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

FORM 10-K

☒ **Annual report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

For the fiscal year ended December 31, 2023
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 001-35853

Harvard Apparatus Regenerative Technology, Inc.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**45-5210462**
(State or other jurisdiction of Incorporation or organization)	(I.R.S. Employer Identification No.)

84 October Hill Road, Suite 11, Holliston, Massachusetts 01746
(Address of Principal Executive Offices, including zip code)

(774) 233-7300
(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered

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

Common Stock, $0.01 par value

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 Section 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, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐	Accelerated filer ☐
Non-accelerated filer ☒	Smaller reporting company ☒
	Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 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 ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, computed by reference to the price at which the common equity was last sold, or the average bid and asked price of such common equity, as of June 30, 2023 was approximately $33.8 million based on the closing sale price on that date of $3.65. Shares of the registrant's common stock held by each officer and director and each person known to the registrant to own 10% or more of the outstanding voting power of the registrant have been excluded in that such persons may be deemed affiliates. This determination of affiliate status is not a determination for other purposes.

At March 18, 2024, there were 13,947,324 shares of the registrant's common stock issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Company's definitive Proxy Statement in connection with the 2024 Annual Meeting of Stockholders, to be filed within 120 days after the end of the Registrant's fiscal year, are incorporated by reference into Part III of this Form 10-K. Except with respect to information specifically incorporated by reference in this Form 10-K, such Proxy Statement is not deemed to be filed as part hereof.

HARVARD APPARATUS REGENERATIVE TECHNOLOGY, INC.
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ANNUAL REPORT ON FORM 10-K
For the Year Ended December 31, 2023

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Forward-Looking Statements

This Annual Report on Form 10-K contains statements that are not statements of historical fact and are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 (the Exchange Act), each as amended. The forward-looking statements are principally, but not exclusively, contained in "Item 1: Business" and "Item 7: Management's Discussion and Analysis of Financial Condition and Results of Operations." These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about management's confidence or expectations and our plans, objectives, expectations and intentions that are not historical facts. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "seek," "expect," "plans," "aim," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "think," "continue," "potential," "is likely," "permit," "objectives," "optimistic," "new," "goal," "target," "strategy" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in detail under the heading "Item 1A. Risk Factors" beginning on page 24 of this Annual Report on Form 10-K. You should carefully review all of these factors, as well as other risks described in our public filings, and you should be aware that there may be other factors, including factors of which we are not currently aware, that could cause these differences. Also, these forward-looking statements represent our estimates and assumptions only as of the date of this Annual Report. We may not update these forward-looking statements, even though our situation may change in the future, unless we have obligations under the federal securities laws to update and disclose material developments related to previously disclosed information. Harvard Apparatus Regenerative Technology, Inc. is referred to herein as "we," "our," "us," and "the Company."

PART I

Item 1. ***Business.***

OVERVIEW

Regenerative Biotech

We are a clinical-stage biotechnology company focused on the development of regenerative medicine treatments for disorders of the gastro-intestinal system and other organs that result from cancer, trauma or birth defects. Our technology is based on our proprietary cell-therapy platform that uses a patient's own stem cells to regenerate and restore function to damaged organs. We believe that our technology represents a next generation solution for restoring organ function because it allows the patient to regenerate their own organ, thus eliminating the need for human donor or animal transplants, the sacrificing of another of the patient's own organs or permanent artificial implants.

Our technology uses mesenchymal stem cells that are retrieved via biopsy from the patient's abdominal adipose, or fat, tissue prior to surgery. These stem cells are isolated, expanded and then cultured on a tubular scaffold made from extremely thin fibers of polyurethane. The scaffold is then incubated in a customized bioreactor where the stem cells continue to grow and adhere to the fibers of the scaffold. The finished graft is then surgically implanted to replace the resected portion of the damaged organ. Several weeks after surgery, once a conduit has been established, the implanted scaffold is removed using an endoscope. No permanent artificial implant remains in the body.

We conducted the world's first successful regeneration of the esophagus in a cancer patient in August 2017. This surgery was performed by Dr. Dennis Wigle, Chair of Thoracic Surgery at the Mayo Clinic in a patient requiring reconstruction of his esophagus following the removal of a large tumor in his chest. The results were published in the Journal of Thoracic Oncology Clinical and Research Reports in August 2021. The procedure demonstrated that using Harvard Apparatus Regenerative Technology, Inc.'s, or HRGN's, technology, we were able to successfully regenerate esophageal tissue, including the mucosal lining, to restore the integrity, continuity and functionality of the esophageal tube.

Based on our successful first-in-human procedure and our preclinical procedures in over 50 pigs, the U.S. Food and Drug Administration, or FDA has approved our Investigational New Drug (IND) application to begin a phase 1 clinical trial for esophageal regeneration. This open-label trial will assess both safety and efficacy in up to ten patients requiring esophageal reconstruction for any reason, including caustic burns, puncture wounds or damage to the esophagus following chemoradiation therapy for esophageal cancer, at up to five U.S. hospitals. We have contracted with IQVIA, a leading global provider of advanced analytics, technology solutions and clinical research services to the life sciences industry, as the contract research organization (CRO) to manage our first clinical trial. We activated two clinical trial sites, the Mayo Clinic and the University of Michigan Medical Center, and started screening patients in the third quarter of 2023. We continue to seek our first eligible patient for enrollment in the trial.

We are initially targeting regeneration of the organs of the gastro-intestinal tract and the airway, where organ transplants are not medically possible today. Human-donor organ transplants or animal xenotransplants are currently not performed for these organs due to high rates of rejection. Additionally, we believe that our technology and intellectual property will allow us to develop organ-regeneration treatments for other organs.

Our product candidates are currently in development and have not yet received regulatory approval for sale anywhere in the world.

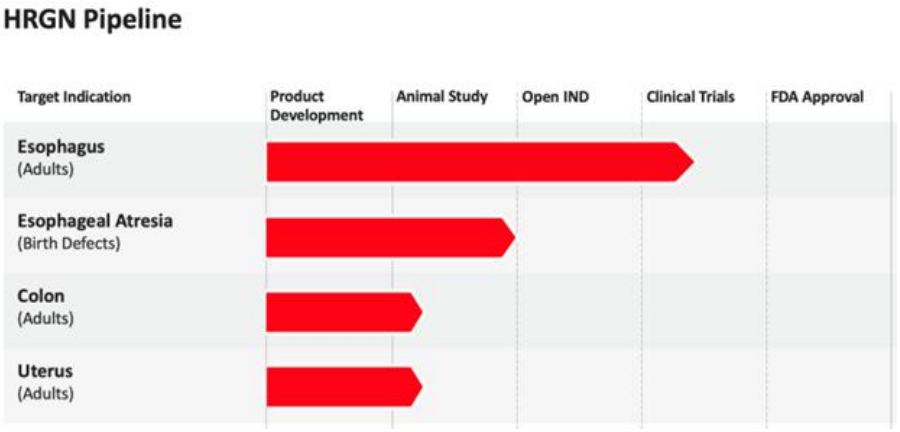
Longevity Products

In the second quarter of 2023, our subsidiary in Hong Kong, Harvard Apparatus Regenerative Technology Limited, or Longevity Products, started focusing on sales of longevity products.

Longevity Products plans to include a broad range of products focused on personal healthcare including longevity dietary supplements. The Company started selling longevity supplements through Longevity Products in the third quarter of 2023. These products are marketed to the general public and initially targeted at consumers in the Great China Region through eCommerce (online sales).

Our Pipeline

We believe our organ-regeneration technology has the potential for broad applications in the field of medicine, for the repair or replacement of diseased or damaged organs. We are initially targeting conditions of the esophagus, including traumatic injury, caustic burns, tissue damage following chemoradiation therapy and birth defects. Additional product candidates in our development pipeline are targeted at the reconstruction of the colon and uterus wound repair.



Our Strategy

Our strategy is to develop and advance our pipeline of products, beginning with our lead product for the treatment of esophageal cancer, through clinical development and commercialization. The key elements of our strategy include:

- Initiate the phase 1 clinical trial for our lead product candidate, the Cellspan^{TM} Esophageal Implant (CEI), for the treatment of severe esophageal disease. Based upon our successful initial case of esophageal regeneration and our animal models, the FDA has approved our IND application to commence a clinical trial in up to ten patients. We activated two clinical trial sites, the Mayo Clinic and the University of Michigan Medical Center, and started screening patients in the third quarter of 2023. We continue to seek our first eligible patient for enrollment in the trial.

- Advance our other pipeline products through clinical development. Based on the establishment of a favorable safety and efficacy profile that we expect to demonstrate in our phase 1 clinical trial for regeneration of the esophagus, we intend to initiate a clinical trial for the treatment of esophageal atresia, a rare birth defect where the esophagus does not fully develop, and the affected infant is unable to swallow food. As we build our safety and efficacy data, we plan to initiate clinical trials in other areas including injury, birth defects and diseases in the colon and other tubular organs that require reconstruction.

- Develop our technology for use in other life-threatening conditions that have a relatively short time to market. We believe our technology has broad applications to treat organ failure. We intend to develop products focused on life-threatening conditions where current treatments are ineffective, expensive or both. Many organ failures are orphan diseases, and we have orphan drug designations from the FDA on our product candidates for severe disease in the esophagus. We believe that developing products for such conditions will require smaller clinical trials and an overall less expensive development pathway than developing treatments for less severe conditions.

- Pursue development pathways in international markets. In addition to the U.S., we intend to pursue regulatory approval for our products in several key international markets, including China, Europe and the U.K. Many of the conditions we are targeting have significantly higher patient populations in foreign countries than in the U.S., thereby making them attractive commercial markets. We intend to engage foreign health regulatory bodies to develop clinical and regulatory strategies to gain international approvals. In addition, we have received Orphan Drug Designation from the European Medicines Agency (EMA) for the use of our CEI for esophageal atresia.

- Collaborate with leading medical and research institutions to develop our products and build awareness. We intend to continue to collaborate with thought-leading medical institutions as we continue clinical development of our products and ultimately reach commercialization. We currently have a co-development initiative with the Mayo Clinic, Connecticut Children's Medical Center, Yale University and the McGowan Institute for Regenerative Medicine at the University of Pittsburgh. We intend to build additional partnerships and collaborations with leading institutions that we believe will help to drive awareness of our products and increase the likelihood of market adoption.

The Problem

According to the American Cancer Society, every year approximately 17,000 Americans are diagnosed with esophageal cancer and approximately 15,000 of these diagnosed patients die from it. A year after being diagnosed with esophageal cancer, 50% of patients die. After five years, 80% of these patients die. According to the World Health Organization's International Agency for Research on Cancer, every year, there are more than 600,000 patients diagnosed with esophageal cancer worldwide.

A current treatment option for patients with esophageal cancer is to receive neoadjuvant therapy which can include definitive chemoradiation treatment. In many cases definitive chemoradiation treatment causes damage to the esophagus leading to severe strictures (constrictions that close the throat and prevent swallowing) or fistulas (holes in the tissue). The current treatment for the removal of the diseased part of the esophagus following chemoradiation is to surgically remove the entire esophagus in a surgical procedure called an esophagectomy. The gap left by the removal of the diseased part of the esophagus is then repaired using one of two difficult and expensive surgeries, both of which have frequent and significant complications. The first type of surgery is gastric pull-up. In this surgery, the patient's stomach is reshaped into a tube and pulled up from the abdomen into the chest to connect to the top of the esophagus. With gastric pull-up, the patient no longer has a stomach with which to digest food. In the second type of surgery, termed colonic interposition, a piece of the patient's bowel is cut out and used to bridge the gap where the diseased esophagus was removed. With colonic interposition, the patient often has insufficient intestine to digest food properly. Both surgical procedures have high rates of complications such as damage to the lungs and infections caused by leakage of stomach acids into the chest. Even with these surgical treatments, esophageal cancer is one of the deadliest forms of cancer.

In addition to cancer, there are other injuries to the esophagus such as fistulas (holes), injuries caused by the accidental ingestion of acids and alkalis, and birth defects. These are all difficult to treat surgically and often have significant long-term complications.

Hence, there is an enormous need for, and a huge market for, a better treatment for cancer, injuries, and birth defects of the esophagus.

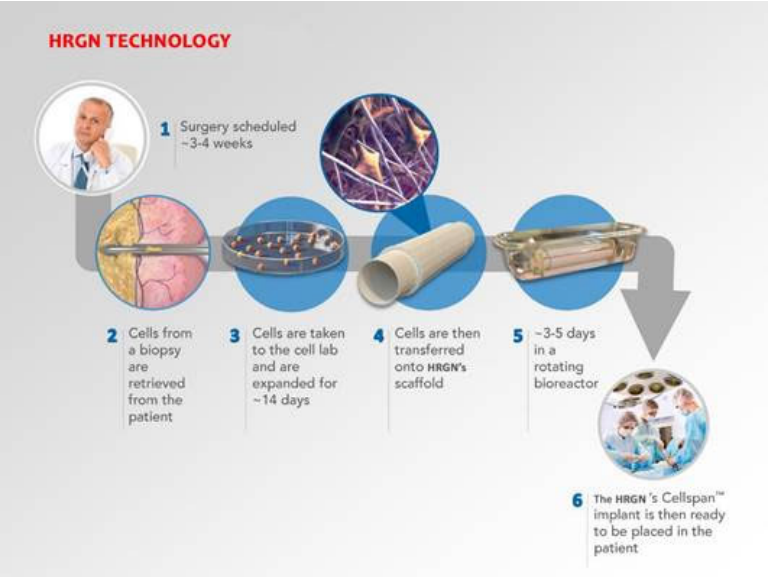
Our Solution –Organ-Regeneration Technology

Our organ-regeneration technology uses a patient's own stem cells seeded on a temporary scaffold to regrow and restore their damaged organ. We believe our technology has numerous advantages over other attempts to restore organ function because our implant is not a transplant of a human-donor or animal organ. It is also not a piece of one of the patient's other organs, and it is not an artificial implant that remains permanently in the body. Rather, our implants will allow the patient to regenerate their own organ inside their own body.

Our esophageal implant consists of a hollow, tubular scaffold consisting of a thin polyurethane fiber mesh that is formed in the shape of the damaged section of the organ. This scaffold is then placed into a customized bioreactor and seeded with the patient's own mesenchymal stem cells which are obtained a few weeks before surgery through a biopsy of adipose (fat) tissue from the patient's abdomen. The stem cells are isolated and expanded and then seeded onto the tubular scaffold for incubation and further cell expansion. During several days of incubation in our bioreactor, the stem cells attach to and grow into the outer 25% of the scaffold. The stem cell-seeded scaffold is then surgically implanted into the patient to bridge the gap created where the diseased or damaged part of the esophagus was removed.

The stem cells then stimulate the body's natural wound-healing process including stimulating new blood vessel formation, scar-tissue formation and the remodeling of that scar tissue into esophageal tissue. The scaffold guides the growth of new cells to regenerate the esophagus. After approximately one month, a complete biological tube, or conduit, has formed and after approximately three months, the tube has developed into a layered structure that contains the critical blood supply, muscles, and mucous-secreting glands to create a functioning esophagus. At this point, the implanted scaffold is removed, as it is not a permanent implant.

Our Technology Platform: How the Esophageal Implant Works



The bioreactor and scaffold are made in our clean-room facilities in Holliston, Massachusetts and the cell seeding is performed at the FDA-approved, clinical-grade human cell culture facility at the University of Texas Medical Branch.

Our manufacturing process for the bioreactors and scaffolds has been approved by the FDA for the clinical trial. Based on expected FDA inspections, additional development may be necessary for product approval.

For our scaffolds, our primary materials are medical-grade plastic resins and solvents used to liquefy the resins in our manufacturing process. These materials are readily available from a variety of suppliers and do not currently represent a large proportion of our total costs. For our automatic cell seeding device and bioreactors, we perform final assembly and testing of components that we buy from third parties like machine shops, parts distributors, molding facilities and printed circuit board manufacturers. These manufacturing operations are performed primarily at our Holliston, Massachusetts headquarters.

Advantages of the Esophageal Implant

Compared with the current standard of care procedures for esophageal cancer patients - gastric pull-up or colonic interposition, our esophageal implant offers the following major advantages:

- Patients can avoid the frequently life-threatening complications of either gastric pull up or colonic interposition surgery;
- Autologous stem cells eliminate the risk of immune system rejection;
- The procedure does not require the sacrifice of the patient's stomach or colon, so those organs remain intact and function accordingly;
- It leaves no permanent implant or artificial structure in the body. Permanent implants can lead to long-term complications, including infection, which can lead to further surgical procedures including removal;
- Patients can remain on a reasonable diet after a procedure with our esophageal implant.

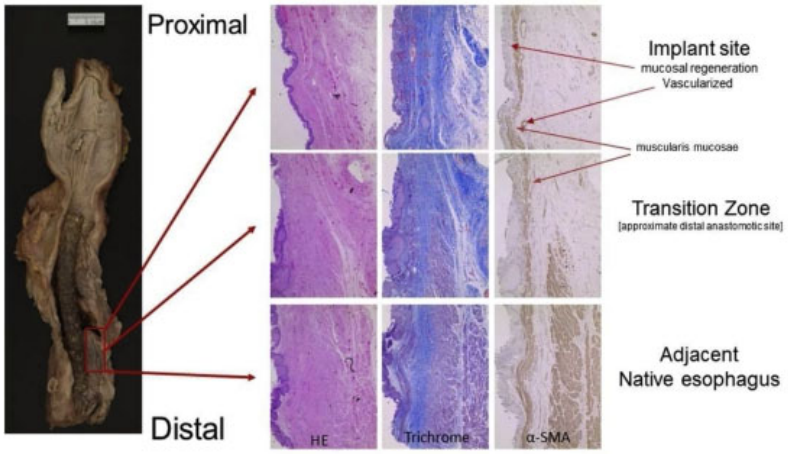
We believe that these significant medical advantages will lead to strong demand from patients and doctors for our esophageal implant. Additionally, we believe that it will receive a favorable reimbursement profile from payors and insurance companies because of the high cost and complications associated with alternative procedures.

First-In-Human Use of the Esophageal Implant and Scientific Proof of Esophageal Regeneration

On August 7, 2017, we announced the use of our esophageal implant in a patient at the Mayo Clinic via an FDA-approved single-use expanded access, or compassionate use, application. The patient was a 75-year-old male with a life-threatening cancerous mass in his chest that spanned his heart, a lung, and his esophagus. The surgery was performed by Dr. Dennis Wigle, Chair of Thoracic Surgery. In order to remove the tumor, a portion of the heart was removed and repaired with a pericardial patch, a portion of the lung was removed, a portion of the vena cava was repaired with a Gortex vascular graft, and a segment of the esophagus was removed and repaired with our CEI. The patient's surgeon informed us at that time that the surgery was successful, and the patient was discharged from the hospital 42 days after implantation. The scaffold and stent were removed on day 104 after implantation.

In February 2018, the surgeon informed us that the patient had died after living approximately eight months after surgery. The surgeon stated that the cause of death was due to a stroke, and that the stroke was unrelated to the esophageal implant. The surgeon also informed us that a preliminary autopsy had shown that the esophageal implant resulted in a regenerated esophageal tube in the patient, except for a very small (approximately 5mm) hole outside the implant zone. The small hole was believed to be caused by abrasion from the Gortex graft used to repair the vena cava. The surgeon also informed us that the esophageal regeneration in this patient was consistent with the regeneration previously observed in our pig studies.

The results were published in the Journal of Thoracic Oncology Clinical and Research Reports in August 2021. The photographs below, taken from the paper, show the explanted esophagus from this procedure. The image on the left is the actual esophagus. The results from this study, in combination with previously published results of esophageal regeneration using the CEI tissue-engineered graft [1,2] confirms that the regeneration process is reproducible in humans. In addition, the data presented confirms that epithelial regeneration occurs during the initial wave of tissue regeneration and is typically complete by 3 months post-implantation.



