Allergan Agreements, the Company agreed to a sale of CCM under a purchase order with Allergan. The CCM sold to Allergan was initially manufactured by the Company for research and development purposes in support of its product candidates. In September 2021, the Company recognized $0.6 million of product revenue related to the sale. The Company does not have any additional purchase orders with Allergan for fulfillment.

2022 Allergan Letter Agreement

Pursuant to the 2017 Allergan Amendment, the Company had the right to a potential milestone payment of $5.5 million if Allergan's net sales of products containing the Company's CCM skin care ingredient exceeds $60.0 million in any calendar year through December 31, 2027. In lieu of the potential milestone payment of $5.5 million, the Company entered into a letter agreement on March 18, 2022 (the "Letter Agreement") with Allergan. In consideration for the execution of the Letter Agreement, the Company received a one-time payment equal to $3.8 million (the "Final Payment") in March 2022. In exchange, among other things, the Company agreed that the Final Payment represents a full and final satisfaction of all money due to the Company pursuant to the License Agreement. The Company

evaluated the 2022 Allergan Letter Agreement under ASC 606 and concluded that the performance obligation has been satisfied and therefore applied point in time recognition. The Company recognized $3.8 million of license revenue related to the Letter Agreement during the year ended December 31, 2022. The Letter Agreement did not have an impact on the remaining performance obligation to share with Allergan any Potential Future Improvements to CCM identified through the Company's research and development efforts.

Remaining Performance Obligation and Deferred Revenue

The remaining performance obligation is the Company's obligation to share with Allergan any Potential Future Improvements to CCM identified through the Company's research and development efforts. Deferred revenue recorded for the Potential Future Improvements was $0.1 million as of both December 31, 2022 and 2021. Deferred revenue is classified in current portion of deferred revenue liabilities when the Company's obligations to provide research for Potential Future Improvements are expected to be satisfied within twelve months of the balance sheet date. The deferred revenue is recognized on a straight-line basis over the remaining life of the licensing patents into early 2028.

Grant Revenue

In March 2017, the National Science Foundation, a government agency, awarded the Company a research and development grant to develop a novel wound dressing for infection control and tissue regeneration. Grant revenue recognized was $0 and $0.1 million for the years ended December 31, 2022 and 2021, respectively. As of March 31, 2021, the Company had completed all obligations under the NSF development grant and, as such, no longer generates any revenues in connection with the research and development grant.

Amerimmune Collaborative Development and Commercialization Agreement

In October 2020, the Company entered into a Collaborative Development and Commercialization Agreement (the "Collaboration Agreement") with Amerimmune to jointly develop emricasan for the potential treatment of COVID-19. The FDA approved an investigational new drug application (IND) to initiate a Phase 1 study of emricasan in mild COVID-19 patients to assess safety and tolerability in 2020. Under the Collaboration Agreement, Amerimmune, at its expense and in collaboration with the Company, was required to use commercially reasonable efforts to lead the development activities for emricasan. Amerimmune was responsible for conducting clinical trials and the Company agreed to provide reasonable quantities of emricasan for such purpose.

Pursuant to the terms of the Collaboration Agreement, each party retained ownership of their legacy intellectual property and responsibility for ongoing patent application prosecution and maintenance costs and jointly owned any intellectual property developed during the term of the agreement. In addition, the Company granted Amerimmune an exclusive option, subject to terms and conditions including completion of a Phase 2 clinical trial by Amerimmune during the research term, to obtain an exclusive license that, if granted by us, would have allowed Amerimmune alone, or in conjunction with one or more strategic partners, to use its commercially reasonable efforts to develop, manufacture, and commercialize emricasan and other caspase modulators, including CTS-2090 and CTS-2096, and the Company would have shared the profits equally with Amerimmune. No consideration would have been transferred to the Company until profits, as defined in the Collaboration Agreement, were generated by Amerimmune from developing or commercializing products.

The Company identified multiple promises to deliver goods and services, which included at the inception of the agreement: (i) a license to technology and patents, information, and know-how; (ii) supply of emricasan, and (iii) collaboration, including the Company's participation in a Joint Development Committee and Joint Partnering Committee. At inception and through December 31, 2022, the Company has identified one performance obligation for all the deliverables under the Collaboration Agreement since the delivered elements were either not capable of being distinct or are not distinct within the context of the contract. No upfront consideration was exchanged between the parties and any consideration received would have been dependent on the successful execution of a qualifying strategic partnership, as defined, on the successful commercialization of emricasan, or upon a change in control of Amerimmune, as defined. Although the Company would have recognized revenue upon the occurrence of one of these events, no such events had occurred as of December 31, 2022.

On January 19, 2022, the Company provided a notice of material breach in connection with Amerimmune's non-performance under the Collaboration Agreement and, on March 3, 2022, filed a demand for arbitration ("Arbitration Demand"). On March 11, 2022, Judicial Arbitration and Mediation Services, Inc. ("JAMS") issued a Notice of Commencement of Arbitration letter, confirming the commencement of the arbitration as of that date.

On March 8, 2022, Amerimmune provided written notice to exercise an option for additional license rights to develop additional products however, the Company has rejected Amerimmune's election of the option and believes that Amerimmune no longer has the right to exercise the option based on, among other reasons, the Company's belief that the Collaboration Agreement is properly terminated as set forth in Histogen's Arbitration Demand.

On November 28, 2022, the Company received an Interim Award ("Interim Award") issued by the Arbitrator presiding over the Arbitration Demand filed by the Company in the County of San Diego, against Amerimmune LLC seeking a declaratory judgment that Amerimmune has materially breached the terms of the Collaboration Agreement to jointly develop emricasan for the potential treatment of COVID-19 entered into by and between the Company and Amerimmune on October 26, 2020, and that the Company therefore was entitled to terminate the Collaboration Agreement.

As affirmed by the Interim Award, the Company has terminated the Collaboration Agreement and all rights and licenses granted to Amerimmune by the Company have been terminated, and Amerimmune shall cease any and all development, manufacture and commercialization activities under the Agreement, and any and all rights granted by the Company to Amerimmune revert to the Company except any such rights that shall survive termination of the Collaboration Agreement.

On January 2, 2023, the arbitrator issued the Final Award affirming the arbitration outcome set forth in the Interim Award. Amerimmune will have 100 days from the date it receives the final award to petition a court to vacate or correct the Final Award. The Company has sought to confirm the award to judgment by filing a petition to confirm award filed (refer to Note 9 for further information).

6. Debt

Paycheck Protection Program Loan

In April 2020, Private Histogen applied for and received loan proceeds in the amount of $0.5 million (the "PPP Loan") under the PPP as government aid for payroll, rent and utilities. The application for these funds required the Company to, in good faith, certify that the current economic uncertainty made the loan request necessary to support the ongoing operations of the Company. This certification further required the Company to take into account its current business activity and its ability to access other sources of liquidity sufficient to support ongoing operations in a manner that is not significantly detrimental to the business. The certification made by the Company did not contain any objective criteria and is subject to interpretation. Based in part on the Company's assessment of other sources of liquidity, the uncertainty associated with future revenues created by the COVID-19 pandemic and related governmental responses, and the going concern uncertainty reflected in the Company's consolidated financial statements as of December 31, 2019, the Company believed in good faith that it met the eligibility requirements for the PPP Loan. If, despite the good-faith belief that given the Company's circumstances all eligibility requirements for the PPP Loan were satisfied, it is later determined that the Company had violated any applicable laws or regulations or it is otherwise determined that the Company was ineligible to receive the PPP Loan, it may be required to repay the PPP Loan in its entirety and/or be subject to additional penalties and potential liabilities.

On June 5, 2020, the Paycheck Protection Program Flexibility Act was signed into law, extending the PPP Loan forgiveness period from eight weeks to 24 weeks after loan origination, extending the initial deferral period of principal and interest payments from six months to ten months after the loan forgiveness period, reducing the required amount of payroll expenditures from 75% to 60%, removing the prior ban on borrowers taking advantage of payroll tax deferral after loan forgiveness and allowing for the amendment of the maturity date on existing loans from two years to five years.

On March 8, 2021 the Company applied for PPP loan forgiveness with its lender and subsequently received approval from the lender on April 2, 2021. The Company, in good faith, believes it maintained compliance with the requirements of the PPP. On May 21, 2021, the Small Business Administration granted its forgiveness of the PPP Loan, including principal and accrued interest, of $0.5 million. The gain on forgiveness is reported as a component of other income on the accompanying consolidated statement of operations.

7. Redeemable Convertible Preferred Stock

The redeemable convertible preferred stock instruments were contingently redeemable preferred stock. Each series contained redemption features, limited voting rights, dividends, and conversion terms. The convertible preferred stock was presented on the consolidated balance sheets as mezzanine equity as of March 31, 2022. All shares of redeemable convertible preferred stock were fully redeemed and are no longer outstanding as of June 30, 2022.

March 2022 Offering

In March 2022, the Company completed a private placement offering (the "March 2022 Offering") of (i) 2,500 shares of the Company's Series A Redeemable Convertible Preferred Stock, par value $0.0001 per share (the "Series A Preferred Stock"), and (ii) 2,500 shares of the Company's Series B Redeemable Convertible Preferred Stock, par value $0.0001 per share (the "Series B Preferred Stock" and together with the Series A Preferred Stock, the "Preferred Stock"), in each case, at an offering price of $952.38 per share, representing a 5% original issue discount to the stated value of $1,000 per share of Preferred Stock, for gross proceeds from the Offerings of approximately $4.76 million, before the deduction of the placement agent's fee and other offering expenses. The shares of Series A Preferred Stock had a stated value of $1,000 per share and were convertible, at a conversion price of $20.00 per share, into 125,000 shares of common stock. The shares of Series B Preferred Stock had a stated value of $1,000 per share and were convertible, at a conversion price of $20.00 per share, into 125,000 shares of common stock. The closing occurred on March 25, 2022. The proceeds of $4.76 million were held in escrow and were only permitted to be disbursed to the Company upon conversion of the Series A and Series B Preferred Stock. Since the redeemable convertible preferred stock could have been redeemed at the option of the holder, but was not mandatorily redeemable, the redeemable preferred stock was classified as mezzanine equity and initially recognized at fair value of $4.76 million as mezzanine equity on the accompanying statement of redeemable convertible preferred stock and stockholders' equity.

The March 2022 Offering generated gross proceeds of $4.76 million and the Company incurred cash-based placement agent fees and other offering expenses of approximately $0.6 million. The proceeds were held in escrow and were only permitted to be disbursed to the Company upon conversion of the Series A and Series B Preferred Stock.

The Company's placement agent was issued compensatory warrants to purchase up to 7.0% of the aggregate number of shares of Preferred Stock sold in the offering (on an as-converted to common stock basis), resulting in common stock warrants to purchase up to 17,501 shares of common stock, with an exercise price of 125% of the offering price, or $25.00 per share, which are exercisable 6 months after issuance on or after September 25, 2022, and expire five and a half (5.5) years following the date of issuance on September 25, 2027.

The placement agent warrants, which are recorded as a component of stockholders' equity, were valued at an aggregate of $34 thousand dollars using the Black Scholes option pricing model based upon the following assumptions: expected volatility of 78.90%, risk-free interest rate of 2.40%, expected dividend yield of 0%, and an expected term of 5.5 years.

As of December 31, 2022, the Company had 17,501 shares of common stock reserved for issuance pursuant to the placement agent's warrants issued by the Company in the March 2022 Offering at an exercise price of $25.00 per share.

Voting Rights

The shares of Preferred Stock had no voting rights, except that they only have the right to vote, with the holders of common stock, as a single class on a proposal to approve an amendment to our certificate of incorporation to effect a reverse stock split of our issued and outstanding common stock within a range, to be determined by our board of directors and set forth in such proposal.

Each share of Series A Preferred Stock outstanding on April 14, 2022 (the "Record Date") had a number of votes equal to the number of shares of Common Stock issuable upon conversion of such share (whether or not such shares are then convertible). Accordingly, as of the Record Date, each share of Series A Preferred Stock had 3,776 votes, which is determined by dividing $1,000, the stated value of one share of Series A Preferred Stock, by $0.2648, the NASDAQ Minimum Price as of the closing on March 25, 2022. The holders of the Series A Preferred Stock agreed to not transfer their shares of Series A Preferred Stock until after the Annual Meeting and to vote all shares of Series A Preferred Stock in favor of the Reverse Stock Split Proposal.

Each share of Series B Preferred Stock outstanding on the Record Date entitled the holder thereof to cast 30,000 votes on the Reverse Stock Split Proposal. The holders of the Series B Preferred Stock agreed to not transfer their shares of Series B Preferred Stock until after the Annual Meeting and to vote all shares of Series B Preferred Stock in the same proportion as the aggregate shares of Common Stock and Series A Preferred Stock are voted on the Reverse Stock Split Proposal. As an example, if 70% of the aggregate votes cast by Common Stock and Series A Preferred Stock voting on the Reverse Stock Split Proposal were voted in favor thereof and 30% of the aggregate votes cast by Common Stock and Series A Preferred Stock voting on the Reverse Stock Split Proposal were voted against such Proposal, then 70% of the votes entitled to be cast by Series B Preferred Stock would have been cast in favor of the proposal and 30% of such votes would have been cast against the proposal.