[1] La Francesca S, et al (2018). Long-term regeneration and remodeling of the pig esophagus after circumferential resection using a retrievable synthetic scaffold carrying autologous cells. Sci Rep.; **8**:4123.

[2] Sundaram, S, et. al. (2022). Esophageal Regeneration following Surgical Implantation of a Tissue Engineered Esophageal Implant in a Pediatric Model. NPJ Regen Med **7:1**.

The dark-brown tube in the center of the esophagus is the stent that was added to avoid narrowing of the esophagus. The stent for this patient was changed twice, once prior to our esophageal implant scaffold removal and once after the scaffold and the second stent were removed. The final stent was removed at five and a half months post-surgery. We anticipate that patients treated with our esophageal implant are likely to undergo at least one stent exchange during their recovery with the discontinuation of stents by six to nine months post-surgery. Stents are deployed and retrieved endoscopically, that is, via the mouth, and accordingly, there is no surgical incision in the chest.

The images on the righthand side are photographs taken under a microscope to show the characteristics of the newly formed tissue extending from the native tissue through a transition zone where the regeneration of the muscle layer begins and then into the center of the implant. The native tissue has multiple layers composed of different cell types, including the mucosal layer on the lumenal surface, a submucosa composed of connective tissue and smooth muscle cells and the muscular adventitia composed of smooth and striated muscle (brown staining structures in the right most actin, α-SMA). In the right most panels, the brown coloration along the left side of the images shows a continuous line of muscles running up the regenerated esophagus (arrows). These muscles are the muscularis mucosae which contract to eject mucous into the esophagus. This mucosal lining is essential to the long-term survival of the patient because it both lubricates the esophagus to allow food to be swallowed and provides a barrier to infection. This mucosal lining was seen at three months in both the human patient and in our pig models.

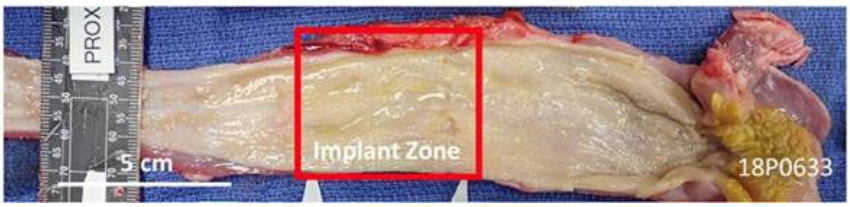
In this patient we saw the development of a tube comprised of the patient's own tissue within one month, and the development of the mucosal lining within three months. In pig models we have observed a similar regeneration process with the development of a tube within one month and the development of the mucosal lining within three months. In our clinical trial, the primary endpoint is the development of the tube of the patient's tissue within three months and one of the secondary endpoints is the development of the mucosal lining within twelve months.

Preclinical Models - Pig Studies

The pre-clinical animal studies using our esophageal implant investigated several key aspects of the product pertaining to the implant procedure, cell survival, the architecture of the regenerated tissue at multiple survival time points, the post-implantation clinical management procedures including Computed Tomography, or CT imaging to assess the growth of new tissue, esophageal stent management, endoscopy procedures, barium swallow tests and nutritional management.

Following implantation, CT imaging revealed early tissue deposition and the formation of a contiguous tissue conduit. Endoscopic evaluation at multiple time points revealed complete epithelialization of the lumenal surface by day 90. Histologic evaluation at several necropsy time points, post-implantation, demonstrated that the tissue continues to remodel over the course of a one-year survival time period, resulting in the development of esophageal structural features, including the mucosal epithelium, muscularis mucosae, lamina propria, as well as smooth muscle proliferation/migration initiating the formation of a laminated adventitia. One-year survival demonstrated restoration of oral nutrition, normal animal growth and the overall safety of this treatment regimen.

The image below is taken from a paper we published in Nature Partner Journals Regenerative Medicine in January 2022, in conjunction with our development partner, Connecticut Children's Medical Center.



This image shows an esophagus explanted from a pig 90 days after our esophageal implant was implanted. The implant zone is visually almost identical to the native tissue to the left and right of it. We note the regeneration of the interior surface of the esophagus and the regeneration of the surrounding tissue that is visible in red at the top of the red box. The red color of the surrounding tissue indicates the presence of a healthy blood supply. We note further the glossy, reflective coating on the inside of the esophagus. This is evidence of the mucosal lining which is essential to the long-term survival of the patient. This mucosal lining was seen at three months in the pigs and was also observed in the human patient. The investigators concluded that at one year it was difficult to distinguish neo-tissue versus the native tissue.

Current Phase 1 Clinical Trial

Based on both the successful in-human procedure at the Mayo Clinic and our extensive large animal research, the FDA has approved our Investigational New Drug application to commence our clinical trial. The trial will be a ten-patient phase 1 trial, in up to five hospitals in the U.S. and is designed to measure both the safety and efficacy of our product candidate in the patient population. Enrollment criteria includes any patient that requires removal of a part of the esophagus that is up to six centimeters long for any medical reason. We expect enrolled patients to include esophageal cancer patients, post-neoadjuvant chemoradiation therapy, but we may enroll patients with other esophageal conditions that require reconstruction and regeneration. We activated two clinical trial sites, the Mayo Clinic and the University of Michigan Medical Center, and started screening patients in the third quarter of 2023. We continue to seek our first eligible patient for enrollment in the trial.

The primary endpoint of the upcoming trial is the establishment of a continuous biological neoconduit, or tube, by three months post-surgery. We saw this tube at one month in the human patient and in the pigs. One of the secondary endpoints will be the development of a mucosal lining in the esophagus by twelve months post-surgery. We saw this mucosal lining by three months in the human patient and the pigs. Because we reached the primary endpoint and one of the secondary endpoints in both the human patient and the pigs, we believe that we have a high likelihood of success in this clinical trial.

Based on the FDA's approval of our clinical trial for any condition that requires removal of part of the esophagus, we believe that we are able to pursue the treatment of multiple diseases, injuries or birth defects with a single clinical trial. As a result, we believe that this clinical trial will advance the Cellspan Esophageal Implant for numerous indications with the possibility of treating esophageal damage due to cancer, Barrett's esophagus, fistulas, traumatic and potentially long-term complications from birth defects in the esophagus. Compared to developing treatments for a single underlying medical condition, we believe that addressing multiple medical conditions in a single clinical trial has the potential to significantly reduce our costs to expand the market for our products.

Preclinical Development

In January 2022, together with Connecticut Children's Medical Center, we published in Nature Partner Journals Regenerative Medicine the results of implanting pediatric-sized esophageal implants in 15 piglets. Numerous survival times were histologically analyzed to understand the tissue development and timing of the regeneration. Overall, the graft implantation procedure was deemed safe and feasible. The piglets showed regeneration of a conduit, or tube, by one month and the regeneration of a normal mucosal lining by three months. Additionally, histological evaluation demonstrated that the tissue continued to develop throughout the course of the one-year survival period. Importantly, the piglets also showed normal growth and weight gain which are considered critical in treating human babies.

This research also utilized post-surgical techniques that closely mimic the hospital care that human infants undergo to treat esophageal atresia. These techniques included non-invasive CT imaging of the regenerated tissue, parenteral feeding via a G tube which are normally used to feed human infants after surgeries in the gastro-intestinal tract as well as endoscopy using a pediatric endoscope.

Clinical Pathway

We believe that this study laid both the scientific and clinical groundwork for treating babies with birth defects in the esophagus with the Cellspan Esophageal Implant. The FDA approval for the clinical trial allows us to treat children once we have established safety in adult patients in the phase 1 clinical trial. Once we have established the safety of the implant in adults, we expect to recruit children into a clinical trial for esophageal atresia.

Orphan Drug Designation – Seven Years of Exclusivity

In November 2016, we were granted Orphan Drug Designation for our esophageal implant by the FDA to restore the structure and function of the esophagus subsequent to esophageal damage due to cancer, injury or congenital abnormalities. We also were granted Orphan Drug Designation for trachea on September 4, 2014.

The Orphan Drug Act provides incentives to manufacturers to develop and market drugs and biologics for rare diseases and conditions affecting fewer than 200,000 persons in the U.S. at the time of application for orphan drug designation, or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the U.S. for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting a new drug application, or NDA, or Biologics License Application or BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. The first developer to receive FDA marketing approval for an orphan biologic is entitled to a seven-year exclusive marketing period in the U.S. for that product as well as a waiver of the BLA user fee. The exclusivity prevents FDA approval of another application for the same product for the same indication for a period of seven years, except in limited circumstances where there is a change in formulation in the original product and the second product has been proven to be clinically superior to the first. In addition, Orphan Drug Designation provides a seven-year marketing exclusivity period against competition in the U.S. from the date of a product's approval for marketing. This exclusivity would be in addition to any exclusivity we may obtain from our patents. Additionally, orphan designation provides certain incentives, including tax credits and a waiver of the BLA fee. We also plan to apply for Orphan Drug Designation for our esophageal implant in Europe. Orphan Drug Designation in Europe would provide market exclusivity in Europe for a period of ten years from the date of the product's approval for marketing.

Our Strategy

Our strategy is to develop and advance our pipeline of products, beginning with our lead product for the treatment of esophageal cancer, through clinical development and commercialization. The key elements of our strategy include:

- **Initiate the phase 1 clinical trial for our lead esophageal implant product candidate for the treatment of severe esophageal disease.** Based upon our successful initial case of esophageal regeneration and our animal models, the FDA has approved our IND application to commence a clinical trial in up to ten patients. We activated two clinical trial sites, the Mayo Clinic and the University of Michigan Medical Center, and started screening patients in the third quarter of 2023. We continue to seek our first eligible patient for enrollment in the trial.

- **Advance our other pipeline products through clinical development.** Based on the establishment of a favorable safety and efficacy profile that we expect to demonstrate in our phase 1 clinical trial for regeneration of the esophagus, we intend to initiate a clinical trial for the treatment of esophageal atresia, a rare birth defect. As we build our safety and efficacy data, we plan to initiate clinical trials in other areas following the demonstration of efficacy in animal models, including colon resection and the prevention of intrauterine adhesions.

- **Develop our technology for use in other life-threatening conditions that have a relatively shorter time to market.** We intend to develop products focused on life-threatening conditions where current treatments are ineffective, expensive or both. Many organ failures are orphan diseases, and we have orphan drug designations from the FDA on our product candidates for severe disease in both the esophagus and the colon. We believe that developing products for such conditions will require smaller clinical trials and an overall less expensive development pathway than developing treatments for less severe conditions.

- **Pursue development pathways in international markets.** In addition to the U.S., we intend to pursue regulatory approval for our products in several key international markets, including China, Europe and the U.K. Many of the conditions we are targeting, have significantly higher patient populations in foreign countries than in the U.S., thereby making them attractive commercial markets. We intend to engage foreign health regulatory bodies to develop clinical and regulatory strategies to gain international approvals.

- **Collaborate with leading medical and research institutions to develop our products and build awareness.** We intend to continue to collaborate with thought-leading medical institutions as we continue clinical development of our products and ultimately reach commercialization. We currently have a co-development initiative with the Mayo Clinic and with the Connecticut Children's Medical Center. We intend to build additional partnerships and collaborations with leading institutions that we believe will help to drive awareness of our products and increase the likelihood of market adoption.

Our Technology

Biocompatible Scaffold Component

Our proprietary biocompatible scaffold component of our esophageal implant is constructed primarily of extremely thin polyurethane fibers. This material was chosen based on extensive testing of various materials. The scaffold is made using a manufacturing process known as electrospinning. The combination of the electrospinning process, which provides control over the desired microstructure of the scaffold fabric, with the polyurethane results in a scaffold that we believe has favorable biocompatibility characteristics.

The Patient's Cells

The cells we seed onto the scaffold are obtained from the patient's adipose tissue, or abdominal fat. This fat tissue is obtained from a standard biopsy during the weeks leading up to the implant surgery. Mesenchymal stem cells are extracted and isolated from the adipose tissue biopsy. The isolated cells are then expanded, or grown, for a short period prior to surgery in order to derive a sufficient cell population to be seeded on the scaffold. The cells are then seeded on the scaffold in our proprietary bioreactor and incubated there before the implant surgery.

Our technology is protected by thirteen issued U.S. patents (including patents on the bioreactor, the structure of the scaffold and the retrievable nature of the scaffold), two Orphan-Drug Designations from the FDA, both of which confer seven years of exclusivity in addition to protection offered by the patents, and our first-mover advantage which allows us to improve the standard of care. Potential competitors would now have to improve upon our new standard of care rather than just improve on the existing standard of care in order to get their product candidates approved by the FDA. In addition, our patent claims cover patches as well as tubular structures. We intend to develop patches for the repair of tubular organs as well as solid organs.

See the "Intellectual Property, Licenses and Related Agreements" section below for more details.

Additional Targeted Diseases

Targeted Diseases

According to the World Health Organization, or WHO, International Agency for Research on Cancer's Global Cancer Observatory database, worldwide there were over 600,000 cases of esophageal cancer in 2020. There are over one million cases of colon cancer. The following are the approximate case counts by certain geographic region pertaining to the cancers noted below:

	Case Count by Geography					
Cancer Type	**USA**	**China**	**Japan**	**Europe**	**ROW**	**Worldwide**
Esophagus Adults	18,309	324,422	26,262	52,993	182,114	604,100
Colon	101,809	306,078	96,781	325,335	318,512	1,148,515
Total	120,118	630,500	123,043	378,328	500,626	1,752,615

Sources: *Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries Hyuna Sung, PhD; Jacques Ferlay, MSc, ME; Rebecca L. Siegel, MPH; Mathieu Laversanne, MSc; Isabelle Soerjomataram, MD, MSc, PhD; Ahmedin Jemal, DMV, PhD; Freddie Bray, BSc, MSc, PhD.*

These numbers of patients do not include those with fistulas, ulcers, injuries or birth defects, all of which we believe may be treatable with our technology.

Because our product candidates are likely to save or extend lives, improve the quality of life, and save money by reducing the complications associated with current surgical repair techniques, we expect to charge more than $250,000 per product in the U.S. market.

Treating even one tenth of only those patients who are diagnosed with esophageal cancer each year could generate billions of dollars in annual revenue. We believe that the market potential for our products is significantly higher.

Esophageal Disease

Esophageal cancer is one of the deadliest types of cancer. According to the American Cancer Society, there are approximately 17,000 new diagnoses of esophageal cancer in the U.S. each year, and there are more than 15,000 deaths. Typically, a year after diagnosis with esophageal cancer, 50% of patients die and after 5 years, 80% die.

There are approximately 600,000 new diagnoses of esophageal cancer globally each year, according to the World Health Organization's International Agency for Research on Cancer.

Hence, there is a vast need for a better treatment for esophageal cancer.

Approximately 5,000 esophagectomy surgeries occur in the U.S. annually to treat esophageal cancer, and approximately 10,000 esophagectomies occur in Europe annually. We believe that approximately one half of the world's esophageal cancer cases occur in China, which would represent the largest potential patient population for our adult esophageal product candidate. We believe that our esophageal implant, if approved, has the potential to provide a major advance over the current esophagectomy procedures for addressing esophageal disease, which have high complication and morbidity rates.

We believe that our esophageal implant has the potential to provide physicians a new, simpler procedure to restore organ function while significantly reducing complication and morbidity rates compared with the current standard of care, and without creating significant quality of life issues for patients.

Pediatric Esophageal Atresia

According to the Centers for Disease Control and Prevention (CDC), each year it is estimated that approximately 4,100 children in the U.S. are born with a congenital birth defect known as esophageal atresia. Esophageal atresia is a condition where an infant is born with an esophagus that does not extend completely from the mouth to the stomach. When a long segment of the esophagus is lacking, the current standard of care is a series of surgical procedures where sutures are applied to both ends of the esophagus in an attempt to stretch them and pull them together so they can be surgically connected at a later date.

This surgical process can take several weeks, and the procedure often involves serious complications and high rates of failure. The infant usually must remain in the neonatal intensive-care unit for this time which can cost thousands of dollars per day. This process also requires at least two separate surgical interventions. Other surgical options include the use of the child's stomach or intestine that would be pulled up into the chest to allow a connection to the mouth. These methods are similar to the use of gastric pull ups and interpositioning used in adult patients and carry similar side effect and safety profiles. We are working in collaboration with the Connecticut Children's Medical Center, to advance an esophageal implant solution to address esophageal atresia that we believe will be more effective, safer, and less expensive than the current procedures.

Colon Cancer

Based on input from our Scientific Advisory Board, which includes certain well-known surgeons in the field of regenerative medicine, we are planning to research regenerating other parts of the gastro-intestinal tract such as the small intestine and colon. All these organs require replacement when they are damaged by cancer, injury, and birth defects. There are over one million patients diagnosed with colon cancer every year.

Infertility

Asherman's Syndrome is a rare, acquired gynecologic condition resulting from the buildup of scar tissue and intrauterine adhesions (IUA). IUA occur primarily after a dilation and curettage (D&C) procedure for elective termination of pregnancy, a missed or incomplete miscarriage, or to treat a retained placenta after delivery. IUA can go undetected, but in many cases can lead to altered menstrual cycles (hypomenorrhea) and can ultimately lead to infertility It is estimated that up to 30% women of reproductive age (15-49 years) in the US that undergo elective pregnancy termination will develop IUA. Based on the CDC recorded number of elective pregnancy termination of over 600,000 per year[3], the incidence of Asherman's syndrome in the US is estimated to be in excess of 100,000 women in ages 15-49. We are currently evaluating our technology to prevent IUA in an animal model of IUA with a prominent laboratory and Chief of Obstetrics and Gynecology.

[3] Data and Statistics - Reproductive Health | CDC

Our History

We were incorporated under the laws of the State of Delaware on May 3, 2012 as a wholly-owned subsidiary of Harvard Bioscience, Inc., or Harvard Bioscience, to provide a means for separating its regenerative medicine business from its other businesses. Harvard Bioscience decided to separate its regenerative medicine business into our company, a separate corporate entity, or the Separation, and it spun off its interest in our business to its stockholders in November 2013. Since the Separation we have been a separately traded public company and Harvard Bioscience has not controlled our operations. Following the Separation, we continued to innovate our bioreactors based on our physiology expertise, we developed our materials science capabilities and we investigated and developed a synthetic tracheal scaffold. By that time, we had built and staffed cell biology laboratories at our Holliston facility, to give ourselves the ability to perform and control our scientific investigation and developments internally. At that point, we began the second phase of our company's development.

In mid-2014, we increased the pace of our scientifically based internal analysis and development of our first-generation tracheal implant product candidate, the HART-Trachea . From large-animal studies conducted thereafter we found that the product candidate elicited an unfavorable inflammatory response after implantation, which required additional development and testing. These requirements extended our expectations regarding our regulatory milestones, and we announced the additional testing and extended milestone expectations in January 2015. During 2015 we isolated and tested all major variables of the organ scaffold and the cell source and protocols, examining the effects of alternatives against the then-existing product approach. Through extensive *in vitro* preclinical studies, and small-animal and large-animal studies, we made dramatic improvements, and discovered that the mechanism of action of our current approach was very different from our hypothesis regarding that of the first-generation product candidate. Our technology uses a different scaffold material and microstructure, a different source and concentration of the patient's cells and several other changes from our earlier trachea initiative. These changes resulted in a scaffold that was temporary and could be removed via the mouth in an endoscopic procedure that did not require major surgery in the chest. The temporary nature of the scaffold reduces the risk of long-term complications that can arise from permanent implants such as those from hernia meshes and breast implants.

Clinical Trials

The FDA has approved our first clinical trial.

Based on both the successful human experience at the Mayo Clinic, and our extensive large-animal research (we have performed surgeries on over 50 pigs including for both adult and pediatric diseases), the FDA has approved our clinical trial. The trial will be a 10-patient phase 1 trial that measures both the safety and efficacy of our product candidate in the patient population. This clinical trial is for any patient that requires removal of a part of the esophagus that is less than 6cm long for any reason. The primary endpoint in the trial is the establishment of a continuous biological neo-conduit, or tube, by three months. In the human patient, this tube was seen in one month. In our pig research, we have seen the formation of a conduit by one month and sometimes by 14 days. One of the secondary endpoints will be the development of a mucosal lining in the esophagus by 12 months or earlier. In the one human patient treated so far, this mucosal lining was seen at three months. In our pig research, we have seen this mucosal lining in three months.