Dividends

The holders of the redeemable convertible preferred stock were entitled to receive dividends on shares of Preferred Stock equal (on an as-if-converted-to-Common-Stock basis, disregarding for such purpose any conversion limitations hereunder) to and in the same form as dividends actually paid on shares of the Common Stock when, as and if such dividends are paid on shares of the Common Stock. No other dividends were payable on shares of Preferred Stock.

Conversion Rights

Each share of Preferred Stock was convertible, at any time and from time to time from and after the Reverse Stock Split Date at the option of the Holder thereof, into that number of shares of Common Stock determined by dividing the stated value per share of preferred stock by the conversion price. The shares of Series A Preferred Stock had a stated value of $1,000 per share and were convertible, at a conversion price of $20.00 per share, into 125,000 shares of common stock. The shares of Series B Preferred Stock had a stated value of $1,000 per share and were convertible, at a conversion price of $20.00 per share, into 125,000 shares of common stock.

Redemption Rights

Each share of Preferred Stock was redeemable after (i) the earlier of (1) the receipt of authorized stockholder approval for the reverse stock split and (2) the date that was 90 days following the Original Issue Date of March 25, 2022, and (ii) before the date that was 120 days after the Original Issue Date or July 23, 2022 (the "Redemption Period"), each stockholder had the right to cause the Company to redeem all or part of such stockholder's shares of Preferred Stock at a price per share equal to 105% of the stated value of $1,000 per share.

Between June 2, 2022, and June 29, 2022, at the request of the holders, the Company redeemed for cash proceeds totaling $5.25 million ($4.76 million payment from escrow and $0.5 million redemption payment by the Company), 2,500 outstanding shares of Series A Preferred Stock and 2,500 outstanding shares of Series B Preferred Stock based on the receipt of the Redemption Notices (the "Preferred Redemption") at a price equal to 105% of the $1,000 stated value per share, which represented all outstanding shares of Preferred Stock. The approximately $1.1 million accretion of the Series A and Series B Preferred Stock to its redemption value was recorded as a reduction to additional paid-in capital. The Company recognized a portion of the accretion as a deemed dividend related to the accretion of the discount and redemption feature of approximately $0.5 million upon redemption of Preferred Stock on the consolidated statement of operations.

On June 30, 2022, the Company filed a Certificate of Elimination with respect to the Series A Preferred Stock and Series B Preferred Stock (the "Series A Certificate of Elimination and the Series B Certificate of Elimination"), which upon filing with the Secretary of State of the State of Delaware ("Delaware Secretary"), eliminated from all matters set forth in the Certificates of Designation of Series A and Series B Preferred Stock.

As of December 31, 2022, all shares of the Series A Preferred Stock and Series B Preferred Stock are no longer outstanding and the Company's only remaining class of outstanding stock is its common stock, par value $0.0001 per share.

8. Stockholders' Equity

Common Stock

January 2021 Offering

In January 2021, the Company completed an S-1 offering (the "January 2021 Offering") of an aggregate of 580,000 shares of common stock, pre-funded warrants to purchase up to 120,000 shares of its common stock, and common stock warrants to purchase up to an aggregate of 700,000 shares of common stock. To the extent that an investor determines, at their sole discretion, that they would beneficially own in excess of the Beneficial Ownership Limitations (or as such investor may otherwise choose), in lieu of purchasing shares of Common Stock and Common Warrants, such investor could have elected to purchase Pre-Funded Warrants and Common Warrants at the Pre-Funded Purchase Price in lieu of the shares of Common Stock and Common Warrants in such a manner to result in the same aggregate purchase price being paid by such investor to the Company. The combined purchase price of one share of common stock and the accompanying common stock warrant was $20.00, and the combined purchase price of one pre-funded warrant and accompanying common stock warrant was $19.998. The common stock warrants are exercisable for five (5) years at an exercise price of $20.00 per share. The pre-funded warrants are immediately exercisable at an exercise price of $0.002 per share and may be exercised at any time until all of the pre-funded warrants are exercised in full. Placement agent warrants were issued to purchase up to 35,000 shares of common stock, are immediately exercisable for an exercise price of $25.00 per share, and are exercisable for five (5) years following the date of issuance. The Company received gross proceeds of $14.0 million and incurred placement agent's fees and other offering expenses of approximately $1.9 million.

The warrants and placement agent warrants were valued at $7.2 million and $0.3 million, respectively, using the Black-Scholes option pricing model based on the following assumptions: expected volatility 80.08%, risk-free interest rate 0.38%, expected dividend yield 0%, and an expected term of 5.0 years.

As of December 31, 2022, a total of 336,060 warrants issued in the January 2021 Offering to purchase shares of common stock have been exercised and the Company issued 336,060 shares of its common stock. The Company received gross proceeds of approximately $6.8 million.

As of December 31, 2022, the Company had 387,565 shares and 11,375 shares of common stock reserved for issuance pursuant to the warrants and placement agent's warrants, respectively, issued by the Company in the January 2021 Offering, at an exercise price of $20.00 per share and $25.00 per share, respectively.

June 2021 Offering

In June 2021, the Company completed a registered direct offering (the "June 2021 Offering") of an aggregate of 298,865 shares of common stock, together with accompanying warrants to purchase up to an aggregate of 239,093 shares of common stock, at a public offering price of $22.00 per share. The accompanying warrants permit the investor to purchase additional shares equal to 80% of the number of shares of the Company's common stock purchased by the investor. The warrants have an exercise price of $20.00 per share, are immediately exercisable, and expire five and a half (5.5) years following the date of issuance. In addition, the Company's placement agent was issued compensatory warrants equal to 5.0%, or 14,946 shares, of the aggregate number of common stock sold in the offering, which are immediately exercisable for an exercise price of $27.50 and expire five (5) years following the date of issuance on June 7, 2026. The Company received gross proceeds of $6.6 million and incurred cash-based placement agent fees and other offering expenses of approximately $0.9 million.

The warrants and placement agent warrants were valued at $3.0 million and $0.2 million, respectively, using a Black-Scholes option pricing model with the following assumptions: expected volatility 81.44% and 80.15%, risk-free interest rate 0.88% and 0.77%, expected dividend yield 0% and 0%, and an expected term of 5.5 years or 5.0 years, respectively.

As of December 31, 2022, no warrants associated with the June 2021 Offering have been exercised.

As of December 31, 2022, the Company had 90,910 shares and 14,946 shares of common stock reserved for issuance pursuant to the warrants and placement agent's warrants, respectively, issued by the Company in the June 2021 Offering, at an exercise price of $20.00 per share and $27.50 per share, respectively. In connection with the July 2022 Offering, the Company agreed to amend warrants, by reducing the exercise price and extending the expiration date, to purchase up to an aggregate of 148,183 shares of common stock of the Company that were originally issued to the investor in the June 2021 Offering. Refer to July 2022 Offering overview below for accounting treatment for the amended warrants.

December 2021 Offering

In December 2021, the Company completed a registered direct offering (the "December 2021 Offering") of an aggregate of 411,764 shares of common stock and 411,766 warrants to purchase up to 411,766 shares of common stock, at a public offering price of $8.50 per share. The accompanying warrants permit the investor to purchase additional shares equal to approximately the same number of shares of the Company's common stock purchased by the investor. The warrants have an exercise price of $8.50 per share, may be exercised any time on or after 6 months and one (1) day after the issuance date, and expire five and a half (5.5) years following the date of issuance. In addition, the Company's placement agent was issued compensatory warrants equal to 5.0%, or 20,590 shares, of the aggregate number of shares of common stock sold in the offering, which are immediately exercisable for an exercise price of $10.626 and expire five and a half (5.5) years following the date of issuance on June 21, 2027. The Company received gross proceeds of $3.5 million and incurred cash-based placement agent fees and other offering expenses of approximately $0.5 million.

The placement agent warrants, which are recorded as a component of stockholders' equity, were valued at an aggregate $0.1 million using the Black-Scholes option pricing model based on the following assumptions: expected volatility of 79.81%, risk-free interest rate of 1.21%, expected dividend yield of 0% and an expected term of 5.5 years.

As of December 31, 2022, no warrants associated with the December 2021 Offering have been exercised.

As of December 31, 2022, the Company had 164,707 shares and 20,590 shares of common stock reserved for issuance pursuant to the warrants and placement agent's warrants, respectively, issued by the Company in the December 2021 Offering, at an exercise price of $8.50 per share and $10.626 per share, respectively. In connection with the July 2022 Offering, the Company agreed to amend warrants, by reducing the exercise price and extending the expiration date, to purchase up to an aggregate of 247,059 shares of common stock of the Company that were originally issued to the investor in the December 2021 Offering. Refer to July 2022 Offering overview below for accounting treatment for the amended warrants.

July 2022 Offering

On July 12, 2022, the Company entered into a Securities Purchase Agreement (the "July 2022 Purchase Agreement") with a single healthcare-focused institutional investor for the sale by the Company of (i) a pre-funded warrant to purchase up to 1,774,309 shares of Common Stock (the "Pre-Funded Warrant"), (ii) a Series A warrant to purchase up to an aggregate of 1,774,309 shares of common stock (the "Series A Warrant"), and (iii) a Series B warrant to purchase up to an aggregate of 1,774,309 shares of common stock (the "Series B Warrant," and together with the Pre-Funded Warrant and the Series A Warrant, the "Warrants"), in a private placement offering (the "Offering"). The combined purchase price of one Pre-Funded Warrant and accompanying Series A Warrant and accompanying Series B Warrant was $2.818.

Subject to certain ownership limitations, the Series A Warrant became exercisable immediately after the issuance date at an exercise price equal to $2.568 per share of common stock, subject to adjustments as provided under the terms of

the Series A Warrant, and has a term of five and a half (5.5) years from the issuance date. Subject to certain ownership limitations, the Series B Warrant became exercisable immediately after the issuance date at an exercise price equal to $2.568 per share of common stock, subject to adjustments as provided under the terms of the Series B Warrant, and has a term of one and a half (1.5) years from the issuance date. Subject to certain ownership limitations described in the Pre-Funded Warrant, the Pre-Funded Warrant was immediately exercisable and may be exercised at an exercise price of $0.0001 per share of common stock any time until all of the Pre-Funded Warrant is exercised in full. As of December 31, 2022, the Pre-Funded Warrant to purchase up to an aggregate of 1,774,309 shares of common stock had been fully exercised and the Company issued 1,774,309 shares of common stock.

The Company also agreed to amend certain warrants to purchase up to an aggregate of 447,800 shares of common stock of the Company that were issued to the investor in the private placement in November 2020, June 2021 and December 2021 with exercise prices ranging from $8.50 to $34.00 per share and expiration dates ranging from May 18, 2026 to June 21, 2027, so that such warrants have a reduced exercise price of $2.568 per share and expiration date of five and a half (5.5) years following the closing of the private placement, for an additional offering price of $0.0316 per amended warrant. The incremental fair value resulting from the modifications to the warrants was adjusted against the gross proceeds from the offering as an equity issuance cost.

The gross proceeds to the Company were approximately $5 million, before deducting the placement agent's fees and other offering expenses, and excluding the proceeds, if any, from the exercise of the Series A Warrant, the Series B Warrant, and amended warrants.

The Series A warrants and placement agent warrants were valued at $3.8 million and $0.2 million, respectively, using the Black-Scholes option pricing model based on the following assumptions: expected volatility 79.28%, risk-free interest rate 3.06%, expected dividend yield 0%, and an expected term of 5.5 years.

The Series B warrants were valued at $2.3 million using the Black-Scholes option pricing model based on the following assumptions: expected volatility 74.25%, risk-free interest rate 3.16%, expected dividend yield 0%, and an expected term of 1.5 years.

The amended warrants were valued at $1.0 million using the Black-Scholes option pricing model based on the following assumptions: expected volatility 79.28%, risk-free interest rate 3.06%, expected dividend yield 0%, and an expected term of 5.5 years. The estimated fair value of the original warrants immediately prior to the warrant amendments was $0.5 million using Black-Scholes option pricing model based on the following assumptions: expected volatility ranging from 81.21 – 83.34%, risk-free interest rates of 3.06 – 3.16%, expected dividend yield 0%, and an expected terms of 3.84 – 4.94 years. The warrant modifications resulted in an estimated value of $0.5 million, measured as the incremental fair value of the amended warrants, and was adjusted against the gross proceeds from the offering.

As of December 31, 2022, no warrants associated with the July 2022 Purchase Agreement have been exercised.

As of December 31, 2022, the Company had 3,996,418 shares and 124,202 shares of common stock reserved for issuance pursuant to the warrants and placement agent's warrants, respectively, issued by the Company in the July 2022 Purchase Agreement, at an exercise price of $2.568 per share and $3.5225 per share, respectively.

Common Stock Purchase Agreement with Lincoln Park

In July 2020, the Company entered into a common stock purchase agreement (the "2020 Purchase Agreement") with Lincoln Park which provided that, upon the terms and subject to the conditions and limitations in the 2020 Purchase Agreement, Lincoln Park was committed to purchase up to an aggregate of $10.0 million of shares of the Company's common stock at the Company's request from time to time during a 24 month period that began in July 2020 and at prices based on the market price of the Company's common stock at the time of each sale. Upon execution of the 2020 Purchase Agreement, the Company sold 16,425 shares of common stock at $60.88 per share to Lincoln Park for gross proceeds of $1.0 million. During the year ended December 31, 2020, the Company sold an

additional 15,000 shares of common stock to Lincoln Park for gross proceeds of approximately $0.5 million. In addition, in consideration for entering into the 2020 Purchase Agreement and concurrently with the execution of the 2020 Purchase Agreement, the Company issued 3,348 shares of its common stock to Lincoln Park. During the years ended December 31, 2022 and 2021, the Company did not sell any shares of common stock to Lincoln Park.