Establishing a safety profile in our current adult clinical trial will allow us to submit an IND for using our technology to treat esophageal atresia in the pediatric population.

Our esophageal implant will not be tested for safety on healthy volunteers (the usual goal of a phase 1 trial) or for dose-response and maximum-tolerated dose (the usual goals of a phase 2 trial). Measuring safety and efficacy in the patient population is normally the goal of a phase 3 clinical trial. Hence, our approved trial is more similar to a small phase 3 clinical trial than a typical first clinical trial. We expect to add patients to this clinical trial, including in Europe and China until we have sufficient data to gain approval.

Unlike the normal drug discovery process, which assesses a drug for its ability to treat a single disease, we can pursue multiple diseases with a single clinical trial. This is because any medical condition that requires the removal of part of the esophagus can be repaired with our esophageal implant. It does not matter that the need to surgically remove part of the esophagus is caused by esophageal cancer, Barrett esophagus (damage to the lower esophagus caused by the reflux of stomach acids into the esophagus), a fistula (a hole in the esophagus), a birth defect, or a wound or injury to the esophagus. Our esophageal implant can be used to treat any of these conditions. Because of this, we believe that the available market in treating the esophagus to be far larger than that for treating esophageal cancer alone. In addition, we can access that large patient population without having to conduct a new clinical trial for each underlying medical condition. Compared to the development of new drugs, this greatly reduces our costs to expand the market size for our products.

We intend to request Fast Track status, Breakthrough Therapy designation, Regenerative Medicine Advanced Therapy, or RMAT, designation, Accelerated Approval, Priority Review and a Priority Review Voucher from the FDA. There are many benefits of such designations, including reduced costs and faster times to market. Please refer to the Regulatory Strategy section for more details.

Our first clinical trial is in the U.S. for patients with cancer, injury, or birth defects in the esophagus. However, there are far more patients with these conditions in Europe and Asia than there are in the U.S. For this reason, we intend to expand our clinical trial to include patients in Europe and Asia and to seek regulatory approval in those countries as well.

In addition to having large patient populations, for product candidates like ours, both the European Union, or E.U., and some countries in Asia allow for "conditional approval". Conditional approval is country specific but, in general, it would allow us to market our products, and obtain revenue from the sales of the respective product, after successful phase 2 clinical trial results. Conditional approval is granted subject to the regulatory authority being able to rescind the approval if something goes wrong as more patients get treated. Hence, it is possible that we could see revenue in either Asia or the E.U. before we see revenue in the U.S.

Research and Development

Our primary research and development activities are focused in three areas: materials science, cell biology and engineering. In materials science, we focus on designing and testing biocompatible organ scaffolds, testing the structural integrity and the cellularization capacities of the scaffolds. In cell biology, we focus on developing and testing isolation and expansion protocols, cell characterization and cell fate studies, investigating the effects of various cell types and concentrations, evaluating the biocompatibility of scaffolds, experimenting with different cell seeding methodologies, and developing protocols for implantation experiments. Our engineering group supports the materials science and cell biology groups across an array of their activities, i.e. designing, engineering and making our proprietary bioreactors and automatic cell seeding device. All three of our research and development groups combine to plan and execute our *in vitro* studies. A fundamental part of our research and development effort in developing our technology has been dedicated to the discovery and development of small and large-animal model studies.

In addition to our in-house engineering and scientific development team, we collaborate with leaders in the field of regenerative medicine who are performing the fundamental research and surgeries in this field to develop and test new product candidates that will advance and improve the procedures being performed. We will work with our collaborators to further enhance our product candidates to make them more efficient and easier to use by surgeons. In the U.S., our principal collaborations have been with Mayo Clinic and Connecticut Children's Medical Center. Collaboration typically involves us developing new technologies specifically to address issues these researchers and clinicians encounter, and then working together to translate our technology from pre-clinical studies to clinical trials. In certain instances, we have entered into agreements that govern the ownership of the technologies developed in connection with these collaborations.

We incurred approximately $3.1 million and $1.7 million of research and development expenses in 2023 and 2022, respectively. As we have not yet applied for or received regulatory approval to market any clinical products, no amount of these research and development costs have been passed on to our customers.

Manufacturing and Resources

The bioreactor and scaffold are made in our clean-room facilities in Holliston, Massachusetts and the cell seeding is currently performed at the FDA-approved clinical-grade human cell culture facility at the University of Texas Medical Branch.

Our manufacturing process for the bioreactors and scaffolds has been approved by the FDA for the clinical trial. Additional development is likely to be necessary for product approval.

For our scaffolds, our primary materials are medical-grade plastic resins and solvents used to liquefy the resins in our manufacturing process. These materials are readily available from a variety of suppliers and do not currently represent a large proportion of our total costs. For our automatic cell-seeding device and bioreactors, we perform final assembly and testing of components that we buy from third parties like machine shops, parts distributors, molding facilities and printed circuit board manufacturers. These manufacturing operations are performed primarily at our Holliston, Massachusetts headquarters.

Sales and Marketing

We expect that most surgeries using our esophageal implant will be performed at a relatively small number of major hospitals in the U.S., Asia and in Europe. In addition, our technology platform is initially aimed at treating the esophagus, the bronchi, and the trachea, all of which are treated by thoracic surgeons. As a result, we expect to employ only a small sales force as compared to companies selling treatments for larger patient populations.

We expect to price the product commensurate with the medical value created for the patient and the costs avoided with the use of our product. Because our products are likely to save or extend lives, improve the quality of life, and save money by reducing the complications associated with current surgical repair techniques, we expect to charge approximately $250,000 per product in the U.S.

We further expect to be paid by the hospital that buys the product from us. Finally, we expect that the hospital would seek reimbursement from government payers, private health insurers and other third-party payers for the entire transplant procedure, including the use of our products.

Intellectual Property, Licenses, and Related Agreements

We have thirteen issued U.S. patents that cover the bioreactor, the scaffold, and the surgical procedure. The patent claims cover the use of synthetic scaffolds for any use in the gastro-intestinal tract and the airways. These patents include the claim of having a removable scaffold. The patent claims cover patches as well as tubes. We intend to research the patch-based approach to treat damage to solid organs. We also have two issued patents in China, one patent issued in Japan, two patents issued in Europe, two U.S. orphan-drug designations which can provide seven years of market exclusivity in the U.S. market after market approval from the FDA and 1 EMA orphan drug designation, which can provide ten years of market exclusivity in the European market after market approval from the EMA. There are numerous other filings pending. We expect these patents to provide protection into the mid to late 2030's.

Sublicense Agreement with Harvard Bioscience

We own the right to use the brand name "Harvard Apparatus Regenerative Technology" in the medical sciences field under a license agreement with Harvard University via a sublicense from Harvard Bioscience. Harvard Bioscience's right to use the name arises from a license agreement, effective December 19, 2002, between it and the President and Fellows of Harvard University. Harvard Bioscience began at Harvard University in 1903 as Harvard Apparatus and has a license to the name Harvard Apparatus in research and industrial fields. Our right to use the name in the medical field arises from the sublicense signed when Harvard Apparatus Regenerative Technology was separated from Harvard Bioscience in 2013 (as more fully described below). Harvard Bioscience delegated its right to use the name in the medical field to us and Harvard Bioscience has no right to use the Harvard mark in the medical field. We intend to use this brand name on our products in the future. We do not have the right to use the Harvard or Harvard Apparatus marks alone but only as Harvard Apparatus Regenerative Technology. We believe we are the only licensee of the Harvard name in the medical products' field. This license is perpetual, worldwide and royalty-free. There are restrictions on our use of the name such as not using it in the color crimson and not using it in a serifed font. We currently have no affiliation with Harvard University.

Separation Agreements with Harvard Bioscience

On November 1, 2013, to effect the Separation, Harvard Bioscience distributed all of the shares of our common stock to the Harvard Bioscience stockholders, or the Distribution. Prior to the Distribution, Harvard Bioscience contributed the assets of its regenerative medicine business, and approximately $15 million in cash, to our company to fund our operations following the Distribution.

In connection with the Separation and immediately prior to the Distribution, we entered into a Separation and Distribution Agreement, Intellectual Property Matters Agreement, Product Distribution Agreement, Tax Sharing Agreement, Transition Services Agreement, and Sublicense Agreement with Harvard Bioscience to effect the Separation and Distribution and provide a framework for our relationship with Harvard Bioscience after the Separation. These agreements govern the current relationships among us and Harvard Bioscience and provided for the allocation among us and Harvard Bioscience of Harvard Bioscience's assets, liabilities, and obligations (including employee benefits and tax-related assets and liabilities) attributable to periods prior to the Separation.

Government Regulation

Our product candidates and our operations are subject to extensive regulation by the U.S. FDA and other federal and state authorities, as well as comparable authorities in foreign jurisdictions, which are discussed below. The FDA is divided into various "Centers" by product type such as the Center for Drug Evaluation and Research, or CDER, the Center for Biologics Evaluation and Research, or CBER, and the Center for Devices and Radiological Health, or CDRH. Different Centers review drug, biologic, or device applications. Our product candidates are subject to regulation as combination products, biologics and medical devices, in the United States under the Federal Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Services Act, or PHS Act, and their implementing regulations as implemented and enforced by the FDA.

CBER regulates medical devices related to licensed blood and cellular products by applying appropriate medical device laws and regulations. Specifically, CBER regulates the medical devices involved in the collection, processing, testing, manufacture and administration of licensed blood, blood components and cellular products. The medical devices regulated by CBER are intimately associated with the blood collection and processing procedures as well as the cellular therapies regulated by CBER. CBER has developed specific expertise in blood, blood products and cellular therapies and the integral association of certain medical devices with those biological products supports the regulation of those devices by CBER. CBER also regulates biologics, which includes cells and tissues, serum, vaccines, blood and blood products, and analogous substances.

After receiving FDA approval or clearance, an approved or cleared product must comply with post-market safety reporting requirements applicable to the product based on the application type under which it received marketing authorization. In the case of current good manufacturing practices, or cGMP, the applicant may take one of two approaches: (1) complying with cGMP for each constituent part, or (2) a streamlined approach specific to combination products, subject to certain limitations.

Regulatory Strategy

Domestic Regulation of our Product Candidates - FDA Approval Process

The FDA extensively regulates, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and import and export of medical products. The FDA governs the following activities that we may perform or that may be performed on our behalf, to ensure that the medical products we may in the future manufacture, promote and distribute domestically or export internationally are safe and effective for their intended uses:

- product design, preclinical and clinical development and manufacture;
- product premarket clearance and approval;
- product safety, testing, labeling and storage;
- recordkeeping procedures;
- product marketing, sales and distribution; and
- post-marketing surveillance, complaint handling and adverse event reporting, including reporting of deaths, serious injuries, malfunctions or other deviations; and
- recall of products, including repairs or remediation.

The labeling, advertising, promotion, marketing and distribution of biologics and medical devices also must be in compliance with the FDA and U.S. Federal Trade Commission, or FTC, requirements which include, among others, standards and regulations for off-label promotion, industry sponsored scientific and educational activities, promotional activities involving the internet, and direct-to-consumer advertising. The FDA and FTC have very broad enforcement authority, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing us to correct deviations from regulatory standards and enforcement actions that can include seizures, injunctions and criminal prosecution. Recently, promotional activities for FDA-regulated products of other companies have been the subject of enforcement action brought under healthcare reimbursement laws and consumer protection statutes. In addition, under the federal Lanham Act and similar state laws, competitors and others can initiate litigation relating to advertising claims. In addition, we are required to meet regulatory requirements in countries outside the U.S., which can change rapidly with relatively short notice.

The FDA has broad post-market and regulatory enforcement powers. Manufacturers of biologics and medical devices are subject to unannounced inspections by the FDA to determine compliance with applicable regulations, and these inspections may include the manufacturing facilities of some of our subcontractors. Failure by manufacturers or their suppliers to comply with applicable regulatory requirements can result in enforcement action by the FDA or other regulatory authorities. Potential FDA enforcement actions include:

- untitled letters, warning letters, fines, injunctions, consent decrees and civil penalties;
- unanticipated expenditures to address or defend such actions
- customer notifications for repair, replacement, refunds;
- recall, detention or seizure of our products;
- operating restrictions or partial suspension or total shutdown of production;
- refusing or delaying our requests for 510(k) clearance or premarket approval of new products or modified products;
- operating restrictions;
- withdrawing 510(k) clearances on PMA approvals that have already been granted;
- refusal to grant export approval for our products; or
- criminal prosecution.

In addition, other government authorities influence the success of our business, including the availability of adequate reimbursement from third party payors, including government programs such as Medicare and Medicaid. Medicare and Medicaid reimbursement policies can also influence corresponding policies of private insurers and managed care providers, which can further affect our business.

Combination Products

A combination product is the combination of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are combined or mixed and produced as a single entity; packaged together in a single package or as a unit; or a drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling, is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

To determine which FDA center or centers will review a combination product candidate submission, companies may submit a request for assignment to the FDA. Those requests may be handled formally or informally. In some cases, jurisdiction may be determined informally based on the FDA's experience with similar products. However, informal jurisdictional determinations are not binding on the FDA. Companies also may submit a formal "Request for Designation" to the FDA Office of Combination Products. The Office of Combination Products will review the request and make its jurisdictional determination within 60 days of receiving a Request for Designation.

The FDA will determine which center or centers within the FDA will review the product candidate and under what legal authority the product candidate will be reviewed. Depending on how the FDA views the product candidates that are developed, the FDA may have aspects of the product candidate reviewed by CBER, CDRH, or CDER, though one center will be designated as the center with primary jurisdiction, based on the product candidate's primary mode of action. The FDA determines the primary mode of action based on the single mode of action that provides the most important therapeutic action of the combination product candidate. This would be the mode of action expected to make the greatest contribution to the overall intended therapeutic effects of the combination product candidate. The review of such combination product candidates is often complex and time consuming, as the FDA may select the combination product candidate to be reviewed and regulated by one, or multiple FDA centers identified above, which could affect the path to regulatory clearance or approval. Furthermore, the FDA may also require submission of separate applications to multiple centers.

Once commercialized, manufacturers of combination products must generally comply with the applicable regulations governing each constituent part. For example, in January 2013, the FDA finalized 21 CFR Part 4, "Current Good Manufacturing Practice Requirements for Combination Products", which was effective July 22, 2013. Associated guidance was also issued in January 2017. Both the rule and guidance reiterate that combination product manufacturers are responsible for compliance with both biologic and device cGMPs when engaging in manufacturing both constituent parts. The guidance allows the use of an abbreviated approach as well. Manufacturers of combination products also must comply with post marketing safety reporting, or PMSR, requirements in accordance with 21 CFR Part 4.

We have been informed by the FDA that our esophageal implant is a combination biologic/device product. Biological products must satisfy the requirements of the PHS Act and the FDCA and their implementing regulations. The lead reviewing FDA Center will be the Center for Biologics Evaluation and Research or CBER. The CBER may choose to consult or collaborate with the FDA's Center for Devices and Radiological Health, or CDRH, with respect to the characteristics of the synthetic scaffold component of our product based on the CBER's determination of need for such assistance. Because the CBER is the lead, in order for our esophageal implant to be legally marketed in the U.S., the product must have a BLA approved by the FDA.

We discuss both the CBER and the CDRH regulatory paradigms below, as potential future products may implicate elements of each, largely at the CBER's discretion to involve the CDRH in the review and approval process.

The BLA Approval Process

The basic steps for obtaining FDA approval of a BLA to market a biopharmaceutical, or biologic product in the U.S. include:

- completion of preclinical laboratory tests, animal studies and formulation studies under the FDA's GLP regulations;
- submission to the FDA of an IND application, for human clinical testing, which must become effective before human clinical trials may begin and which must include Institutional Review Board, or IRB, approval at each clinical site before the trials may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with Good Clinical Practices, or GLP, to establish the safety, purity, and potency of the product for each indication;
- submission to the FDA of a BLA, which contains detailed information about the chemistry, manufacturing and controls for the product, reports of the outcomes of the clinical trials, and proposed labeling and packaging for the product;
- the FDA's acceptance of the BLA for filing;
- satisfactory review of the contents of the BLA by the FDA, including the satisfactory resolution of any questions raised during the review or by the advisory committee, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP regulations, to assure that the facilities, methods and controls are adequate to ensure the product's identity, strength, quality and purity; and
- FDA approval of the BLA.

In order to obtain approval to market a biological product in the United States, a marketing application must be submitted to the FDA that provides sufficient data establishing the safety, purity and potency of the proposed biological product for its intended indication. The application includes all relevant data available from pertinent preclinical 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 things. 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. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the biological product to the satisfaction of the FDA.

The results of product development, preclinical 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 a BLA requesting approval to market the product. The submission of a BLA is subject to the payment of user fees; a waiver of such fees may be obtained under certain limited circumstances. The FDA initially reviews all BLAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA generally completes this preliminary review within 60 calendar days. The FDA may request additional information rather than accept a BLA for filing. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. FDA may refer the BLA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The approval process is lengthy and often difficult, and the FDA may refuse to approve a BLA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. FDA reviews a BLA to determine, among other things whether the product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. Before approving a BLA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA may issue a complete response letter, which may require additional clinical or other data or impose other conditions that must be met in order to secure final approval of the BLA, or an approval letter following satisfactory completion of all aspects of the review process.

BLAs may receive either standard or priority review. Under current FDA review goals, standard review of an original BLA will be 10 months from the date that the BLA is filed. A biologic representing a significant improvement in treatment, prevention or diagnosis of disease may receive a priority review of six months. Priority review does not change the standards for approval but may expedite the approval process.

If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it will either issue "not approvable" letter or an "approvable" letter. A "not approvable" letter means that the FDA refuses to approve the application because the BLA or manufacturing facilities do not satisfy the regulatory criteria for approval. An "approvable" letter means that the FDA considers the BLA and manufacturing facilities to be favorable, but the letter will outline the deficiencies and provide the applicant with an opportunity to submit additional information or data to address the deficiencies. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. If a product receives regulatory approval, the approval may be limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase IV testing which involves clinical trials designed to further assess a drug's safety and effectiveness after BLA approval and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. Separate approval is required for each proposed indication. If we want to expand the use of an approved product, we will have to design additional clinical trials, submit the trial designs to the FDA for review and complete those trials successfully.

The Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted in 2012, made permanent the Pediatric Research Equity Act, or PREA, which requires a sponsor to conduct pediatric studies for most biologics with a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, BLAs and supplements thereto, must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before pediatric studies can begin. After April 2013, the FDA must send a non-compliance letter to any sponsor that fails to submit a required pediatric assessment within specified deadlines or fails to submit a timely request for approval of a pediatric formulation, if required.

Priority or Expedited Review Pathways for BLAs

Companies may seek fast track designation for their products. Fast track products are those that are intended for the treatment of a serious or life-threatening condition and that demonstrate the potential to address unmet medical needs for such a condition. If awarded, the fast track designation applies to the product only for the indication for which the designation was received. Fast track products are eligible for two means of potentially expediting product development and FDA review of BLAs. First, a fast track product may be approved on the basis of either a clinical endpoint or a surrogate endpoint that is reasonably likely to predict clinical benefit. Approvals of this kind may be subject to requirements for appropriate post-approval studies to validate the surrogate endpoint or otherwise confirm the effect on the clinical endpoint, and to certain other conditions. Second, if the FDA determines after review of preliminary clinical data submitted by the sponsor that a fast track product may be effective, it may begin review of portions of a BLA before the sponsor submits the complete BLA, thereby accelerating the date on which review of a portion of the BLA can begin. There can be no assurance that any of our other products will receive designation as fast track products. And even if they are designated as fast track products, we cannot assure you that our products will be reviewed or approved more expeditiously for their fast track indications than would otherwise have been the case or will be approved promptly, or at all. Furthermore, the FDA can revoke fast track status at any time.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-approval clinical trials to verify and further define the drug's clinical benefit and safety profile. There can be no assurance that any of our products will receive accelerated approval. Even if accelerated approval is granted, the FDA may withdraw such approval if the sponsor fails to conduct the required post-approval clinical trials, or if the post-approval clinical trials fail to confirm the early benefits seen during the accelerated approval process.