The 2020 Purchase Agreement expired automatically pursuant to its term on August 1, 2022, and the Company did not sell any additional shares of common stock to Lincoln Park through the date of expiration of the 2020 Purchase Agreement.

Common Stock Warrants

In 2016, Private Histogen issued warrants to purchase common stock as consideration for settlement of prior liability claims. The warrants for the purchase of up to 180 common shares at an exercise price of $461.60 per share expired on July 31, 2021.

In addition, at December 31, 2022, warrants to purchase 68 shares of common stock with an exercise price of $1,486.00 per share remain outstanding that were issued by Conatus in connection with obtaining financing in 2016. These warrants expire on July 3, 2023.

See warrant discussion above in connection with the January 2021 Offering, the June 2021 Offering, the December 2021 Offering, and the July 2022 Offering.

Stock-Based Compensation

Equity Incentive Plans

On December 18, 2017, Private Histogen established the Histogen Inc. 2017 Stock Plan (the "2017 Plan"). Under the 2017 Plan, Private Histogen was authorized to issue a maximum aggregate of 41,861 shares of common stock with adjustments for unissued or forfeited shares under the predecessor plan (the Histogen Inc. 2007 Stock Plan). In April 2019, Private Histogen amended the 2017 Plan, which increased the number of common stock available for grants by 16,336 shares. The 2017 Plan permitted the issuance of incentive stock options ("ISOs"), non-statutory stock options ("NSOs"), and Stock Purchase Rights. NSOs could be granted to employees, directors, or consultants, while ISOs could be granted only to employees. Options granted vest over a maximum period of four years and expire ten years from the date of grant. In connection with the closing of the Merger, no further awards will be made under the 2017 Plan.

In May 2020, in connection with the closing of the Merger, the Company's stockholders approved the Company's 2020 Incentive Award Plan (the "2020 Plan"). The maximum number of shares of the Company's common stock available for issuance under the 2020 Plan equals the sum of (a) 42,500 shares; (b) any shares of common stock of the Company which are subject to awards under the Conatus 2013 Equity Incentive Plan (the "Conatus 2013 Plan") as of the effective date of the 2020 Plan which become available for issuance under the 2020 Plan after such date in accordance with its terms; and (c) an annual increase on the first day of each calendar year beginning with the January 1 of the calendar year following the effectiveness of the 2020 Plan and ending with the last January 1 during the initial ten-year term of the 2020 Plan, equal to the lesser of (i) five percent of the number of shares of the Company's common stock outstanding (on an as-converted basis) on the final day of the immediately preceding calendar year, and (ii) such lesser number of shares of the Company's common stock as determined by the Company's board of directors.

Additionally, in connection with the closing of the Merger, no further awards will be made under the Conatus 2013 Plan. As of December 31, 2022, 4,887 fully vested options remain outstanding under the Conatus 2013 Plan with a weighted average exercise price of $859.59 per share.

The following summarizes activity related to the Company's stock options under the 2017 Plan and the 2020 Plan for the year ended December 31, 2022:

	Options Outstanding	Weighted-average Exercise Price	Weighted-average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	111,418	$ 37.62	6.78	$ —
Granted	67,300	4.54		
Cancelled / Forfeited	(65,439)	31.83		
Outstanding at December 31, 2022	113,279	21.30	8.09	$ —
Vested and exercisable at December 31, 2022	41,101	$ 39.60	6.54	$ —

Prior Chief Executive Officer Stock Options

On January 24, 2019, the Company issued 22,909 stock options to its then newly appointed Chief Executive Officer. In accordance with the original award agreement, 40% of the options would vest immediately upon an initial public offering or 45 days following a change in control, as defined in the award agreement, while the remaining 60% are subject to vesting, of which 25% vest on the first anniversary of the grant date and then ratably over the remaining 36 months.

On January 28, 2020, the award agreement was amended, which became effective upon the close of the Merger in May 2020, whereby the 40% of stock options ("Liquidity Option Shares") subject to vesting upon an initial public offering or 45 days following a change in control will now vest immediately upon meeting certain performance and market condition-based criteria. The vesting of the Liquidity Option Shares is divided into four separate tranches, each vesting 25% of the Liquidity Option Shares, upon: (1) the closing of the proposed merger with Conatus; (2) the date that the market capitalization of the Company exceeds $200.0 million; (3) the date that the market capitalization of the Company exceeds $275.0 million, and; (4) the date that the market capitalization of the Company exceeds $300.0 million. Each vesting tranche represents a unique derived service period and therefore stock-based compensation expense for each vesting tranche is recognized on a straight-line basis over its respective derived service period. Additionally, in the event that the Chief Executive Officer's employment with the Company is terminated without cause or he resigns for good reason, an additional portion of the stock options award will vest equal to the number of such options which would have vested in the 12 months following the date of such termination.

On May 26, 2020, in connection with the closing of the Merger, 2,426 options of the Liquidity Option Shares became fully vested as the performance condition was achieved.

In November 2021, the Company's then President and Chief Executive Officer voluntarily resigned. No further stock-based compensation expense related to the market-based options will be recognized. As of December 31, 2022, the vested option awards expired unexercised.

Board of Directors and Employee Stock Options

In March 2021, in conjunction with a former Board Member's voluntary resignation, the Company modified stock-based payment awards by accelerating the vesting of all awards that were unvested at the time of his voluntary resignation and by extending the exercise period through December 31, 2021. As a result of the modification, the Company recorded an immaterial amount of additional stock-based compensation expense during the year ended December 31, 2021. As of December 31, 2022, the awards expired unexercised.

In June 2021, in conjunction with a former employees' voluntary resignation, the Company modified stock-based payment awards by accelerating the vesting of all awards that were unvested at the time of the voluntary resignation and by extending the exercise period through August 29, 2023.

Valuation of Stock Option Awards

The following weighted-average assumptions were used to calculate the fair value of awards granted to employees, non-employees and directors:

	Years Ended December 31,	
	2022	2021
Expected volatility	78.95%	78.69%
Risk-free interest rate	2.14%	0.85%
Expected option life (in years)	6.02	6.08
Expected dividend yield	—%	—%

Restricted Stock Units

On November 8, 2021, the Company granted 23,423 restricted stock units to the Company's Interim Chief Executive Officer, Chief Financial Officer, and Senior Vice President of Technical Operations. The fair value of the RSUs was $14.58 per share, which was the closing market price of the Company's common stock on the date of grant. The RSUs vest in full upon the earlier of (1) 12 months following the grant date and (2) a change of control of the Company, as defined in the Company's 2020 Plan, subject to continued service to the Company. Prior to RSU vesting, the Company and the RSU recipients mutually agreed to enter into RSU Cancellation Agreements such that the RSU awards shall no longer be outstanding. As of December 31, 2022, no restricted stock units remain outstanding.

Stock-based Compensation Expense

The compensation cost that has been included in the Company's consolidated statements of operations for all stock-based compensation arrangements is detailed as follows (in thousands):

	Years Ended December 31,	
	2022	2021
General and administrative	$ 470	$ 520
Research and development	32	184
Total	$ 502	$ 704

As of December 31, 2022, total unrecognized compensation cost related to unvested options was approximately $0.5 million which is expected to be recognized over a weighted-average period of 2.29 years.

Common Stock Reserved for Future Issuance

Common stock reserved for future issuance is as follows:

	December 31,	
	2022	2021
Common stock warrants	4,876,639	1,186,307
Common stock options issued and outstanding	118,166	116,311
Common stock available for issuance under stock plan	100,577	2,309
	5,095,382	1,304,927

9. Commitments and Contingencies

Leases

In January 2020, Private Histogen entered into a long-term operating lease with San Diego Sycamore, LLC ("Sycamore") for its headquarters that includes office and laboratory space. The lease commenced on March 1, 2020 and expires on August 31, 2031, with no options to renew or extend. The lease was accounted for as a modification of Private Histogen's existing lease with Sycamore as the lease agreement did not grant Private Histogen an additional right-of-use asset.

The terms of the lease agreement include seven months of rent abatement at lease commencement and a tenant improvement allowance of up to $2.2 million. The tenant improvements are required to be permanently affixed to the leased office and laboratory space and do not constitute leasehold improvements of the Company. During the construction period of the tenant improvements, the lease agreement requires the Company to relocate its operations to a similar Sycamore property whereby monthly rent is substantially reduced for the duration of the construction period. The lease is subject to additional variable charges for common area maintenance, insurance, taxes and other operating costs. At lease commencement, the Company recognized a right-of-use asset and operating lease liability totaling approximately $4.5 million. The Company used a discount rate based on its estimated incremental borrowing rate to determine the right-of-use asset and operating lease liability amounts to be recognized. The Company determined its incremental borrowing rate based on the term and lease payments of the new operating lease and what it would normally pay to borrow, on a collateralized basis, over a similar term for an amount equal to the lease payments. Operating lease expense is recognized on a straight-line basis over the lease term. The terms of the lease required the Company to provide the landlord a security deposit of $0.3 million as collateral for a letter of credit issued to be held throughout the lease term. This security deposit is shown as restricted cash on the accompanying consolidated balance sheets.

In June 2021, the Company entered into the First Amendment to Lease (the "Amendment"). Pursuant to the Amendment, among other things, the Company and Sycamore agreed (i) to substitute the temporary premises, (ii) to delay the start of construction and the timing of the Company's relocation to the replacement temporary premises, (iii) to increase the tenant improvement allowance from $2.2 million to $2.3 million, (iv) to increase the letter of credit amount from $0.3 million to $0.4 million upon commencement of the tenant improvements, and (v) to review potential subsequent reductions to the security deposit and related letter of credit requirement at certain time intervals along the lease term provided that the Company is not in default. As a result of the modification, the lease liability was remeasured using the incremental borrowing rate at the modification date and a corresponding reduction of $0.3 million was recorded to both the lease liability and right-of-use-asset.

During the year ended December 31, 2022, the Company completed construction of the building improvements. Due to construction delays, the tenant improvement construction period was extended by two months for which the Company was granted an incremental two-month extension of rent abatement and effectively shortened the lease term. Upon completion of the improvements, the building improvement costs in excess of the tenant improvement allowance that was funded by the Company were capitalized to the right-of-use-asset, to be amortized over the remaining lease term. As a result of the modification, the lease liability was remeasured and a corresponding increase of $0.4 million was recorded to both the lease liability and right-of-use-asset.

The Company leases certain office equipment that is classified as a finance lease. As of December 31, 2022, the weighted-average remaining term of the Company's operating lease and finance lease was approximately 8.7 years and 1.5 years, respectively.

The Company recognizes right-of-use assets and lease liabilities at the lease commencement date based on the present value of future minimum lease payments over the lease term. The discount rate used to determine the present value of the lease payments is the rate implicit in the lease unless that rate cannot be readily determined, in which case, the Company utilizes its incremental borrowing rate in determining the present value of the future minimum lease payments. At the inception dates of the leases, the weighted-average discount rate for the Company's operating and finance lease was 12.2% and 10.0%, respectively.

The Company does not record leases with an initial term of 12 months or less on the consolidated balance sheets. Expense for these short-term leases is recognized on a straight-line basis over the lease term. The Company has elected the practical expedient to combine lease and non-lease components into a single component for all classes of underlying assets.

The Company's lease assets and lease liabilities were as follows (in thousands):

	Balance Sheet Classification	December 31, 2022	December 31, 2021
Assets			
Operating lease	Right-of-use asset	$ 4,658	$ 4,432
Finance lease	Property and equipment, net	12	20
Total lease assets		$ 4,670	$ 4,452
Liabilities			
Current			
Operating lease liability	Current portion of lease liability	$ 238	$ 127
Finance lease liability	Accrued liabilities	9	9
Total current liabilities		247	136
Noncurrent			
Operating lease liability	Noncurrent portion of lease liability	4,379	4,617
Finance lease liability	Other liabilities	5	14
Total noncurrent liabilities		4,384	4,631
Total lease liabilities		$ 4,631	$ 4,767

The components of lease expense were as follows (in thousands):

	Statement of Operations Classification	Years Ended December 31, 2022	Years Ended December 31, 2021
Operating lease cost:			
Research and development		$ 597	$ 210
General and administrative		694	428
Total operating lease cost		$ 1,291	$ 638
Finance lease cost:			
Amortization of fixed assets	Property and equipment, net	$ 8	$ 9
Interest on lease liabilities	Interest expense	1	3
Total finance lease cost		$ 9	$ 12

Supplemental cash flow information related to leases were as follows (in thousands):

	Years Ended December 31, 2022	Years Ended December 31, 2021
Cash paid for amounts included in the measurement of lease liabilities		
Operating cash flows from operating lease	$ (78)	$ 111
Operating cash flows from finance lease	1	3
Financing cash flows from finance lease	9	9

At December 31, 2022, future minimum payments of lease liabilities were as follows (in thousands):

	Operating Lease	Finance Lease
2023	$ 780	$ 10
2024	803	5
2025	827	—
2026	853	—
Thereafter	4,330	—
Total minimum lease payments	7,593	15
Less: imputed interest	(2,976)	(1)
Total future minimum lease payments	4,617	14
Less: current obligations under leases	(238)	(9)
Noncurrent lease obligations	$ 4,379	$ 5

Material Contracts

Pfizer Inc.