Fast-Track designation and accelerated approval should be distinguished from priority review although products awarded fast track status may also be eligible for priority review. Products regulated by the CBER may receive priority review if they provide significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious or life-threatening disease. Products awarded priority review are given abbreviated review goals by the agency. Under the Prescription Drug User Fee Act of 2007, the agency has agreed to the performance goal of reviewing products awarded priority review within six months, whereas products under standard review receive a ten-month target. The review process, however, is often significantly extended by FDA requests for additional information or clarification regarding information already provided in the submission. Priority review is requested at the time the BLA is submitted, and the FDA makes a decision as part of the agency's review of the application for filing. We plan to seek priority review for our trachea transplant products but cannot guarantee that the FDA will grant the designation and cannot predict if awarded, what impact, if any, it will have on the review time for approval of our product.

We intend to request Fast Track status, Breakthrough Therapy designation, Regenerative Medicine Advanced Therapy, or RMAT, designation, Accelerated Approval and Priority Review. If we are awarded any of these designations, combined with our Orphan Drug designations, discussed below, we believe that our future clinical trial designs and approval pathway may be streamlined and expedited. Although, if granted, Fast-Track designation, accelerated approval, and priority review may expedite the approval process, they do not change the standards for approval. On September 30, 2020, Congress provided a short-term extension of the rare pediatric disease Priority Review Voucher Program. According to the current statutory sunset provisions:

1) After December 11, 2020, the FDA may only award a voucher for an approved RPD product application if the sponsor has RPD designation for the drug and that designation was granted by December 11, 2020.

2) After December 11, 2022, the FDA may not award any RPD priority review vouchers.

The Creating Hope Reauthorization Act, which was received in the Senate on September 30, 2020, proposes to replace those cutoffs with "September 30, 2024" and "September 30, 2026", respectively, thus extending the authorized period for RPD designation and granting of RPD priority review vouchers from the 21st Century Cures Act by four years. We cannot be certain that this extension will be granted.

Clinical Trials

BLAs generally require clinical data in order for FDA review and approval. Clinical trials are subject to extensive monitoring, recordkeeping and reporting requirements. Clinical trials must be conducted under the oversight of an IRB for the relevant clinical trial sites and must comply with FDA regulations, including but not limited to those relating to GCP. Adverse events must be reported and investigated timely. To conduct a clinical trial, a company is also required to obtain the patients' informed consent in form and substance that complies with both FDA requirements and state and federal privacy and human subject protection regulations. The sponsor, the FDA or the IRB could suspend a clinical trial at any time for various reasons, including a belief that the risks to trial subjects outweigh the anticipated benefits. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each site at which the trial is conducted must approve the protocol and any amendments. Foreign studies performed under an IND must meet the same requirements that apply to U.S. studies. The FDA will accept a foreign clinical trial not conducted under an IND only if the trial is well-designed, well-conducted, performed by qualified investigators in accordance with international principles for GCP, and conforms to the ethical principles contained in the Declaration of Helsinki, or with the laws and regulations of the country in which the research was conducted, whichever provides greater protection of the human subjects. The FDA, however, has substantial discretion in deciding whether to accept data from foreign non-IND clinical trials.

Clinical trials involving biopharmaceutical products are typically conducted in three sequential phases. The phases may overlap or be combined. A fourth, or post-approval, phase may include additional clinical trials. These phases are described generally below. Briefly, the phases of clinical development generally include the following:

- *Phase I.* Phase I clinical trials involve the initial introduction of the medicine into human subjects to determine the adverse effects associated with increasing doses. Such Phase I studies frequently are highly abbreviated or combined with Phase II studies (as outlined below).

- *Phase II.* Phase II clinical trials usually involve studies in a limited patient population to evaluate the efficacy of the product for specific, targeted indications to identify possible adverse effects and safety risks.

- *Phase III.* If the biologic is found to be potentially effective and to have an acceptable safety profile in Phase II (or sometimes Phase I) trials, the clinical trial program will be expanded to further demonstrate clinical efficacy, optimal dosage and safety within an expanded patient population at geographically dispersed clinical trial sites. As noted, the exact number of subjects needed, the duration of clinical follow-up, and the endpoints by which safety and efficacy are demonstrated are based on the condition being treated.

- *Post-Approval (Phase IV).* Post-approval clinical trials are required of or agreed to by a sponsor as a condition of, or subsequent to marketing approval. Further, if the FDA becomes aware of new safety information about an approved product, it is authorized to require post approval trials of the biological product. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase IV clinical trial requirement. These clinical trials are often referred to as Phase III/IV post approval clinical trials. Failure to promptly conduct Phase IV clinical trials could result in withdrawal of approval for products approved under accelerated approval regulations.

Medical devices, however, typically rely on one or a few pivotal studies rather than Phase I, II, and III clinical trials.

During the development of a new medical product, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND or IDE, at the end of Phase II, and before a BLA or PMA is submitted. Meetings at other times may be requested. 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 FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase II meeting to discuss their Phase II clinical results and present their plans for the pivotal Phase III clinical trial that they believe will support approval of the new biologic. Similarly, sponsors typically use the end of feasibility studies to do the same for planning for their pivotal trial or trials for a medical device.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of a biologic and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. For biologics, the manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final 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. Before approving a BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in full compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PHSA in particular emphasizes the importance of manufacturing control for products like biologics whose attributes cannot be precisely defined.

Based on the FDA's approval of our clinical trial for any condition that requires removal of part of the esophagus, we believe that we are able to pursue the treatment of multiple diseases, injuries or birth defects with a single clinical trial. As a result, we believe that this clinical trial will advance our esophageal implant for numerous indications including to treat esophageal cancer, Barrett esophagus, fistulas, traumatic injury to the esophagus and birth defects in the esophagus. Compared to developing treatments for a single underlying medical condition, we believe that addressing multiple medical conditions in a single clinical trial has the potential to significantly reduce our costs to expand the market for our products. Based on discussions with the FDA, we also expect clinical trials for our esophageal implant product candidates to be conducted in two sequential phases:

- An initial trial that combines both phase 1 and phase 2 into a single trial. This trial has already been approved by the FDA.
- If successful, the initial trial would be followed by a phase 2 Registration, or Pivotal Trial, to test the product candidate's safety and efficacy in a larger patient population. We believe that the nature of the our esophageal implant and the sizes of their targeted patient populations would lead to a small number of patients in this trial, relative to most biotechnology clinical trials.

As with any clinical trial, clinical testing of our esophageal implant may not be completed successfully within any specified time period, if at all. The FDA closely monitors the progress of each phase of clinical trials that are conducted under an IND and may, at its discretion, reevaluate, alter, suspend, or terminate the testing based upon the data accumulated to that point and the FDA's assessment of the risk/benefit ratio to the patient. The FDA or the sponsor may suspend or terminate clinical trials at any time for various reasons, including a finding that the subjects or patients are being exposed to an unacceptable health risk. The FDA can also request that additional pre-clinical studies or clinical trials be conducted as a condition to product approval.

We will submit a BLA once we have sufficient data from the clinical trials to assess the safety and efficacy of our esophageal implant. We estimate that this process may span a period of three to six years, or longer, considering the uncertainty of a successful clinical trial. We anticipate approvals in countries outside of the United States may be shorter, however, we can give no assurance of such approvals.

Post-Approval Requirements

After BLA approval is obtained, companies are required to comply with a number of post-approval requirements relating to manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, distribution and recordkeeping. For example, as a condition of approval of a BLA, the FDA may require post-approval testing and surveillance to monitor the product's safety or efficacy. In addition, holders of an approved BLA are required to keep extensive records, to report certain adverse reactions and production deviations and problems to the FDA, to provide updated safety and efficacy information and to comply with requirements concerning advertising and promotional labeling for their products. If we fail to comply with the regulatory requirements of the FDA and other applicable U.S. and foreign regulatory authorities, or previously unknown problems with any approved commercial products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions or other setbacks. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

Specifically, our products could be subject to voluntary recall if we or the FDA determine, for any reason, that our products pose a risk of injury or are otherwise defective. Moreover, the FDA can order a mandatory recall if there is a reasonable probability that our device would cause serious adverse health consequences or death. In addition, the FDA could suspend the marketing of or withdraw a previously approved product from the market upon receipt of newly discovered information regarding the drug's safety or effectiveness.

Orphan Drug Designation

In November 2016, we were granted Orphan Drug Designation for our esophageal implant by the FDA to restore the structure and function of the esophagus subsequent to esophageal damage due to cancer, injury or congenital abnormalities. We also were granted Orphan Drug Designation for trachea on September 4, 2014.

The Orphan Drug Act provides incentives to manufacturers to develop and market drugs and biologics for rare diseases and conditions affecting fewer than 200,000 persons in the U.S. at the time of application for orphan drug designation, or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the U.S. for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting a new drug application, or NDA, or BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. The first developer to receive FDA marketing approval for an orphan biologic is entitled to a seven year exclusive marketing period in the U.S. for that product as well as a waiver of the BLA user fee. The exclusivity prevents FDA approval of another application for the same product for the same indication for a period of seven years, except in limited circumstances where there is a change in formulation in the original product and the second product has been proven to be clinically superior to the first. In addition, Orphan Drug Designation provides a seven-year marketing exclusivity period against competition in the U.S. from the date of a product's approval for marketing. This exclusivity would be in addition to any exclusivity we may obtain from our patents. Additionally, orphan designation provides certain incentives, including tax credits and a waiver of the Biologics License Application, or BLA, fee. We also plan to apply for Orphan Drug Designation for our esophageal implant in Europe. Orphan Drug Designation in Europe would provide market exclusivity in Europe for a period of ten years from the date of the product's approval for marketing.

International

We plan to seek required regulatory approvals and comply with extensive regulations governing product safety, quality, manufacturing and reimbursement processes in order to market our products in other major foreign markets.

In addition to having large patient populations, both the E.U. and some countries in Asia allow for "conditional approval" for product candidates like ours. Conditional approval is country specific but, in general, it would allow us to market our products, and obtain revenue from the sales of them, after successful phase 2 results. Conditional approval is granted subject to the regulatory authority being able to rescind the approval if something goes wrong in as more patients get treated. Hence, it is possible that we could see revenue in either Asia or the E.U. before we see revenue in the U.S.

The regulation of our products in the Asian and European markets, and in other foreign markets varies significantly from one jurisdiction to another. The classification of the particular products and related approval or CE marking procedures can involve additional product testing and additional administrative review periods. The time required to obtain these foreign approvals or to CE mark our products may be longer or shorter than that required in the U.S., and requirements for approval may differ from the FDA requirements. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Legislation similar to the Orphan Drug Act has been enacted in other jurisdictions, including the E.U. The orphan legislation in the E.U. is available for therapies addressing conditions that affect five or fewer out of 10,000 persons. The marketing exclusivity period is for ten years, although that period can be reduced to six years if, at the end of the fifth year, available evidence establishes that the product is sufficiently profitable not to justify maintenance of market exclusivity. We intend to apply for orphan drug-designation for our esophageal implant in Europe.

We have also formed a subsidiary in Hong Kong, Harvard Apparatus Regenerative Technology Limited, as we continue to assess the market and regulatory approval pathway in China as to our product candidates. We have other subsidiaries in the U.K. and Germany. Any development and capital raising efforts in China may include a joint venture in relation to our Hong Kong subsidiary, and would also involve a number of commercial variables, including rights and obligations pertaining to licensing, development and financing, among others. Our failure to receive or obtain such clearances or approvals on a timely basis or at all, whether that be in the U.S., China or otherwise, would have an adverse effect on our results of operations.

Employees and Human Capital Resources

As of December 31, 2023, our consolidated business employed 18 individuals. Our employees are located in the U.S. and Asia and the laws regarding employee relationships are different by jurisdiction. None of our employees are unionized. In general, we consider our relations with our employees to be good. Our employees are highly skilled, and many hold advanced degrees. Our future performance depends significantly upon the continued service of our key scientific, technical and senior management personnel and our continued ability to attract and retain highly skilled employees. We have taken proactive steps throughout the COVID-19 pandemic to protect the health and safety of our employees. We expect to continue to implement these measures until we determine that the COVID-19 pandemic is adequately contained for purposes of our business. We may take further actions, in compliance with all appropriate government regulations, that we determine to be in the best interest of our employees.

Competition

We are not aware of any companies whose products are directly competitive with our cell-seeded biocompatible synthetic-scaffold system. However, in our key markets we may in the future compete with multiple pharmaceutical, biotechnology, and medical device companies, many of which have substantially greater financial, technological, research and development, marketing and personnel resources than we do. In addition, there are many academic and clinical centers that are developing regenerative technologies that may one day become competitors of ours.

We expect that other products will compete with our products and potential products based on efficacy, safety, cost, and intellectual property positions. While we believe that these will be the primary competitive factors, other factors include, in certain instances, obtaining marketing exclusivity under the Orphan Drug Act, availability of supply, manufacturing, marketing and sales expertise and capability, and reimbursement coverage.

Information about our Executive Officers

The following table shows information about our executive officers as of March 18, 2024:

Name	Age	Position(s)
Junli (Jerry) He	49	Chief Executive Officer
Hong Yu	51	President
Dr. William Fodor	65	Chief Scientific Officer
Joseph Damasio, Jr.	49	Chief Financial Officer

Junli (Jerry) He – Chairman and Chief Executive Officer

Mr. He was appointed as our Chairman and Chief Executive Officer (CEO) on March 1, 2023. He has served as a member of our Board of Directors since September 1, 2021. Mr. He serves as the Executive Vice Chairman of Bright Scholar Holdings and has been in that position since January 2019. Prior to the promotion, Mr. He had served as the CEO of Bright Scholar. Prior to joining Bright Scholar, Mr. He was a Managing Director at Tstone Corp, and served as Chief Financial Officer, CEO and a director of Noah Education Holdings Ltd., a former NYSE listed private education services provider in China. Mr. He was a portfolio manager at Morgan Stanley Global Wealth Management from June 2008 to June 2009 and was employed by Bear Stearns from November 2006 to May 2008. Mr. He obtained a bachelor’s degree in science from Peking University and an M.B.A. with Honors from the University of Chicago, Booth School of Business. Mr. He is also a Certified Financial Analyst (CFA) charter holder.

Hong Yu, BS, MS, CFA – President

Mr. Yu has served as our President since May 31, 2018 and has raised over $20 million in capital for Harvard Apparatus Regenerative Technology. Mr. Yu is a seasoned executive with extensive experience in fundraising, strategic analytics, wealth management, and investment research. Prior to Harvard Apparatus Regenerative Technology, Mr. Yu was a Senior Vice President at Bank of America, where he was employed for nearly 20 years. During his career, Mr. Yu has developed an expertise in matching emerging companies with cross-border investors. Mr. Yu holds a B.S. degree from Peking University (Beijing, China), and a M.S. degree from University of Illinois (Chicago, IL). Mr. Yu is a Chartered Financial Analyst.

Dr. William Fodor – Chief Scientific Officer

Dr. William Fodor has served as our Chief Scientific Officer since July 2017. On July 2, 2018, Dr. Fodor became an employee of Harvard Apparatus Regenerative Technology after serving as a consultant to the Company. Dr. Fodor was a founding scientist at Alexion Pharmaceuticals, where he served as an executive management team member and Senior Director of the Cell/Tissue Engineering, Transgenic Animal and Transplant Programs. He has also served as an Associate Professor at the University of Connecticut Department of Molecular Cell Biology and the Center for Regenerative Biology, extending research areas into stem cells and cell engineering. Dr. Fodor was Senior Director of Product Development at ViaCell Inc., leading programs in hematopoietic stem cell process development and manufacturing, mesenchymal stem cell basic research and manufacturing for cardiac repair and pancreatic stem cell research. He was a consultant for the biotechnology industry, serving clients in stem cell research, gene therapy, stem cell manufacturing and stem cell genome engineering. Dr. Fodor has expertise in programs targeting transplant immunology, hematopoiesis, cardiac repair, stem cell potency, gene therapy for liver diseases, tissue engineering, design and oversight of pre-clinical non-Good Laboratory Practices (GLP) and GLP animal models and IND Applications (Pre-clinical and Chemistry, Manufacturing and Control (CMC) Modules). Dr. Fodor earned a PhD. In genetics from Ohio State University. He completed post-doctoral work at Yale University School of Medicine in the department of immunobiology, investigating the regulation of Major histocompatibility complex (MHC) class I and MHC class II genes in the histocompatibility complex.

Joseph Damasio, Jr. – Chief Financial Officer

Mr. Damasio has served as our Chief Financial Officer since August 8, 2022. He has over 20 years of finance and accounting experience. Prior to joining our company, he was Vice President of Finance at Inhibikase Therapeutics, a publicly-traded clinical stage biopharmaceutical company, since October 2021. Before joining Inhibikase, Mr. Damasio was Controller at Cue Biopharma from June 2020 to October 2021, Controller at XL Fleet from February 2019 to June 2020, and Chief Financial Officer at Pressure BioSciences, Inc. from April 2017 to February 2019. Mr. Damasio earned a bachelor's degree in accounting, with honors, from the University of Massachusetts. He holds an MBA and MSF from Boston College and is a Certified Public Accountant in Massachusetts.

Available Information and Website

Our website address is *www.hregen.com*. Our Annual Reports on Form 10-K, our Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and exhibits and amendments to those reports filed or furnished with the Securities and Exchange Commission, or SEC, pursuant to Section 13(a) of the Exchange Act are available for review on our website and the SEC website at www.sec.gov. Any such materials that we file with, or furnish to, the SEC in the future will be available on our website as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information on our website is not incorporated by reference into this Annual Report on Form 10-K.

Item 1A. ***Risk Factors.***

Summary of Risk Factors

Below is a summary of the principal factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading "Risk Factors" and should be carefully considered, together with other information in this Annual Report on Form 10-K and our other filings with the SEC before making an investment decision regarding our common stock.

- Our audited financial statements for the year ended December 31, 2023 contain a going concern qualification. Our financial status creates doubt whether we will continue as a going concern. We will need additional funds in the near future and our operations will be adversely affected if we are unable to obtain needed funding.
- We have generated an insignificant amount of revenue from commercial operations to date and have an accumulated deficit. We anticipate that we will incur losses for the foreseeable future. We may never achieve or sustain profitability.
- The COVID-19 pandemic could continue to adversely impact our business, including clinical trials.
- Our product candidates are in an early stage of development. If we are unable to develop or market any of our product candidates, our financial condition will be negatively affected, and we may have to curtail or cease our operations.
- Our product candidates will subject us to liability exposure.
- The results of our clinical trials or pre-clinical development efforts may not support our product candidates claims or may result in the discovery of adverse side effects.
- If we fail to obtain, or experience significant delays in obtaining, regulatory approvals in the U.S., China or the E.U. for our product candidates, including those for the esophagus and airways, or are unable to maintain such clearances or approvals for our product candidates, our ability to commercially distribute and market these products would be adversely impacted.
- Even if our product candidates are cleared or approved by regulatory authorities, if we or our suppliers fail to comply with ongoing FDA or other foreign regulatory authority requirements, or if we experience unanticipated problems with our product candidates, these product candidates could be subject to restrictions or withdrawal from the market.
- General market conditions, including the effects of Russia's invasion of Ukraine and attendant economic sanctions, high inflation, and rising interest rates as well as the effects of laws and regulations on foreign investment in the United States under the jurisdiction of the Committee on Foreign Investment in the United States (CFIUS), and other agencies and related regulations, including the Foreign Investment Risk Review Modernization Act (FIRRMA), adopted in August 2018, may make it difficult for us to seek financing from the capital markets.
- Our principal stockholders hold a significant percentage of our voting power and will be able to exert significant control over us.
- We do not intend to pay cash dividends on our common stock.

Risk Factors

The following factors should be reviewed carefully, in conjunction with the other information contained in this Annual Report on Form 10-K. As previously discussed, our actual results could differ materially from our forward-looking statements. Our business faces a variety of risks. We describe below what we believe are currently the material risks and uncertainties we face, but they are not the only risks and uncertainties we face. Additional risks and uncertainties of which we are unaware, or that we currently believe are not material, may also become important factors that adversely affect our business. In addition, past financial performance may not be a reliable indicator of future performance and historical trends should not be used to anticipate results or trends in future periods. If any of the following risks and uncertainties develops into actual events, these events could have a material adverse effect on our business, financial condition or results of operations. In such case, the trading price of our common stock could decline, and you may lose all or part of your investment in our securities. The risk factors generally have been separated into three groups: (i) risks relating to our business, (ii) risks relating to the Separation and (iii) risks relating to our common stock. These risk factors should be read in conjunction with the other information in this Annual Report on Form 10-K.

Risks Relating to Our Financial Position, Need for Capital and Operating Risks

Our audited financial statements for the year ended December 31, 2023 contain a going concern qualification. Our financial status creates doubt whether we will continue as a going concern. We will need additional funds in the near future and our operations will be adversely affected if we are unable to obtain needed funding.

We ended the year 2023 with approximately $0.4 million of operating cash on-hand and received debt financing of $0.5 million in gross proceeds subsequent to December 31, 2023 and will need to raise additional capital in the first quarter and beyond to fund operations. If we do not raise additional capital from outside sources during the first quarter of 2024, we may be forced to further curtail or cease our operations. Based on these circumstances, our ability to continue as a going concern is at risk and our independent registered public accounting firm included a "going concern" explanatory paragraph as to our ability to continue as a going concern in their audit report dated March 28, 2024, included in this Form 10-K. Our cash requirements and cash resources will vary significantly depending upon the timing, and the financial and other resources that will be required to complete ongoing development and pre-clinical and clinical testing of our product candidates, regulatory efforts and collaborative arrangements necessary for our product candidates that are currently under development. In addition to development and other costs, we expect to incur capital expenditures from time to time. These capital expenditures will be influenced by our regulatory compliance efforts, our success, if any, at developing collaborative arrangements with strategic partners, our needs for additional facilities and capital equipment and the growth, if any, of our business in general. We will require additional funding to continue our anticipated operations and support our capital and operating needs. We are currently seeking and will continue to seek financings from other existing and/or new investors to raise necessary funds through a combination of public or private equity offerings. We may also pursue debt financings, other financing mechanisms, strategic collaborations and licensing arrangements. We may not be able to obtain additional financing on terms favorable to us, if at all. In addition, general market conditions, including the effects of Russia's invasion of Ukraine and attendant economic sanctions, high inflation, rising interest rates and the COVID-19 pandemic on financial markets, as well as the effects of laws and regulations on foreign investment in the United States under the jurisdiction of the Committee on Foreign Investment in the United States (CFIUS), and other agencies and related regulations, including the Foreign Investment Risk Review Modernization Act (FIRRMA), adopted in August 2018, may make it difficult for us to seek financing from the capital markets.

Any additional equity financings could result in significant dilution to our stockholders and possible restrictions on subsequent financings. Debt financing, if available, could result in agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring additional debt, making capital expenditures or paying dividends. Other financing mechanisms may involve selling intellectual property rights, payment of royalties or participation in our revenue or cash flow. In addition, in order to raise additional funds through strategic collaborations or licensing arrangements, we may be required to relinquish certain rights to some or all of our technologies or product candidates. If we cannot raise funds or engage strategic partners on acceptable terms when needed, we may not be able to continue our research and development activities, develop or enhance our product candidates, take advantage of future opportunities, grow our business, respond to competitive pressures or unanticipated requirements, or at worst may be forced to curtail or cease our operations.

We have generated insignificant revenue to date and have an accumulated deficit. We anticipate that we will incur losses for the foreseeable future. We may never achieve or sustain profitability.

We have generated insignificant revenues to date, and we have generated no revenues from sales of any clinical product candidates, and, as of December 31, 2023, we had an accumulated deficit of approximately $92.0 million. We expect to continue to experience losses in the foreseeable future due to our limited anticipated revenues and significant anticipated expenses. We do not anticipate that we will achieve meaningful revenues for the foreseeable future. In addition, we expect that we will continue to incur significant operating expenses as we continue to focus on additional research and development, preclinical testing, clinical testing and regulatory review and/or approvals of our product candidates and technologies. As a result, we cannot predict when, if ever, we might achieve profitability and cannot be certain that we will be able to sustain profitability, if achieved.

Our product candidates are in an early stage of development. If we are unable to develop or market any of our product candidates, our financial condition will be negatively affected, and we may have to curtail or cease our operations.

We are in the early stage of product development. Investors must evaluate us in light of the uncertainties and complexities affecting an early-stage biotechnology company. Our product candidates require additional research and development, preclinical testing, clinical testing and regulatory review and/or approvals or clearances before marketing. In addition, we may not succeed in developing new products as an alternative to our existing portfolio of product candidates. If we fail to successfully develop and commercialize our product candidates, including our esophageal or airway product candidates, our financial condition may be negatively affected, and we may have to curtail or cease our operations.

We have a limited operating history and it is difficult to predict our future growth and operating results.

We have a limited operating history and limited operations and assets. Accordingly, investors should consider our prospects in light of the costs, uncertainties, delays and difficulties encountered by companies in the early stage of development, particularly companies in new and evolving markets, such as bioengineered organ implants, and regenerative medicine. These risks include, but are not limited to, unforeseen capital requirements, delays in obtaining regulatory approvals, failure to gain market acceptance and competition from foreseen and unforeseen sources. As such, our development timelines have been and may continue to be subject to delay that could negatively affect our cash flow and our ability to develop or bring product candidates to market, if at all. Our estimates of patient population are based on published data and analysis of external databases by third parties and are subject to uncertainty and possible future revision as they often require inference or extrapolations from one country to another or one patient condition to another. The effect of any or all of the foregoing could cause a material adverse effect on our business, financial condition or results of operations.

If we fail to retain key personnel and/or attract satisfactory replacements, we may not be able to compete effectively, which would have an adverse effect on our operations.

Our success is highly dependent on the continued services of key management, technical and scientific personnel and collaborators. Our management and other employees may voluntarily terminate their employment at any time upon short notice. The loss of the services of any member of our senior management team, including our Chief Executive Officer Jerry He, our President Hong Yu, our Chief Scientific Officer Dr. William Fodor, and our Chief Financial Officer Joseph Damasio, and our other key scientific, technical and management personnel, may significantly delay or prevent the achievement of product development and other business objectives. We can give no assurance that we could find satisfactory replacements for our current and future key scientific and management employees, including recently terminated executives, on terms that would not be unduly expensive or burdensome to us.

If our collaborators do not devote sufficient time and resources to successfully carry out their duties or meet expected deadlines, we may not be able to advance our product candidates in a timely manner or at all.

We are currently collaborating with multiple academic researchers and clinicians at a variety of research and clinical institutions. Our success depends in part on the performance of our collaborators. Some collaborators may not be successful in their research and clinical trials or may not perform their obligations in a timely fashion or in a manner satisfactory to us. Typically, we have limited ability to control the amount of resources or time our collaborators may devote to our programs or potential product candidates that may be developed in collaboration with us. Our collaborators frequently depend on outside sources of funding to conduct or complete research and development, such as grants or other awards. In addition, our academic collaborators may depend on graduate students, medical students, or research assistants to conduct certain work, and such individuals may not be fully trained or experienced in certain areas, or they may elect to discontinue their participation in a particular research program, creating an inability to complete ongoing research in a timely and efficient manner. As a result of these uncertainties, we are unable to control the precise timing and execution of any experiments that may be conducted.

Although we have co-development collaboration arrangements with Mayo Clinic and Connecticut Children's Medical Center, we do not have formal agreements in place with other collaborators, and most of our collaborators retain the ability to pursue other research, product development or commercial opportunities that may be directly competitive with our programs. If any of our collaborators elect to prioritize or pursue other programs in lieu of ours, we may not be able to advance product development programs in an efficient or effective manner, if at all. If a collaborator is pursuing a competitive program and encounters unexpected financial or capability limitations, they may be motivated to reduce the priority placed on our programs or delay certain activities related to our programs. Any of these developments could harm or slow our product and technology development efforts.

Public perception of ethical and social issues surrounding the use of cell technology may limit or discourage the use of our technologies, which may reduce the demand for our products and technologies and reduce our revenues.

Our success will depend in part upon our and our collaborators' ability to develop therapeutic approaches incorporating, or discovered through, the use of cells. If bioengineered organ implant technology is perceived negatively by the public for social, ethical, medical or other reasons, governmental authorities in the U.S. and other countries may call for prohibition of, or limits on, cell-based technologies and other approaches to bioengineering and tissue engineering. Although our product candidates have not, to date, used the more controversial stem cells derived from human embryos or fetuses in the human transplant surgeries using our product candidates, claims that human-derived stem cell technologies are ineffective or unethical may influence public attitudes. The subject of cell and stem cell technologies in general has at times received negative publicity and aroused public debate in the U.S. and some other countries. Ethical and other concerns about such cells could materially harm the market acceptance of our product candidates.

Our products will subject us to liability exposure.

We face an inherent risk of product liability claims, especially with respect to our products that will be used within the human body, including the scaffolds we manufacture. Product liability coverage is expensive and sometimes difficult to obtain, if it can be obtained at all. We may not be able to obtain or maintain insurance at a reasonable cost. We have and in the future may be subject to claims for liabilities for unsuccessful outcomes of surgeries involving our products, which may include claims relating to patient suffering and death. We may also be subject to claims for liabilities relating to patients that suffer serious complications or death during or following implantations involving our products, including the patients who had surgeries utilizing our first-generation scaffold device or our bioreactor technology or our esophageal implant, or patients that may have surgeries utilizing any of our products in the future. On April 27, 2022, we and Harvard Bioscience executed a settlement, relating to an ongoing wrongful death lawsuit, which resolved all claims relating to the litigation. The settlement resulted in the dismissal with prejudice of the wrongful death claim, and neither we nor Harvard Bioscience admitted any fault or liability in connection with the claim. The settlement also resolved any and all claims by and between the parties and our products liability insurance carriers, which resulted in the dismissal with prejudice of all claims asserted by or against those carriers, us and Harvard Bioscience. Our current product liability coverage is $10 million per occurrence and in the aggregate. We will need to increase our insurance coverage if and when we begin commercializing any of our products. There can be no assurance that existing insurance coverage will extend to other products in the future. Any product liability insurance coverage may not be sufficient to satisfy all liabilities resulting from product liability claims. Furthermore, insurance carriers may deny that coverage exists after a claim is made. A successful claim may prevent us from obtaining adequate product liability insurance in the future on commercially desirable items, if at all. If claims against us substantially exceed our coverage, then our business could be adversely impacted. Regardless of whether we are ultimately successful in any product liability litigation, such litigation could consume substantial amounts of our financial and managerial resources and could result in, among others:

- significant awards or judgments against us;
- substantial litigation costs;
- injury to our reputation and the reputation of our products;
- withdrawal of clinical trial participants; and
- adverse regulatory action.

Any of these results would substantially harm our business.

If restrictions on reimbursements or other conditions imposed by payers limit our customers' actual or potential financial returns on our products, our customers may not purchase our products or may reduce their purchases.

Our customers' willingness to use our products will depend in part on the extent to which coverage for these products is available from government payers, private health insurers and other third-party payers. These payers are increasingly challenging the price of medical products and services. Significant uncertainty exists as to the reimbursement status of newly approved treatments and products in the fields of biotechnology and regenerative medicine, and coverage and adequate payments may not be available for these treatments and products. In addition, third-party payers may require additional clinical trial data to establish or continue reimbursement coverage. These clinical trials, if required, could take years to complete and could be expensive. There can be no assurance that the payers will agree to continue reimbursement or provide additional coverage based upon these clinical trials. Failure to obtain adequate reimbursement would result in reduced sales of our products, which could have a material adverse effect on our business, financial condition and results of operations.

We depend upon single-source suppliers for the hardware used for our proprietary automatic cell seeder, bioreactor control and acquisition system. The loss of a single source supplier, or future single-source suppliers we may rely on, or their failure to provide us with an adequate supply of their products or services on a timely basis, could adversely affect our business.

We currently have single-source suppliers for certain components that we use for our proprietary automatic cell seeder, bioreactor control and acquisition systems as well as materials used in scaffolds. We may also rely on other single-source suppliers for critical components of our products in the future. If we were unable to acquire hardware or other products or services from applicable single-source suppliers, we could experience a delay in developing and manufacturing our products, which could have a material adverse effect on our business, financial condition and results of operations.

We use and generate hazardous materials in our business and must comply with environmental laws and regulations, which can be expensive.

Our research, development and manufacturing involve the controlled use of hazardous chemicals, and we may incur significant costs as a result of the need to comply with numerous laws and regulations. For example, certain volatile organic laboratory chemicals we use, such as fluorinated hydrocarbons, must be disposed of as hazardous waste. We are subject to laws and regulations enforced by the FDA, foreign health authorities and other regulatory requirements, including the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other current and potential federal, state, local and foreign laws and regulations governing the use, manufacturing, storage, handling and disposal of our products, materials used to develop and manufacture our products, and resulting waste products. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, our operations could be interrupted. Further, we could be held liable for any damages that result and any such liability could exceed our resources.

Our products are novel and will require market acceptance.

Even if we receive regulatory approvals for the commercial use of our product candidates, their commercial success will depend upon acceptance by physicians, patients, third party payers such as health insurance companies and other members of the medical community. Market acceptance of our products is also dependent upon our ability to provide acceptable evidence and the perception of the positive characteristics of our products relative to existing or future treatment methods, including their safety, efficacy and/or other positive advantages. If our products fail to gain market acceptance, we may be unable to earn sufficient revenue to continue our business. Market acceptance of, and demand for, any product that we may develop and commercialize will depend on many factors, both within and outside of our control. If our products receive only limited market acceptance, our business, financial condition and results of operations would be materially and adversely affected.

Our long-term growth depends on our ability to develop products for other organs.

Our growth strategy includes expanding the use of our products in treatments pertaining to organs other than the esophagus and airways, such as the lungs, gastrointestinal tract, and others. These other organs are more complex than the esophagus and airways. There is no assurance that we will be able to successfully apply our technologies to these other more complex organs, which might limit our expected growth.

Our success will depend partly on our ability to operate without infringing on, or misappropriating, the intellectual property or confidentiality rights of others.

We may be sued for infringing on the intellectual property or confidentiality rights of others, including the patent rights, trademarks and trade names and confidential information of third parties. To the extent that any of such claims are valid, if we had utilized, or were to utilize, such patent applications or patents without an agreement from the owner thereof, it could result in infringement of the intellectual property rights of the respective owner. Intellectual property and related litigation is costly and the outcome is uncertain. If we do not prevail in any such intellectual property or related litigation, in addition to any damages we might have to pay, we could be required to stop the infringing activity, or obtain a license to or design around the intellectual property or confidential information in question. If we are unable to obtain a required license on acceptable terms or are unable to design around any third-party patent, we may be unable to sell some of our products and services, which could result in reduced revenue.

We may be involved in lawsuits to protect or enforce our patents that would be expensive and time consuming.

In order to protect or enforce our patent and trademark rights, we may initiate litigation against third parties. We may also become subject to interference proceedings conducted in the patent and trademark offices of various countries to determine the priority of inventions. The defense and prosecution, if necessary, of intellectual property suits, interference proceedings and related legal and administrative proceedings would be costly and may divert our technical and management personnel from their normal responsibilities. We may not prevail in any of these suits should they occur. An adverse determination of any litigation or defense proceedings could put our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of being rejected and patents not being issued.

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 this type of litigation. For example, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments in the litigation. Securities analysts or investors may perceive these announcements to be negative, which could cause the market price of our stock to decline.

If we are unable to effectively protect our intellectual property, third parties may use our technology, which would impair our ability to compete in our markets.

Our continued success will depend significantly on our ability to obtain and maintain meaningful patent protection for certain of our products throughout the world. Patent law relating to the scope of claims in the biotechnology, regenerative medicine, and medical device fields in which we operate is still evolving. The degree of future protection for our proprietary rights is uncertain. We may rely on patents to protect a significant part of our intellectual property and to enhance our competitive position. However, our presently pending or future patent applications may not be accepted and patents might not be issued, and any patent previously issued to us may be challenged, invalidated, held unenforceable or circumvented. Furthermore, the claims in patents which have been issued or which may be issued to us in the future may not be sufficiently broad to prevent third parties from producing competing products similar to our products. We may also operate in countries where we do not have patent rights and in those countries we would not have patent protection. We also rely on trademarks and trade names in our business. The laws of various foreign countries in which we compete may not protect our intellectual property to the same extent as do the laws of the U.S. If we fail to obtain adequate patent protection for our proprietary technology, our ability to be commercially competitive could be materially impaired. It is also possible that our intellectual property may be stolen via cyber-attacks or similar methods.

In addition to patent protection, we also rely on protection of trade secrets, know-how and confidential and proprietary information. To maintain the confidentiality of trade-secrets and proprietary information, we generally seek to enter into confidentiality agreements with our employees, consultants and strategic partners upon the commencement of a relationship. However, we may not be able to obtain these agreements in all circumstances in part due to local regulations. In the event of unauthorized use or disclosure of this information, these agreements, even if obtained, may not provide meaningful protection for our trade-secrets or other confidential information. In addition, adequate remedies may not exist in the event of unauthorized use or disclosure of this information. The loss or exposure of our trade secrets and other proprietary information would impair our competitive advantages and could have a materially adverse effect on our operating results, financial condition and future growth prospects.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- we or any collaborators might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; and
- we may not develop additional proprietary technologies that are patentable.

Our competitors and potential competitors may have greater resources than we have and may develop products and technologies that are more effective or commercially attractive than our products and technologies or may develop competing relationships with our key collaborators.

We expect to compete with multiple pharmaceutical, biotechnology, medical device and scientific research product companies. In addition, there are many academic and clinical centers that are developing bioengineered or regenerative organ technologies that may one day become competitors for us. Many of our competitors and potential competitors have substantially greater financial, technological, research and development, marketing, and personnel resources than we do. We cannot, with any accuracy, forecast when or if these companies are likely to bring bioengineered organ or regenerative medicine products to market for indications that we are also pursuing. Many of these potential competitors may be further along in the process of product development and also operate large, company-funded research and development programs.

We expect that other products will compete with our current and future products based on efficacy, safety, cost, and intellectual property positions. While we believe that these will be the primary competitive factors, other factors include obtaining marketing exclusivity under certain regulations, availability of supply, manufacturing, marketing and sales expertise and capability, and reimbursement coverage. Our competitors may develop or market products that are more effective or commercially attractive than our current or future products and may also develop competing relationships with our key collaborators. In addition, we may face competition from new entrants into the field. We may not have the financial resources, technical expertise or marketing, distribution or support capabilities to compete successfully in the future. The effects of any such actions of our competitors may have a materially adverse effect on our business, operating results and financial condition.

Cyber-attacks or other failures in telecommunications or information technology systems and deficiency in our, or those of third parties upon which we rely, cybersecurity could result in information theft, data corruption and significant disruption of our business operations.

In the ordinary course of business, we and the third parties upon which we rely and may process proprietary, confidential, and sensitive data, including personal data (such as health-related data), intellectual property, and trade secrets (collectively, sensitive information). Cyber-attacks, malicious internet-based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our sensitive information and information technology systems, and those of the third parties upon which we rely. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer "hackers," threat actors, "hacktivists," organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation-state-supported actors.