In July 2010, Conatus entered into a Stock Purchase Agreement with Pfizer, pursuant to which it acquired all of the outstanding capital stock of Idun Pharmaceuticals, Inc., which was subsequently spun off to Conatus stockholders in January 2013. Under the stock purchase agreement, the Company may be required to make payments to Pfizer totaling $18.0 million upon the achievement of specified regulatory milestones. In accordance with authoritative guidance, amounts for the milestone payments will be recognized when it is probable that the related contingent liability has been incurred and the amount owed is reasonably estimated. No amounts for the milestone payments have been recorded during the years ended December 31, 2022 and 2021.

Prior to the termination of the Collaboration Agreement with Amerimmune on November 28, 2022, the obligations pursuant to the Stock Purchase Agreement were the responsibility of our former collaboration partner, Amerimmune. In accordance with authoritative guidance, amounts for the milestone payments will be recognized when it is probable that the related contingent liability has been incurred and the amount owed is reasonably estimated. No amounts for the milestone payments have been recorded during the year ended December 31, 2022.

PUR Settlement

In April 2019, Private Histogen entered into a Settlement, Release and Termination Agreement ("PUR Settlement") with PUR Biologics, LLC and its members which terminated the License, Supply and Operating Agreements between Private Histogen and PUR, eliminated Private Histogen's membership interest in PUR and returned all in-process research and development assets to Private Histogen (the "Development Assets"). The agreement also provided indemnifications and complete releases by and among the parties. The acquisition of the Development Assets was accounted for as an asset acquisition in accordance with ASC 805-50-50, Acquisition of Assets Rather than a Business.

As consideration for the reacquisition of the Development Assets, Private Histogen compensated PUR with both equity and cash components, including 8,366 shares of Series D convertible preferred stock with a fair value of $1.75 million and a potential cash payout of up to $6.25 million (the "Cap Amount"). Private Histogen paid PUR $0.5 million in upfront cash, forgave approximately $22 thousand of accounts receivable owed by PUR to Private Histogen, and settled an outstanding payable of PUR of approximately $23 thousand owed to a third party. The Company is also obligated to make milestone and royalty payments, including (a) a $0.4 million payment upon the unconditional acceptance and approval of a New Drug Application or Pre-Market Approval Application by the FDA related to the Development Assets, (b) a $0.4 million commercialization milestone upon reaching gross sales (by the Company or licensee) of the $0.5 million of products incorporating the Development Assets, and (c) a five percent (5%) royalty on net revenues collected by the Company from commercial sales (by the Company or licensee) of products incorporating the Development Assets. The aforementioned cash payments, along with any future milestone and royalty payments, are all applied against the Cap Amount. In accordance with authoritative guidance, amounts for the milestone and royalty payments will be recognized when it is probable that the related contingent liability has been incurred and the amount owed is reasonably estimated. No amounts for the milestone and royalty payments have been recorded during the years ended December 31, 2022 and 2021.

Litigation and Legal Matters

The Company is subject to claims and legal proceedings that arise in the ordinary course of business. Such matters are inherently uncertain, and there can be no guarantee that the outcome of any such matter will be decided favorably to the Company or that the resolution of any such matter will not have a material adverse effect upon the Company's consolidated financial statements. The Company accrues a liability for such matters when it is probable that future expenditures will be made, and such expenditures can be reasonably estimated. As of December 31, 2022, no accruals have been made and no liability recognized related to commitments and contingencies.

Employee Litigation

On or about February 17, 2022, two former employees, each of whom separately resigned and terminated their employment with Histogen, filed a complaint in the Superior Court of California, County of San Diego against the Company, the Company's Board of Directors, the Company's former Chief Executive Officer, as well as three individuals that are currently employed by the Company. Although the complaint lists the "Histogen Board of Directors, a business entity form unknown" as a defendant, the complaint does not specifically list the names of the board members. The plaintiffs allege whistleblower status, retaliation, discrimination, unfair business practices, wrongful termination, violation of civil rights, and other California state law claims. The Company has tendered the complaint to its liability insurer and engaged outside litigation counsel, as approved by its carrier, to defend Histogen, the Board of Directors and the individuals in this matter. The Company objects to the naming of each of the defendants in this matter and denies each of the plaintiffs' claims. The plaintiffs agreed to pre-arbitration mediation, which was conducted on May 4, 2022, as was required by the arbitration agreement executed by each of the plaintiffs. Considering that the parties did not resolve the matter through this mediation, the Company petitioned the San Diego Superior Court for an order that the matter be submitted to arbitration consistent with each of the plaintiff's arbitration agreements. The hearing for the motion to compel arbitration was held on August 12, 2022 and the San Diego Superior Court issued a ruling to uphold the binding arbitration agreements signed by both plaintiff's. The matter is expected to proceed to arbitration but is the responsibility of the plaintiffs to initiate the arbitration proceeding. The Company believes that our defense costs, settlement monies, damages or any other awards would be covered by our liability insurance; provided, however, insurance may not cover all claims or could exceed our insurance coverage. The Company believes that there are substantial defenses to this lawsuit, and we intend to vigorously defend against each of these claims. While this litigation matter is in the early stages, the Company believes the action is without merit. Nonetheless, the ultimate outcome is unknown at this time.

Amerimmune Collaborative Development and Commercialization Agreement Arbitration

On March 3, 2022, the Company filed a demand for arbitration ("Arbitration Demand") with JAMS in the county of San Diego, against Amerimmune LLC ("Amerimmune") seeking a declaratory judgment that Amerimmune has materially breached the Collaboration Agreement entered into by and between the Company and Amerimmune on October 26, 2020, and that the Company is therefore entitled to terminate the Collaboration Agreement in accordance with its terms. On November 28, 2022, the arbitrator issued an interim award in favor of the Company, granting the Company's request for declaratory relief and specific performance terminating the Collaboration Agreement and denying each of Amerimmune's counterclaims. On January 2, 2023, the arbitrator issued a final award affirming the arbitration outcome set forth in the interim award and further awarding the Company its costs in pursuing the arbitration. On February 9, 2023, the Company filed a petition in the Superior Court of California, County of San Diego, seeking to confirm the arbitration award. A hearing on the petition is currently scheduled for May 26, 2023.