Some actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties upon which we rely may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability conduct our research and development programs and our clinical trials. We and the third parties upon which we rely may be subject to a variety of evolving threats, including but not limited to social-engineering attacks (including through phishing attacks and deep fakes, which may be increasingly more difficult to identify as fake), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks, credential stuffing attacks, credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, and other similar threats. In particular, severe ransomware attacks are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, disruption of clinical trials, loss of sensitive data (including data related to clinical trials), loss of income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. Remote work has become more common and has increased risks to our information technology systems and data, as more of our employees utilize network connections, computers, and devices outside of our premises or network, including working at home, while in transit and in public locations. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies.

In addition, our reliance on third-party service providers could introduce new cybersecurity risks and vulnerabilities, including supply-chain attacks, and other threats to our business operations. We may rely on third- party service providers and technologies to operate critical business systems to process sensitive information in a variety of contexts, including, without limitation, third-party providers of information technology infrastructure, cloud-based infrastructure, encryption and authentication technology, employee email, content delivery to customers, CROs for managing clinical trial data, and other functions. We may also rely on third-party service providers to provide other products, services, parts, or otherwise operate our business. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, the liability of such third party may be limited such that any award may be insufficient to cover our damages, or we may be unable to recover any such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third-party partners' supply chains have not been compromised.

We may expend significant resources or modify certain of our business activities (which could include our clinical trial activities) to try to protect against security incidents. Certain data privacy and security obligations may require us to implement and maintain specific security measures, industry-standard or reasonable security measures to protect our information technology systems and sensitive information.

While we have established physical, electronic and organizational security measures designed to safeguard and secure our systems against security incidents, there can be no assurance that these measures will be effective. We take steps designed to detect, mitigate and remediate vulnerabilities in our information technology systems (such as our hardware and/or software, including that of third parties upon which we rely). We may not, however, detect and remediate all such vulnerabilities including on a timely basis. Further, we may experience delays in developing and deploying remedial measures and patches designed to address identified vulnerabilities.

Vulnerabilities could be exploited and result in a security incident. Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties upon whom we rely. A security incident or other interruption could disrupt our ability (and that of third parties upon whom we rely) to provide our products. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences. If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences. These consequences may include: government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing sensitive information (including personal data); litigation (including class-action claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position.

If we do not successfully manage our growth, our business goals may not be achieved.

To manage growth, we will be required to continue to improve existing, and implement additional, operational and financial systems, procedures and controls, and hire, train and manage additional employees. Our current and planned personnel, systems, procedures and controls may not be adequate to support our anticipated growth and we may not be able to hire, train, retain, motivate and manage required personnel. Competition for qualified personnel in the biotechnology and regenerative medicine area is intense, and we operate or plan to operate in geographic locations where labor markets are particularly competitive, including Boston, Massachusetts, where demand for personnel with these skills is extremely high and is likely to remain high. As a result, competition for qualified personnel is intense and the process of hiring suitably qualified personnel is often lengthy and expensive, and may become more expensive in the future. If we are unable to hire and retain a sufficient number of qualified employees or otherwise manage our growth effectively, our ability to conduct and expand our business could be seriously reduced.

Risks Associated with Clinical Trials and Pre-Clinical Development

The results of our clinical trials or pre-clinical development efforts may not support our product claims or may result in the discovery of adverse side effects.

Even if our pre-clinical development efforts or clinical trials are completed as planned, we cannot be certain that their results will support our product claims or that the U.S. Food and

Drug Administration, or FDA, foreign regulatory authorities or notified bodies will agree with our conclusions regarding them. Although we have obtained some positive results from the use of our scaffolds and bioreactors for esophageal and trachea implants performed to date, we also discovered that our first-generation trachea product design encountered certain body response issues that we have sought to resolve with our ongoing development of our implant design. We cannot be certain that our implant design or any future modifications or improvements with respect thereto will support our claims, and any such developments may result in the discovery of further adverse side effects. We also may not see positive results when our product candidates undergo clinical testing in humans in the future. Success in pre-clinical studies and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure that the later trials will replicate the results of prior trials and pre-clinical studies. Our pre-clinical development efforts and any clinical trial process may fail to demonstrate that our product candidates are safe and effective for the proposed indicated uses, which could cause us to abandon a product candidate and may delay development of others. Also, patients receiving surgeries using our product candidates under compassionate use or in clinical trials may experience significant adverse events following the surgeries, including serious health complications or death, which may or may not be related to materials provided by us. In 2017, our esophageal implant candidate was used in a human surgery at Mayo Clinic via an FDA-approved single-use expanded access application. In 2013 and 2014 we had provided a previous generation trachea scaffold device that was used in implants in human patients under compassionate use. To date, we believe that at least four of the six patients who received those tracheal implants have died. While we believe that none of those patients died because of a failure of the applicable device, these and any other such events have and may cause or contribute to the delay or termination of our clinical trials or pre-clinical development efforts. Any delay or termination of our pre-clinical development efforts or clinical trials will delay the filing of our product submissions and, ultimately, our ability to commercialize our products and generate revenues. It is also possible that patients enrolled in clinical trials will experience adverse side effects that are not currently part of the product candidate’s profile.

Regulatory approval delays due to COVID-19

COVID-19 may impede clinical trials and slow down regulatory actions. It could adversely affect the entire clinical trial spectrum from enrollment to data analysis. Assuming patients enroll, clinical trials may face disruptions to protocol schedules for treatment and follow-up visits. Reports from Europe have noted overwhelmed facilities where all non-critical visits have been postponed or canceled. Many U.S. hospitals have followed suit to limit exposure and allow for care of COVID-19 patients. Deviations from trial protocols could present challenges when it comes time to analyze the related data set. Some clinics may stop allowing clinical trial monitors on site. Without reconciling the data, we may be unable to "lock" the trial database, an essential step that precedes the analysis of the data.

We rely on regular interaction and guidance from the FDA and other regional/country regulatory authorities/agencies to plan research and development activities across all stages. Due to the COVID-19 pandemic, the FDA and worldwide regulatory authorities have a great deal of resources dedicated to COVID-19 related matters, resulting in disruption in their ability to fully support the regulatory clearance/approval processes. As resources continue to be diverted, regulatory clearances/approvals may continue to be delayed, until the pandemic is under control. Therefore, delays with approvals, clearances, inspections, and meetings that are currently being experienced may continue for the foreseeable future. Postponement of these interactions could delay us from bringing our product candidates to market.

Clinical trials necessary to support a biological product license or other marketing authorization for our product candidates will be expensive and will require the enrollment of sufficient patients to adequately demonstrate safety and efficacy for the product's target populations. Suitable patients may be difficult to identify and recruit. Delays or failures in our clinical trials will prevent us from commercializing any products and will adversely affect our business, operating results and prospects.

In the U.S., initiating and completing clinical trials necessary to support Biological License Applications, or BLAs, will be time consuming, expensive and the outcome uncertain. Moreover, the FDA may not agree that clinical trial results support an application for the indications sought in the application for the product. In other jurisdictions such as the E.U., the conduct of extensive and expensive clinical trials may also be required in order to demonstrate the quality, safety and efficacy of our product candidates, depending on each specific product candidate, the claims being studied, and the target condition or disease. The outcome of these clinical trials, which can be expensive and are heavily regulated, will also be uncertain. Moreover, the results of early clinical trials are not necessarily predictive of future results, and any product candidate we advance into clinical trials following initial positive results in early clinical trials may not have favorable results in later clinical trials.

Conducting successful clinical trials will require the enrollment of a sufficient number of patients to support each trial's claims, and suitable patients may be difficult to identify and recruit. Patient enrollment in clinical trials and completion of patient participation and follow-up depends on many factors, including the size of the patient population, the nature of the trial protocol, the attractiveness of, or the discomfort and risks associated with, the treatments received by enrolled subjects, the availability of appropriate clinical trial investigators, support staff, and proximity of patients to clinical sites and ability to comply with the eligibility and exclusion criteria for participation in the clinical trial and patient compliance. For example, patients may be discouraged from enrolling in our clinical trials if the trial protocol requires them to undergo extensive post-treatment procedures or follow-up to assess the safety and effectiveness of our product candidates, or if they determine that the treatments received under the trial protocols are not attractive or involve unacceptable risks or discomfort. Also, patients may not participate in our clinical trials if they choose to participate in contemporaneous clinical trials of competitive products. In addition, patients participating in clinical trials may die before completion of the trial or suffer adverse medical events unrelated to investigational products.

Development of sufficient and appropriate clinical protocols to demonstrate safety and efficacy are required and we may not adequately develop such protocols to support clearance and approval. Further, the FDA and foreign regulatory authorities may require us to submit data on a greater number of patients than we originally anticipated and/or for a longer follow-up period or change the data collection requirements or data analysis applicable to our clinical trials. Delays in patient enrollment or failure of patients to continue to participate in a clinical trial may cause an increase in costs and delays in the approval and attempted commercialization of our products or result in the failure of the clinical trial. In addition, despite considerable time and expense invested in our clinical trials, the FDA and foreign regulatory authorities may not consider our data adequate to demonstrate safety and efficacy. Although FDA regulations allow submission of data from clinical trials outside the U.S., there can be no assurance that such data will be accepted or that the FDA will not apply closer scrutiny to such data. Increased costs and delays necessary to generate appropriate data, or failures in clinical trials could adversely affect our business, operating results and prospects.

If the third parties on which we rely to conduct our clinical trials and to assist us with pre-clinical development do not perform as contractually-required or expected, we may not be able to obtain regulatory approval for or commercialize our product candidates.

We do not have the ability to independently conduct our pre-clinical and clinical trials for our product candidates and we must rely on third parties, such as contract research organizations, medical institutions, clinical investigators and contract laboratories to conduct, or assist us in conducting, such trials, including data collection and analysis. We do not have direct control over such third parties' personnel or operations. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if these third parties 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 clinical protocols or any regulatory requirements, or for other reasons, our pre-clinical development activities or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to seek or obtain regulatory approval for, or successfully commercialize, our product candidates on a timely basis, if at all. Our business, operating results and prospects may also be adversely affected. Furthermore, any third-party clinical trial investigators pertaining to our product candidates may be delayed in conducting our clinical trials for reasons outside of their control.

Risks Associated with Regulatory Approvals

If we fail to obtain, or experience significant delays in obtaining, regulatory approvals in the U.S., China or the E.U. for our products, including those for the esophagus and airways, or are unable to maintain such clearances or approvals for our products, our ability to commercially distribute and market these products would be adversely impacted.

We currently do not have regulatory approval to market any of our implant product candidates, including those for the esophagus, colon, and uterus. Our product candidates are subject to rigorous regulation by the FDA, and numerous other federal and state governmental authorities in the U.S., as well as foreign governmental authorities. In the U.S., the FDA permits commercial distribution of new medical products only after approval of a Premarket Approval, or PMA, New Drug Application, or NDA, or BLA, unless the product is specifically exempt from those requirements. A PMA, NDA or BLA must be supported by extensive data, including, but not limited to, technical, pre-clinical, clinical trial, manufacturing and labeling data, to demonstrate to the FDA's satisfaction the safety and efficacy of the product for its intended use. There are similar approval processes in China, the E.U. and other foreign jurisdictions. Our failure to receive or obtain such clearances or approvals on a timely basis or at all would have an adverse effect on our results of operations.

The first bioengineered trachea implant approved in the U.S. using our first-generation trachea scaffold in an implant was approved under the IND pathway through the FDA's Center for Biologics Evaluation and Research, or CBER, for a single compassionate use. Such initial U.S. surgery was led by Professor Paolo Macchiarini, M.D., a surgeon pioneering tracheal replacement techniques. Dr. Macchiarini was not employed or affiliated with our company, and we did not pay him any compensation or consulting fees. In June 2014, we ceased support of any human surgeries with Dr. Macchiarini. Since the time we withdrew from involvement with Dr. Macchiarini, allegations that Dr. Macchiarini had failed to obtain informed consent and accurately report patient conditions, among other things, for surgeries performed at the Karolinska Institutet in Stockholm, Sweden, were made public.

The Karolinska Institutet investigated the allegations and concluded that while in some instances Dr. Macchiarini did act without due care, his actions did not qualify as scientific misconduct. Subsequent to this investigation, further negative publicity and claims continued to be released questioning the conduct of Dr. Macchiarini, the Karolinska Institutet, the Krasnodar Regional Hospital in Krasnodar, Russia as well as our company relating to surgeries performed by Dr. Macchiarini and other surgeons at such facilities. In February 2015, the Karolinska Institutet announced that it would conduct an additional investigation into the allegations made about Dr. Macchiarini and the Karolinska Institutet's response and actions in the earlier investigation. In March 2015, the Karolinska Institutet announced that it was terminating Dr. Macchiarini's employment, and in December 2016 the Karolinska Institutet found Dr. Macchiarini, along with three co-authors, guilty of scientific misconduct. In May 2022, Dr. Macchiarini was tried in Solna District Court in Sweden for aggravated assault against three patients treated at the Karolinska University Hospital. On June 16, 2022, Dr. Macchiarini was acquitted in two of these cases and in the third was found guilty of causing bodily harm to the patient and was given a suspended sentence for two years. These allegations, the results of the investigation and any further actions that may be taken in connection with these matters, have and may continue to harm the perception of our product candidates or company and make it difficult to recruit patients for any clinical trials, which could have a material adverse effect on our business, financial condition or results of operations.

The FDA has informed us that our esophageal implant would be viewed by the FDA as a combination product comprised of a biologic, or cells, and a medical device component. Nevertheless, we cannot be certain how the FDA will regulate our products. The FDA may require us to obtain marketing clearance and approval from multiple FDA centers. The review of combination products is often more complex and more time consuming than the review of products under the jurisdiction of only one center within the FDA.

While the FDA has informed us that our esophageal implant would be regulated by the FDA as a combination product, we cannot be certain that any of our other products would also be regulated by the FDA as a combination product. For a combination product, the Office of Combination Products, or OCP, within FDA can determine which center or centers within the FDA will review the product and under what legal authority the product will be reviewed. Generally, the center within the FDA that has the primary role in regulating a combination product is determined based on the primary mode of action of the product. Generally, if the primary mode of action is as a device, the FDA's Center for Devices and Radiological Health, or CDRH, takes the lead. Alternatively, if the primary mode of action is cellular, then the CBER takes the lead. On October 18, 2016, we also received written confirmation from the CBER that the FDA intends to regulate our esophageal implant as a combination product under the primary jurisdiction of CBER. We further understand that CBER may choose to consult or collaborate with CDRH with respect to the characteristics of the synthetic scaffold component of our product based on CBER's determination of need for such assistance.

The process of obtaining FDA marketing approval is lengthy, expensive, and uncertain, and we cannot be certain that our product candidates, including product candidates pertaining to the esophagus, airways, or otherwise, will be cleared or approved in a timely fashion, or at all. In addition, the review of combination products is often more complex and can be more time consuming than the review of a product under the jurisdiction of only one center within the FDA.

We cannot be certain that the FDA will not elect to have our combination product candidates reviewed and regulated by only one FDA center and/or different legal authority, in which case the path to regulatory approval would be different and could be more lengthy and costly.

If the FDA does not approve or clear our products in a timely fashion, or at all, our business, financial condition or operations will be adversely affected.

In the E.U., our esophagus product candidate will likely be regulated as a combined advanced therapy medicinal product and our other product candidates, including for the colon and uterus, may also be viewed as advanced therapy medicinal products, which could delay approvals and clearances and increase costs of obtaining such approvals and clearances.

On May 28, 2014, we received notice from the European Medicines Agency, or EMA, that our first-generation trachea product candidate would be regulated as a combined advanced therapy medicinal product. While we have not had any formal interaction with the EMA with respect to our esophageal implant, we believe that such implant technology would likely be regulated as a combined advanced therapy medicinal product. In the event of such classification, it would be necessary to seek a marketing authorization for these products granted by the European Commission before being marketed in the E.U.

Other products we may develop, including any products pertaining to the airways or otherwise, may similarly be regulated as advanced therapy medicinal products or combined advanced therapy medicinal products. The regulatory procedures leading to marketing approval of our products vary among jurisdictions and can involve substantial additional testing. Compliance with the FDA requirements does not ensure clearance or approval in other jurisdictions, and the ability to legally market our products in any one foreign country does not ensure clearance, or approval by regulatory authorities in other foreign jurisdictions. The foreign regulatory process leading to the marketing of the products may include all of the risks associated with obtaining FDA approval in addition to other risks. In addition, the time required to comply with foreign regulations and market products may differ from that required to obtain FDA approval, and we may not obtain foreign approval or clearance on a timely basis, if at all.

Risk Associated with Product Marketing

Even if our products are cleared or approved by regulatory authorities, if we or our suppliers fail to comply with ongoing FDA or other foreign regulatory authority requirements, or if we experience unanticipated problems with our products, these products could be subject to restrictions or withdrawal from the market.

Any product for which we obtain clearance or approval in the U.S., China, or Europe, and the manufacturing processes, reporting requirements, post-approval clinical data and promotional activities for such product, will be subject to continued regulatory review, oversight and periodic inspections by the FDA and other domestic and foreign regulatory authorities or notified bodies. In particular, we and our suppliers are required to comply with the FDA's Quality System Regulations, or QSR, and current Good Manufacturing Practices, or cGMP, for our medical products, and International Standards Organization, or ISO, regulations for the manufacture of our products and other regulations which cover the methods and documentation of the design, testing, production, control, quality assurance, labeling, packaging, storage and shipping of any product for which we obtain clearance or approval. Manufacturing may also be subject to controls by the FDA for parts of the system or combination products that the FDA may find are controlled by the biologics regulations. Equivalent regulatory obligations apply in foreign jurisdictions. Regulatory authorities, such as the FDA, China's National Medical Products Administration, the competent authorities of the E.U. Member States, the EMA and notified bodies, enforce the QSR, cGMP and other applicable regulations in the U.S. and in foreign jurisdictions through periodic inspections. The failure by us or one of our suppliers to comply with applicable statutes and regulations administered by the FDA and other regulatory authorities or notified bodies in the U.S. or in foreign jurisdictions, or the failure to timely and adequately respond to any adverse inspectional observations or product safety issues, could result in, among other things, any of the following enforcement actions:

- untitled letters, warning letters, fines, injunctions, consent decrees and civil penalties;
- unanticipated expenditures to address or defend such actions;
- customer notifications for repair, replacement, or refunds;
- recall, detention or seizure of our products;
- operating restrictions or partial suspension or total shutdown of production;
- withdrawing BLA or NDA approvals that have already been granted;
- withdrawal of the marketing authorization granted by the European Commission or delay in obtaining such marketing authorization;
- withdrawal of the CE Certificates of Conformity granted by the notified body or delay in obtaining these certificates;
- refusal to grant export approval for our products; and
- criminal prosecution.

The occurrence of any of these events could have a material adverse effect on our business, financial condition or results of operations.

Post-market enforcement actions can generate adverse commercial consequences.

Even if regulatory approval of a product is granted, such clearance or approval may be subject to limitations on the intended uses for which the product may be marketed and reduce our potential to successfully commercialize the product and generate revenue from the product. If the FDA or a foreign regulatory authority determines that our promotional materials, labeling, training or other marketing or educational activities constitute promotion of an unapproved use, it could request that we cease or modify our training or promotional materials or subject us to regulatory enforcement actions. It is also possible that other federal, state or foreign enforcement authorities might take action if they consider our training or other promotional materials to constitute promotion of an unapproved use, which could result in significant fines or penalties under other statutory authorities, such as laws prohibiting false claims for reimbursement. In addition, we may be required to conduct costly post-market testing and surveillance to monitor the safety or effectiveness of our products, and we must comply with medical products reporting requirements, including the reporting of adverse events and malfunctions related to our products. Later discovery of previously unknown problems with our products, including unanticipated adverse events or adverse events of unanticipated severity or frequency, manufacturing problems, or failure to comply with regulatory requirements such as QSR, may result in changes to labeling, restrictions on such products or manufacturing processes, withdrawal of the products from the market, voluntary or mandatory recalls, a requirement to repair, replace or refund the cost of any medical device we manufacture or distribute, fines, suspension of regulatory approvals, product seizures, injunctions or the imposition of civil or criminal penalties which would adversely affect our business, operating results and prospects.

Economic, political and other risks associated with our international operations could adversely affect our revenues and international growth prospects.

The Company started selling longevity supplements through Longevity Products in the third quarter of 2023. These products are marketed to the general public and initially targeted at consumers in the Great China Region through eCommerce (online sales).

Longevity Products plans to include a broad range of products focused on personal healthcare including longevity dietary supplements. Our international operations are subject to a number of risks inherent to operating in foreign countries, and any expansion of our international operations will amplify the effects of these risks, which include, among others:

- political and economic instability of foreign markets;
- foreign governments' restrictive trade policies or the impact of trade tensions amongst nations;
- inconsistent product regulation or sudden policy changes by foreign agencies or governments;
- the imposition of, or increase in, duties, taxes, government royalties or non-tariff trade barriers;
- difficulty in collecting international accounts receivable and potentially longer payment cycles;
- difficulty of enforcing contractual obligations of foreign partners;
- increased costs in maintaining international marketing efforts;
- problems entering international markets with different cultural bases and consumer preferences;
- compliance with foreign regulatory requirements such as the General Data Protection Regulation (GDPR), domestic laws and regulations applicable to international operations, such as the Foreign Corrupt Practices Act and regulations promulgated by the Office of Foreign Asset Control, as well as regulatory laws, regulations and restrictions that may impact or target dietary supplement retailers and manufacturers;
- fluctuations in foreign currency exchange rates; and
- operating in new, developing or other markets in which there are significant uncertainties regarding the interpretation, application and enforceability of laws and regulations relating to contract and intellectual property rights.

Any of these risks could have a material adverse effect on our international operations and our growth strategy.

Additionally, if the opportunity arises, we may expand our operations into new and high-growth international markets. However, there is no assurance that we will expand our operations in such markets in our desired time frame. To expand our operations into new international markets, we may enter into business combination transactions, make acquisitions or enter into strategic partnerships, joint ventures or alliances, any of which may be material. We may enter into these transactions to acquire other businesses or products to expand our products or take advantage of new developments and potential changes in the industry. Our lack of experience operating in new international markets and our lack of familiarity with local economic, political and regulatory systems could prevent us from achieving the results that we expect on our anticipated time frame or at all. If we are unsuccessful in expanding into new or high-growth international markets, it could adversely affect our operating results and financial condition.

Additionally, our business is increasingly exposed to operational risks in China. These include, among others, changes in economic conditions (including consumer spending, unemployment levels and wage and commodity inflation), consumer preferences, the regulatory environment, and tax laws and regulations, as well as increased media scrutiny, fluctuations in foreign exchange rates, increased restrictions or tariffs on imported supplies as a result of trade disputes and increased competition. Any significant or prolonged deterioration in U.S.-China relations could adversely affect our operations in China if Chinese consumers reduce the frequency of their purchases of our products. Chinese law regulates our business conducted within China. In addition, if we are unable to enforce our intellectual property or contract rights in China, it could result in an interruption in the operation of our brands, which could negatively impact our financial results. If our business is harmed or development of our Chinese operations is slowed in China due to any of these factors, it could negatively impact our overall financial results or our growth prospects.

Risks Relating to Our Common Stock

Our principal stockholders hold a significant percentage of our voting power and will be able to exert significant control over us.

The stockholders who purchased shares of our common stock and related warrants pursuant to a Securities Purchase Agreement dated December 27, 2017 collectively hold shares of common stock that represent approximately 32% of all outstanding voting power, and as such may significantly influence the results of matters voted on by our shareholders. The interests of these stockholders may conflict with your interests. This significant concentration of share ownership may adversely affect the trading price for our common stock because investors may perceive disadvantages in owning stock in companies with controlling stockholders.

A trading market that will provide you with adequate liquidity may not develop for our common stock.

The current public market for our common stock has limited trading volume and liquidity. We cannot predict the extent to which investor interest in our company will lead to the development of a more active trading market in our common stock, or how liquid that market might be.

Our revenues, operating results and cash flows may fluctuate in future periods and we may fail to meet investor expectations, which may cause the price of our common stock to decline.

Variations in our quarterly and year-end operating results are difficult to predict and may fluctuate significantly from period to period. If our revenues or operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially, which could have a material adverse effect on our ability to raise additional capital, to use our stock as consideration for future acquisitions or for compensation of our employees. In addition to the other factors discussed under these "Risk Factors," specific factors that may cause fluctuations in our operating results include:

- demand and pricing for our products;
- government or private healthcare reimbursement policies;
- adverse events or publicity related to our products, our research or investigations, or our collaborators or other partners;
- physician and patient acceptance of any of our current or future products;
- manufacturing stoppages or delays;
- introduction of competing products or technologies;
- our operating expenses which fluctuate due to growth of our business; and
- timing and size of any new product or technology acquisitions we may complete.

Substantial sales of common stock have and may continue to occur, or may be anticipated, which have and could continue to cause our stock price to decline.

We expect that we will seek to raise additional capital from time to time in the future, which may involve the issuance of additional shares of common stock, or securities convertible into or exercisable for common stock. The purchasers of the shares of common stock and warrants to purchase shares of common stock from our public offerings and private placements may sell significant quantities of our common stock in the market, which may cause a decline in the price of our common stock. Further, we cannot predict the effect, if any, that any additional market sales of common stock, or anticipation of such sales, or the availability of those shares of common stock for sale will have on the market price of our common stock. Any future sales of significant amounts of our common stock, or the perception in the market that this will occur, may result in a decline in the price of our common stock.

Your percentage ownership will be diluted in the future.

Your percentage ownership will be diluted in the future because of equity awards that we expect will be granted to our directors, officers and employees, as well as shares of common stock, or securities convertible into common stock, we issue in connection with future capital raising or strategic transactions. Our Amended and Restated Equity Incentive Plan provides for the grant of equity-based awards, including restricted stock, restricted stock units, stock options, stock appreciation rights and other equity-based awards to our directors, officers and other employees, advisors and consultants. The issuance of any shares of our stock would dilute the proportionate ownership and voting power of existing security holders.

Provisions of Delaware law, of our amended and restated charter and amended and restated bylaws may make a takeover more difficult, which could cause our stock price to decline.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws and in the Delaware corporate law may make it difficult and expensive for a third party to pursue a tender offer, change in control or takeover attempt, which is opposed by management and the Board of Directors. Public stockholders who might desire to participate in such a transaction may not have an opportunity to do so. We have a staggered Board of Directors that makes it difficult for stockholders to change the composition of the Board of Directors in any one year. Any removal of directors will require a super-majority vote of the holders of at least 75% of the outstanding shares entitled to be cast on the election of directors which may discourage a third party from making a tender offer or otherwise attempting to obtain control of us. These anti-takeover provisions could substantially impede the ability of public stockholders to change our management and Board of Directors. Such provisions may also limit the price that investors might be willing to pay for shares of our common stock in the future.

The market price of our shares may fluctuate widely.

The market price of our common stock may fluctuate widely, depending upon many factors, some of which may be beyond our control, including:

- the success and costs of preclinical and clinical testing and obtaining regulatory approvals or clearances for our products;
- the success or failure of surgeries and procedures involving the use our products;
- a shift in our investor base;
- our quarterly or annual results of operations, or those of other companies in our industry;
- actual or anticipated fluctuations in our operating results due to factors related to our business;
- changes in accounting standards, policies, guidance, interpretations or principles;
- announcements by us or our competitors of significant acquisitions, dispositions or intellectual property developments or issuances;
- the failure of securities analysts to cover our common stock;
- changes in earnings estimates by securities analysts or our ability to meet those estimates;
- the operating and stock price performance of other comparable companies; our issuance of equity, debt or other financing instruments;
- overall market fluctuations; and
- general macroeconomic conditions.

Stock markets in general have experienced volatility that has often been unrelated to the operating performance of a particular company. These broad market fluctuations may adversely affect the trading price of our common stock.

Any issuance of preferred stock in the future may dilute the rights of our common stockholders.

Our Board of Directors has the authority to issue up to 2,000,000 shares of preferred stock and to determine the price, privileges and other terms of these shares. Our Board of Directors is empowered to exercise this authority without any further approval of stockholders. The rights of the holders of common stock may be adversely affected by the rights of future holders of preferred stock.

We have in the past issued, and we may at any time in the future issue, additional shares of authorized preferred stock. For example, in our December 2017 private placement transaction, we authorized 12,000 shares of Series D convertible preferred stock, of which we issued 3,108 shares, all of which have been converted into shares of common stock, and in June 2022 we also issued 4,000 shares of Series E convertible preferred stock, and additional shares of Series E convertible preferred stock thereafter in relation to dividends on such Series E convertible preferred stock. The Company issued an aggregate of 180 and 77 shares of Series E convertible preferred stock relating to accrued dividends during the years ended December 31, 2022 and 2023, respectively. All shares of Series E convertible preferred stock have been converted into shares of common stock as of December 31, 2023.

We do not intend to pay cash dividends on our common stock.

Currently, we do not anticipate paying any cash dividends to holders of our common stock. As a result, capital appreciation, if any, of our common stock will be a stockholder's sole source of gain.

Our common stock has been delisted on the NASDAQ Capital Market, which may negatively impact the trading price of our common stock and the levels of liquidity available to our stockholders.

Our common stock was suspended from trading on the NASDAQ Capital Market, prior to the opening of the market on October 6, 2017 and began quotation on the OTCQB Venture Market on that date, retaining the symbol "BSTG". On December 7, 2017, the NASDAQ Capital Market filed a Form 25-NSE with the SEC to complete the delisting process. The trading of our common stock on the OTCQB Venture Market rather than The NASDAQ Capital Market may negatively impact the trading price of our common stock and the levels of liquidity available to our stockholders.

Upon such delisting, our common stock became subject to the regulations of the SEC relating to the market for penny stocks. A penny stock is any equity security not traded on a national securities exchange that has a market price of less than $5.00 per share. The regulations applicable to penny stocks may severely affect the market liquidity for our common stock and could limit the ability of shareholders to sell securities in the secondary market. Accordingly, investors in our common stock may find it more difficult to dispose of or obtain accurate quotations as to the market value of our common stock, and there can be no assurance that our common stock will continue to be eligible for trading or quotation on the OTCQB Venture Market or any other alternative exchanges or markets.

The delisting of our common stock from the NASDAQ Capital Market may adversely affect our ability to raise additional financing through public or private sales of equity securities, may significantly affect the ability of investors to trade our securities, and may negatively affect the value and liquidity of our common stock. Such delisting may also have other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest and fewer business development opportunities. Furthermore, because of the limited market and low volume of trading in our common stock that could occur, the share price of our common stock could more likely be affected by broad market fluctuations, general market conditions, fluctuations in our operating results, changes in the market's perception of our business, and announcements made by us, our competitors, parties with whom we have business relationships or third parties.

If securities or industry analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us and our business. Securities or industry analysts may elect not to provide coverage of our common stock, and such lack of coverage may adversely affect the market price of our common Stock. In the event we do not secure additional securities or industry analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more securities or industry analysts downgrade our stock or issue other unfavorable commentary or research. If one or more securities or industry analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

General Risk Factors

Impact of COVID-19, Supply Chain Disruptions and Other Matters

The impact of the COVID-19 outbreak has subsided substantially in the U.S. but continues to result in reduced activity levels outside of the U.S., such as continued restrictions on travel and business operations and advising or requiring individuals to limit or forego their time outside of their homes or places of business. In response to the global supply chain instability and inflationary cost increases, we have taken action to minimize, as much as possible, any potential adverse impacts by working with our suppliers to monitor the availability of raw material components (e.g., polymers and organic solvents), lead times, and freight carrier availability. We expect global supply chain instability will continue to have an impact on our business, but to date that has not been material to our financial performance or the development of our products. The consequences of the pandemic, global supply chain instability and inflationary cost increases and their adverse impact to the global economy, continue to evolve. Accordingly, the significance of the future impact to our business, financial condition and results of operations remains subject to significant uncertainty.

We are subject to new U.S. foreign investment regulations, which may impose additional burdens on or may limit certain investors' ability to purchase our common stock, potentially making our common stock less attractive to investors, and may also impact our ability to generate revenues outside of the U.S.

In October 2018, the U.S. Department of Treasury announced a pilot program to implement part of the Foreign Investment Risk Review Modernization Act of 2018 (FIRRMA), effective November 10, 2018. The pilot program expands the jurisdiction of CFIUS to include certain direct or indirect foreign investments in a defined category of U.S. companies, which may include companies such as Harvard Apparatus Regenerative Technology in the biotechnology industry. Among other things, FIRRMA empowers CFIUS to require certain foreign investors to make mandatory filings and permits CFIUS to charge filing fees related to such filings. Such filings are subject to review by CFIUS. Any such restrictions on the ability to purchase shares of our common stock may have the effect of delaying or deterring any particular investment and could also affect the price that some investors are willing to pay for our common stock. In addition, such restrictions could also limit the opportunity for our stockholders to receive a premium for their shares of our common stock in relation to any potential change in control.

We intend to generate significant revenues outside the U.S., including in China and the E.U. Restrictions, such as those related to CFIUS, not only affect foreign ownership and investments, but also the transfer or licensing of technology from the U.S. into certain foreign markets, including China. Such restrictions, including to the extent they block strategic transactions that might otherwise be in stockholder's interests, may materially and adversely affect our ability to generate revenues in those foreign markets and the results of our operations.

If we incur higher costs as a result of trade policies, treaties, government regulations or tariffs, it could have a materially adverse effect on our business, financial condition or results of operations.

There is currently significant uncertainty about the future relationship between the United States and China, including with respect to trade policies, treaties, government regulations and tariffs. The current United States administration has called for substantial changes to U.S. foreign trade policy including greater restrictions on international trade and significant increases in tariffs on goods imported into the U.S. Under the current status, we do not expect that this tariff will significantly impact any Harvard Apparatus Regenerative Technology products and thus the tariff should not have a materially adverse effect on our business, financial condition or results of operations. We are unable to predict whether or when additional tariffs will be imposed or the impact of any such future tariff increases.

We are exposed to a variety of risks relating to our potential international sales and operations, including fluctuations in exchange rates, local economic conditions and delays in collection of accounts receivable.

We intend to generate significant revenues outside the U.S. in multiple foreign currencies including Chinese Renminbi, Euros, British pounds, and in U.S. dollar-denominated transactions conducted with customers who generate revenue in currencies other than the U.S. dollar. In such instances, for those foreign customers who purchase our products in U.S. dollars, currency fluctuations between the U.S. dollar and the currencies in which those customers do business may have a negative impact on the demand for our products in foreign countries where the U.S. dollar has increased in value compared to the local currency.

Since we may have vendors and customers outside the U.S. and we may generate revenues and incur operating expenses in multiple foreign currencies, we will experience currency exchange risk with respect to any foreign currency-denominated revenues and expenses. We cannot predict the consolidated effects of exchange rate fluctuations upon our future operating results because of the number of currencies involved, the variability of currency exposure and the potential volatility of currency exchange rates. Our international activities subject us to laws regarding sanctioned countries, entities and persons, customs, import-export, laws regarding transactions in foreign countries, the U.S. Foreign Corrupt Practices Act and local anti-bribery and other laws regarding interactions with healthcare professionals. Among other things, these laws restrict, and in some cases prohibit, U.S. companies from directly or indirectly selling goods, technology or services to people or entities in certain countries. In addition, these laws require that we exercise care in structuring our sales and marketing practices in foreign countries.

Local economic conditions, legal, regulatory or political considerations, disruptions from strikes, the effectiveness of our sales representatives and distributors, local competition and changes in local medical practice could also affect our sales to foreign markets. Relationships with customers and effective terms of sale frequently vary by country, often with longer-term receivables than are typical in the U.S.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

In December 2017, the U.S. government enacted the Tax Cuts and Jobs Act of 2017, or TCJA, which significantly reforms the Internal Revenue Code of 1986, as amended. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, effective January 1, 2018; limitation of the tax deduction for interest expense; limitation of the deduction for net operating losses and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such tax losses may be carried forward indefinitely); and modifying or repealing many business deductions and credits, including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as “orphan drugs”. The tax rate change resulted in (i) a reduction in the gross amount of our deferred tax assets recorded as of December 31, 2017, without an impact on the net amount of our deferred tax assets, which are recorded with a full valuation allowance. We continue to examine the impact this tax reform legislation may have on our business. However, the effect of the TCJA on us and our affiliates, whether adverse or favorable, is uncertain and may not become evident for some period of time. We urge investors to consult with their legal and tax advisers regarding the implications of the TCJA on an investment in our common stock.

Changes in the European regulatory environment regarding privacy and data protection regulations could have a materially adverse impact on our results of operations.

The European Union, or E.U., has adopted a comprehensive overhaul of its data protection regime in the form of the General Data Protection Regulation, or GDPR, which came into effect in May 2018. GDPR extends the scope of the existing E.U. data protection law to foreign companies processing personal data of E.U. residents. The regulation imposes a strict data protection compliance regime with severe penalties of 4% of worldwide turnover or €20 million, whichever is greater, and includes new rights such as the right of erasure of personal data. Although the GDPR will apply across the E.U., as has been the case under the current data protection regime, E.U. Member States have some national derogations and local data protection authorities that will still have the ability to interpret the GDPR, which has the potential to create inconsistencies on a country-by-country basis. Implementation of, and compliance with the GDPR could increase our cost of doing business and/or force us to change our business practices in a manner adverse to our business. In addition, violations of the GDPR may result in significant fines, penalties and damage to our brand and business which could, individually or in the aggregate, materially harm our business and reputation.

Healthcare legislative reform measures may have a materially adverse effect on our business and results of operations.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Affordable Care Act, or ACA, was passed, which substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (70% commencing January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to Judicial and Congressional challenges, as well as efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, former President Trump signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA.

Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The TCJA includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, former President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax, an annual fee on certain high-cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the Medical Device Excise Tax, or MDET, on non-exempt medical devices. Since then, The Further Consolidated Appropriations Act, 2020 H.R. 1865, signed into law on December 20, 2019, repealed the MDET. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to reduce the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The effect that the ACA and its possible repeal and replacement may have on our business remains unclear.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2027 unless additional congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, the Middle Class Tax Relief and Job Creation Act of 2012 required that the Centers for Medicare & Medicaid Services, or CMS, the agency responsible for administering the Medicare program, reduce the Medicare clinical laboratory fee schedule by 2% in 2013, which served as a base for 2014 and subsequent years. In addition, effective January 1, 2014, CMS also began bundling the Medicare payments for certain laboratory tests ordered while a patient received services in a hospital outpatient setting. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for any product candidate we develop or complementary diagnostics or companion diagnostics or additional pricing pressures.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

Most recently, the Inflation Reduction Act of 2022 included a number of significant drug pricing reforms, which include the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that requires manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, the establishment of rebate payment requirements on manufacturers under Medicare Parts B and D to penalize price increases that outpace inflation, and a redesign of the Part D benefit, as part of which manufacturers are required to provide discounts on Part D drugs.

Any of these regulatory changes and events could limit our ability to form collaborations and our ability to commercialize our products, and if we fail to comply with any such new or modified regulations and requirements it could adversely affect our business, operating results and prospects.

If we fail to complete the required IRS forms for exemptions, make timely semi-monthly payments of collected excise taxes, or submit quarterly reports as required by the MDET, we may be subject to penalties, such as Section 6656 penalties for any failure to make timely deposits.

Section 4191 of the Internal Revenue Code, enacted by Section 1405 of the Health Care and Education Reconciliation Act of 2010, Public Law 111-152 (124 Stat. 1029 (2010)), in conjunction with the Patient Protection and the ACA, Public Law 111-148 (124 Stat. 119 (2010)), imposed as of January 1, 2013, an excise tax on the sale of certain medical devices. The MDET imposed by Section 4191 is 2.3% of the price for which a taxable medical device is sold within the U.S.