10. Income Taxes

The reconciliation of income taxes computed using the statutory U.S. income tax rate and the provision is as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Tax computed at federal statutory rate	$ (2,235)	$ (3,152)
State tax, net of federal tax benefits	(5)	(908)
Tax credits	(368)	(325)
Valuation allowance	1,825	5,320
PPP loan forgiveness	—	(126)
Other	783	(809)
Provision for income taxes	$ —	$ —

Significant components of the Company's net deferred tax assets are as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Deferred tax assets:		
Tax loss carryforward	$ 19,250	$ 18,041
R&D credits and other tax credits	2,201	1,834
Stock-based compensation	132	152
Compensation	26	58
Deferred revenue	4	5
Lease liability	970	1,283
Capitalized research and development	1,992	2,607
Section 174	1,056	—
Other	33	80
Total deferred tax assets	25,664	24,060
Less: valuation allowance	(24,686)	(22,861)
Deferred tax assets, net	978	1,199
Deferred tax liability:		
Right-of-use assets	(978)	(1,199)
Net deferred tax assets	$ —	$ —

The Company records a valuation allowance against deferred tax assets to the extent that it is more likely than not that some portion, or all, the deferred tax assets will not be realized. Due to the substantial doubt related to the Company's ability to utilize its deferred tax assets, the Company recorded a valuation allowance against the deferred tax assets. The change in the valuation allowance is an increase of $1.8 million and $5.3 million for the years ended December 31, 2022 and 2021, respectively.

As of December 31, 2022, the Company had federal and California net operating loss ("NOL") carryforwards of approximately $72.0 million and $57.4 million, respectively. Additionally, as of December 31, 2022, Adaptive Biologix has federal and state net operating losses of $0.4 million each. The Company has federal net operating loss carryforwards of $41.3 million that are not subject to expiration. No California NOLs expired in 2022. As of December 31, 2022, the Company had federal and California research and development ("R&D") credit carryforwards of approximately $1.7 million and $1.6 million, respectively. The federal R&D tax credit carryforwards will begin to expire in 2027 unless previously utilized. The California R&D credit carryforwards will carry forward indefinitely.

Under Sections 382 and 383 of the Internal Revenue Code ("IRC"), substantial changes in the Company's ownership may limit the amount of NOL and research and development credit carryforwards that could be used annually in the future to offset taxable income. The tax benefits related to future utilization of federal and state NOL carryforwards, credit carryforwards, and other deferred tax assets may be limited or lost if cumulative changes in ownership exceeds 50% within any three-year period. The Company has not completed an IRC Section 382/383 analysis regarding the limitation of net operating loss and research and development credit carryforwards, and therefore, the ability of the Company to utilize its NOL and R&D credits is unknown.

Uncertain Tax Positions

The FASB ASC Topic 740, *Income Taxes*, addresses the determination of whether tax benefits claimed or expected to be claimed on a tax return should be recorded in the financial statements. Under ASC Topic 740-10, the Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities, based on the technical merits of the position. For fiscal years through December 31, 2022, the Company generated research and development credits but has not conducted a study to document the qualified activities. This study may result in an adjustment to the Company's research and development tax credit carryforwards; therefore, based on the accumulation of research and development tax credits since the Company's inception and the Company's uncertainty around its ability to utilize those tax credits until a study is completed, the Company has reserved a portion of those credits as an uncertain tax position as of December 31, 2022. A full valuation allowance has been provided against the Company's research and development tax credit carryforwards and, if an adjustment were to be required, this adjustment would be offset by a corresponding reduction to the valuation allowance.

The following table summarizes the activity related to our unrecognized tax benefits (in thousands):

	Years Ended December 31,	
	2022	2021
Gross unrecognized tax benefits at the beginning of the year	$ 683	$ 561
Additions from tax positions taken in the current year	133	118
Additions from tax positions taken in prior years	—	4
Reductions for tax positions from prior year	—	—
Gross unrecognized tax benefits at end of the year	$ 816	$ 683

Due to the existence of the valuation allowance, future changes in the Company's unrecognized tax benefits will not impact the Company's effective tax rate. The Company does not anticipate that there will be a substantial change in unrecognized tax benefits within the next twelve months.

The Company has not recognized any interest and penalties related to income taxes in the accompanying consolidated balance sheets or statements of operations. The Company is subject to taxation in the U.S. and state jurisdictions. The Company's income tax returns for all years beginning January 1, 2018 and subsequent are still open to audit by the taxing authorities.

CARES ACT

On March 27, 2020, the United States enacted the Coronavirus Aid, Relief and Economic Security Act (CARES Act). The Cares Act is an emergency economic stimulus package that includes spending and tax breaks to strengthen the United States economy and fund a nationwide effort to curtail the effect of COVID-19. While the CARES Act provides sweeping tax changes in response to the COVID-19 pandemic, some of the more- significant provisions which are expected to impact the Company's consolidated financial statements include removal of certain limitations on utilization of net operating losses, increasing the loss carryback period for certain losses to five years, and increasing the ability to deduct interest expense, as well as amending certain provisions of the previously enacted Tax Cuts and Jobs Act. Due to the loss position of the U.S. entities, many provisions of the CARES Act do not impact the Company and the CARES Act did not have an impact on the Company's income tax provision for the years ended December 31, 2022 and 2021.

11. Related Parties

Lordship

Lordship, with its predecessor entities along with its principal owner, Jonathan Jackson, have invested and been affiliated with Private Histogen since 2010. As of December 31, 2022 and 2021, Lordship controlled approximately 2.8% and 4.7% of the Company's outstanding voting shares, respectively, and currently holds two Board of Director seats.

In November 2012, Private Histogen entered into a Strategic Relationship Success Fee Agreement with Lordship (the "Success Fee Agreement"). The Success Fee Agreement causes certain payments to be made from the Company to Lordship equal to 1% of certain product revenues and 10% of certain license and royalty revenues generated from our Human Multipotent Cell Conditioned Media, or CCM, and our Human Extracellular Matrix, or hECM, in connection with the Company's biologics technology platform. The Success Fee Agreement also stipulates that if the Company engages in a merger or sale of all or substantially all (defined as 90% or more) of its assets or equity to a third party, then the Company has the option to terminate the agreement by paying Lordship the fair market value of future payments with the minimum payment being at least equal to the most recent annual payments Lordship has received. The Success Fee Agreement was amended in August 2016, but continues to carry the same rights to certain payments. The Company recognized an expense to Lordship for the years ended December 31, 2022 and 2021 totaling $375 thousand and $10 thousand, respectively, all of which is included in general and administrative expenses on the accompanying consolidated statements of operations. As of December 31, 2022 and 2021, there was a balance of $10 thousand and $12 thousand, respectively, paid to Lordship included as a component of other assets on the accompanying consolidated balance sheets in connection with the deferral of revenue from the Allergan license transfer agreements.