We are a smaller reporting company and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

We are a smaller reporting company, or SRC, and a non-accelerated filer, which allows us to take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not SRCs or non-accelerated filers, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, reduced disclosure obligations, including disclosures regarding executive compensation, in our Annual Report and our periodic reports and proxy statements and providing only two years of audited financial statements in our Annual Report and our periodic reports. We will remain an SRC until (a) the aggregate market value of our outstanding common stock held by non-affiliates as of the last business day our most recently completed second fiscal quarter exceeds $250 million or (b) in the event we have over $100 million in annual revenues, and the aggregate market value of our outstanding common stock held by non-affiliates as of the last business day our most recently completed second fiscal quarter exceeds $700 million. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile and may decline.

We incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we incur significant legal, accounting, and other expenses that we did not incur as a private company. These costs generally increase for a company whose shares are listed on the NYSE American or Nasdaq Capital Market as compared to the costs for a company for whose shares are quoted on the OTCQB Venture Market. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, FINRA rules and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

We continue to evaluate these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

We will likely in the future have assets held at financial institutions that may exceed the insurance coverage offered by the Federal Deposit Insurance Corporation ("FDIC"), the loss of which would have a severe negative affect on our operations and liquidity.

We currently have the majority of our cash and cash equivalents held in deposit at East West Bank. While the amounts held in the deposit accounts as of December 31, 2023 were less than the insurance coverage offered by the FDIC, in the future, we will likely maintain our cash assets at financial institutions in the U.S. in amounts that may be in excess of the FDIC insurance limit of $250,000. Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank, or SVB, was closed by the California Department of Financial Protection and Innovation, which appointed the FDIC as receiver. In the event of a failure or liquidity issue of or at any of these financial institutions where we maintain our deposits or other assets, we may incur a loss, and to the extent such loss exceeds the FDIC insurance limitation it could have a material adverse effect upon our liquidity, financial condition and our results of operations.

Item 1B. ***Unresolved Staff Comments.***

None.

Item 1C. ***Cybersecurity.***

Risk management and strategy

With the assistance of our IT vendor, we established policies and processes for assessing, identifying, and managing material risk from cybersecurity threats and have integrated these processes into our overall risk management systems and processes. We routinely assess material risks from cybersecurity threats, including any potential unauthorized occurrence on or conducted through our information systems that may result in adverse effects on the confidentiality, integrity, or availability of our information systems or any information residing therein. Primary responsibility for assessing, monitoring and managing our cybersecurity risks rests with an information technology (IT) consultant who reports to our Chief Financial Officer, to manage the risk assessment and mitigation process. Our Board of Directors provides oversight to our cybersecurity efforts to ensure effective governance in managing risks associated with cybersecurity threats. Our CFO provides periodic updates to the Board of Directors regarding our cybersecurity program, including information about cyber risk management governance and status updates on various projects intended to enhance the overall cybersecurity posture of the Company.

We conduct periodic risk assessments to identify cybersecurity threats, as well as assessments in the event of a material change in our business practices that may affect information systems that are vulnerable to such cybersecurity threats. These risk assessments include identification of reasonably foreseeable internal and external risks, the likelihood and potential damage that could result from such risks, and the sufficiency of existing policies, procedures, systems, and safeguards in place to manage such risks.

Following these risk assessments, responses may include re-design, implementation, and maintenance of reasonable safeguards to minimize identified risks and address any identified gaps in existing safeguards; and regularly monitoring of the effectiveness of our safeguards.

As part of our overall risk management system, we monitor and test our safeguards and train our employees on these safeguards, in collaboration with IT and management. Personnel at all levels and departments are made aware of our cybersecurity policies through trainings.

We engage consultants, or other third parties in connection with our risk assessment processes. These service providers assist us to design and implement our cybersecurity policies and procedures, as well as to monitor and test our safeguards.

We have not encountered cybersecurity challenges that have materially impaired our operations or financial standing. For additional information regarding risks from cybersecurity threats, please refer to "*Cyber-attacks or other failures in telecommunications or information technology systems and deficiency in our, or those of third parties upon which we rely, cybersecurity could result in information theft, data corruption and significant disruption of our business operations."* under Item 1A, "Risk Factors," in this annual report on Form 10-K.

Governance

One of the key functions of our board of directors is informed oversight of our risk management process, including risks from cybersecurity threats. Our board of directors is responsible for monitoring and assessing strategic risk exposure, and our executive officers are responsible for the day-to-day management of the material risks we face. Our board of directors administers its cybersecurity risk oversight function directly as a whole, as well as through the audit committee.

Our Chief Financial Officer is primarily responsible to assess and manage our material risks from cybersecurity threats with assistance from third-party service providers.

Our Chief Financial Officer oversees our cybersecurity policies and processes, including those described in "Risk Management and Strategy" above. The cybersecurity risk management program includes tools and activities to prevent, detect, and analyze current and emerging cybersecurity threats, and plans and strategies to address threats and incidents.

Item 2. ***Properties.***

On November 1, 2013 we entered into a sublease of approximately 17,000 square feet of mixed-use space of the facility located at 84 October Hill Road, Suite 11, Holliston, Massachusetts, which is our corporate headquarters, from Harvard Bioscience. Our principal facilities incorporate manufacturing, laboratory, development, sales and marketing, and administration functions. We believe our current facilities are adequate for our needs for the foreseeable future.

Item 3. ***Legal Proceedings.***

From time to time, we may be involved in various claims and legal proceedings arising in the ordinary course of business. There are no such matters pending that we expect to be material in relation to our business, financial condition, and results of operations or cash flows.

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

The Company filed an amendment (the "Certificate of Amendment") to its Amended and Restated Certificate of Incorporation (the "Certificate of Incorporation") with the Secretary of State for the State of Delaware to change its name from Biostage, Inc. to Harvard Apparatus Regenerative Technology, Inc. The Company also amended and restated its Amended and Restated Bylaws, solely to reflect the name change (as amended, the "Third Amended and Restated Bylaws"). The Certificate of Amendment and the Third Amended and Restated Bylaws each became effective on July 20, 2023.

In connection with the name change, the Company traded on the OTCQB under the new ticker symbol "HRGN". The new ticker symbol was effective at the open of the market on July 20, 2023. Prior to that time, our common stock traded on the OTCQB under the symbol "BSTG."

There were 140 holders of record of our common stock as of March 18, 2024, which does not include persons or entities that hold their stock in nominee or "street" name through various brokerage firms. We believe that the number of beneficial owners of our common stock at that date was substantially greater.

Dividend Policy

We have never declared or paid cash dividends on our common stock in the past and do not intend to pay cash dividends on our common stock in the foreseeable future. Any future determination to pay cash dividends will be at the discretion of our Board of Directors and will depend on our financial condition, results of operations, capital requirements and other factors our Board of Directors deems relevant.

Recent Sales of Unregistered Securities

During the fiscal year ended December 31, 2023, all of our unregistered sales were previously disclosed in our Quarterly Reports on Form 10-Q or in Current Reports on Form 8-K in relation to the applicable periods, which such issuances were done without registration under the Securities Act in reliance on the exemptions provided by Section 4(a)(2) of the Securities Act as transactions not involving a public offering and Rule 506 promulgated under the Securities Act as sales to an accredited investor, and in reliance on similar exemptions under applicable state laws.

Item 6. ***Selected Financial Data.***

Not Applicable.

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

Forward-Looking Statements

The following section of this Annual Report on Form 10-K entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" contains statements that are not statements of historical fact and are forward-looking statements within the meaning of federal securities laws. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties.

In some cases, you can identify forward-looking statements by terms such as "believe," "may," "estimate," "continue," "anticipate," "intend," "should," "could," "would," "target," "seek," "aim," "believe," "predicts," "think," "objectives," "optimistic," "new," "goal," "strategy," "potential," "is likely," "will," "expect," "plan" "project," "permit" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events, are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail in Item 1A."Risk Factors" of this Annual Report on Form 10-K. You should carefully review all of these factors, as well as the comprehensive discussion of forward-looking statements on page ii of this Annual Report on Form 10-K.

Overview

We are a clinical-stage biotechnology company focused on the development of regenerative medicine treatments for disorders of the gastro-intestinal system and other organs that result from cancer, trauma or birth defects.

We believe that our technology represents a next generation solution for restoring organ function because it allows the patient to regenerate their own organ, thus eliminating the need for human donor or animal transplants, the sacrificing of another of the patient's own organs or permanent artificial implants.

Our first esophageal product candidate, our esophageal implant was used in the first successful regeneration of the esophagus in a patient with esophageal cancer. This successful first-in-human experience, plus the research we have performed on over 50 pigs, led the FDA to approve our 10-patient phase 1 clinical trial. This combination trial will measure both safety and efficacy in the patient population.

We have contracted with IQVIA, a leading global provider of advanced analytics, technology solutions and clinical research services to the life sciences industry, as the contract research organization (CRO) to manage our first clinical trial. We activated the first clinical trial site and started screening patients in the third quarter of 2023. Our product candidates are currently in development and have not yet received regulatory approval for sale anywhere in the world.

In addition to our development of regenerative medicine treatments, we also sell longevity dietary supplements. In the second quarter of 2023, the Company's subsidiary in Hong Kong, Harvard Apparatus Regenerative Technology Limited, or Longevity Products, started focusing on longevity products. Longevity Products plans to include a broad range of products focused on personal healthcare including longevity dietary supplements. Longevity Products started selling longevity supplements in the third quarter of 2023. These products are marketed to the general public and initially targeted at consumers in the Great China Region through eCommerce (online sales).

We were incorporated and commenced operations on November 1, 2013 as a result of a spin-off from Harvard Bioscience, Inc., or Harvard Bioscience. On that date, we became an independent company that operates the regenerative medicine business previously owned by Harvard Bioscience. The spin-off was completed through the distribution of all the shares of common stock of Harvard Apparatus Regenerative Technology to Harvard Bioscience stockholders.

We continue to assess the market and regulatory approval pathway in China as to our implant products. We are not certain at this time as to which market, including U.S. or China for example, may provide the most viable initial pathway for regulatory approval to a commercial product. This will depend on a number of factors, including the approval and development processes, related costs, ability to raise capital and the terms and conditions thereof, among other factors. Any development and capital raising efforts in China may include a joint venture in relation to our Hong Kong subsidiary, and would also involve a number of commercial variables, including rights and obligations pertaining to licensing, development, and financing, among others. Our failure to receive or obtain such clearances or approvals on a timely basis or at all, whether that be in the U.S., China or otherwise, would have an adverse effect on our results of operations.

Since our incorporation, we have devoted substantially all of our resources to developing our programs, building our intellectual property portfolio, business planning, raising capital and providing selling, general and administrative support for these operations. To date, we have financed our operations with proceeds from the sales of common stock and preferred stock. In December 2017, we sold the inventory and rights to manufacture and sell research-only versions of our bioreactors to Harvard Bioscience.

We have incurred substantial operating losses since our inception, and as of December 31, 2023 had an accumulated deficit of approximately $92.0 million and will require additional financing to fund future operations. We expect that our operating cash on-hand as of December 31, 2023 of approximately $0.4 million and debt financing of $0.5 million received in gross proceeds subsequent to December 31, 2023 will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2024. We expect to continue to incur operating losses and negative cash flows from operations in future years. Therefore, as disclosed in Note 1 to our Consolidated Financial Statements, these conditions raise substantial doubt about our ability to continue as a going concern.

We will need to raise additional funds to fund our operations. In the event we do not raise additional capital from outside sources during the first quarter of 2024, we may be forced to curtail or cease our operations. Cash requirements and cash resource needs will vary significantly depending upon the timing of the financial and other resource needs that will be required to complete ongoing development, pre-clinical and clinical testing of product candidates, as well as regulatory efforts and collaborative arrangements necessary for our products that are currently under development. We are currently seeking and will continue to seek financings from other existing and/or new investors to raise necessary funds through a combination of public or private equity offerings. We may also pursue debt financings, other financing mechanisms, research grants, or strategic collaborations and licensing arrangements. We may not be able to obtain additional financing on favorable terms, if at all.

Our operations will be adversely affected if we are unable to raise or obtain needed funding and may materially affect our ability to continue as a going concern. Our consolidated financial statements have been prepared assuming that we will continue as a going concern and therefore, the consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amount and classifications of liabilities that may result from the outcome of this uncertainty.

Business Segments

The Company has two separate reportable segments. The Company has one segment, Harvard Apparatus Regenerative Technology, Inc., or Regenerative Biotech, focused on the development and commercialization of therapies to cure patients of cancers, injuries, and birth defects of the gastro-intestinal tract and the airways. The other segment, Longevity Products, is focused on personal healthcare including longevity dietary supplements.

2023 Financing Activities

During the year ended December 31, 2023, we completed the following financing activities:

- On April 12, 2023 and on March 31, 2023, the Company entered into Securities Purchase Agreements, each a Purchase Agreement, with new and existing investors, the Investors, pursuant to which the Investors purchased in a private placement an aggregate of 1,000,967 shares of common stock for the aggregate purchase price of approximately $6 million with a purchase price per unit of $6.00.

2022 Financing Activities

During the year ended December 31, 2022, we completed the following financing activities:

- In May 2022, we sold 854,771 shares of common stock and warrants to purchase 427,390 shares of common stock for the aggregate purchase price of approximately $5.1 million and a purchase price per unit of $5.92. Each unit consisted of one share of common stock and a warrant to purchase one half of one share of common stock, subject to adjustment as provided in the warrants. The warrants have an exercise price of $8.88 per share, subject to adjustments as provided under the terms thereof, and were immediately exercisable. The warrants are exercisable until five years (5) from the warrant issuance date. In May 2022, we also issued options to acquire 38,564 shares of common stock to satisfy sales commissions in the approximate amount of $155,660 incurred in relation to this private placement.
- In June 2022, the Company issued 4,000 shares of Series E Convertible Preferred Stock at a price of $1,000 per share to satisfy certain indemnification obligations in the amount of $4.0 million, in lieu of paying cash. The Company issued an aggregate of 180 shares of Series E Convertible Preferred Stock relating to accrued dividends during the year ended December 31, 2023.

Management

Effective as of November 26, 2021, we appointed David Green as Chief Executive Officer. Effective as of March 1, 2023, we transitioned the role of Chief Executive Officer to Junli (Jerry) He, our existing director, and Mr. Green remains on our Board of Directors.

On August 8, 2022, we appointed Joseph Damasio Jr. as Chief Financial Officer. In such role, Mr. Damasio serves as the Company's principal accounting officer and principal financial officer.

As of December 31, 2023, our consolidated business employed 18 individuals.

Components of Operating Loss

Product revenue. Product revenue consists of longevity product sales, launched in the Asia region in the third quarter of 2023. We had not generated any revenue prior to the launch of our longevity products.

Research and development expense. Research and development expense consists of salaries and related expenses, including share-based compensation, for personnel and contracted consultants and various materials and other costs to develop our new products, primarily: synthetic scaffolds, including investigation and development of materials and investigation and optimization of cellularization, as well as studies of cells and cell behavior. Other research and development expenses include the costs of outside service providers and material costs for prototype and test units and outside laboratories and testing facilities performing cell growth and materials experiments, as well as the costs of all other preclinical research and testing including animal studies and expenses related to potential patents. We expense research and development costs as incurred.

Sales and marketing expense. Sales and marketing costs include advertising and payroll and related expenses for personnel engaged in marketing and selling activities.

General and administrative expense. General and administrative expense consists primarily of salaries and other related expenses, including share-based compensation. Other costs include professional fees for legal and accounting services, insurance, investor relations and facility costs.

Changes in Fair Value of Warrant Liability. Changes in fair value of warrant liability represent the change in the fair value of outstanding common stock warrants that were classified as liability awards during the year ended December 31, 2022. We used the Black-Scholes pricing model to value the related warrant liability.

Critical Accounting Estimates

Management's 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 Generally Accepted Accounting Principles in the United States (U.S. GAAP). The preparation of these consolidated financial statements requires us to make estimates and assumptions for the reported amounts of assets, liabilities, revenues, expenses and related disclosures. We believe the following policies to be critical to the judgments and estimates used in the preparation of our financial statements.

Share-based Compensation

We account for our share-based compensation in accordance with the fair value recognition provisions of current authoritative guidance. Share-based awards, including stock options, are measured at fair value as of the grant date and recognized as expense over the requisite vesting period (generally the service period), which we recognize on a straight-line basis. Expense on share-based awards for which vesting is performance or milestone based is recognized on a straight-line basis from the date when we determine the achievement of the milestone is probable to the vesting/milestone achievement date. We estimate the fair value of options granted using the Black-Scholes option valuation model. Significant judgment is required in determining the proper assumptions used in these models. The assumptions used include the risk-free interest rate, expected term, expected volatility and expected dividend yield. We base our assumptions on historical data when available or, when not available, on a peer group of companies. However, these assumptions consist of estimates of future market conditions, which are inherently uncertain and subject to our judgment, and therefore any changes in assumptions could significantly impact the future grant date fair value of share-based awards.

Total share-based compensation expense for each of the years ended December 31, 2023 and 2022 was approximately $3.5 million and $1.0 million, respectively. Share-based compensation is further described in Note 15 to our Consolidated Financial Statements included in Item 15 of this Annual Report on Form 10-K.

Warrant Liability

Most of the warrants to purchase shares of our common stock have been classified on our consolidated balance sheets as equity. We classify warrants as a liability in our consolidated balance sheets if the warrant is a free-standing financial instrument that may require us to transfer cash consideration upon exercise and that cash transfer event would be out of our control. Such a "liability warrant" is initially recorded at fair value on the date of grant using the Black-Scholes model, net of issuance costs, and it is subsequently re-measured to fair value at each subsequent balance sheet date. Changes in fair value of the warrant are recognized as a component of other income (expense) in the consolidated statements of operations. We continued to adjust the liability for changes in fair value until the expiration of the warrant liability in February 2022.

Results of Operations

The following table summarizes the results of our operations for the years ended December 31, 2023 and 2022 ($ in thousands):

	Year Ended December 31,		Change 2023 vs. 2022	
	2023	2022	$ Change	%
Product revenue	$ 103	$ —	$ 103	100%
Operating expenses				
Cost of sales	24	—	24	100%
Research and development	3,062	1,742	1,320	76%
Sales and marketing	294	—	294	100%
General and administrative	5,713	4,411	1,302	30%
Total operating expenses	9,093	6,153	2,940	48%
Other income (expense), net				
Sublease income	—	87	(87)	(100)%
Change in fair value of warrant liability	—	2	(2)	(100)%
Interest income	64	—	64	100%
Interest expense	(14)	(9)	(5)	(56)%
Other expense	(5)	—	(5)	(100)%
Total other income, net	45	80	(35)	(44)%
Net loss	$ (8,945)	$ (6,073)	$ 2,872	47%

Year Ended December 31, 2023 Compared to Year Ended December 31, 2022

Product Revenue

Product revenue was $103,000 and zero for the year ended December 31, 2023 and 2022, respectively. Product revenue consists of longevity product sales launched in the Asia region in the third quarter of 2023. We had not generated any revenue prior to the launch of our longevity products.

Cost of Sales

Cost of sales was $24,000 and zero for the year ended December 31, 2023 and 2022, respectively. Cost of sales consists of the purchase price of consumer products, taxes, inbound and outbound shipping costs.

Research and Development Expense

Research and development expense increased approximately $1.3 million, or 76%, to approximately $3.1 million for the year ended December 31, 2023 as compared to approximately $1.7 million for the year ended December 31, 2022. This was due primarily to higher headcount and preclinical trial activities to increase our product pipeline and clinical trial activities resulting in our first site activation in the third quarter of 2023.

Sales and Marketing Expense

Longevity Products launched its longevity products business in the second quarter of 2023 so there were no prior period costs. Selling and marketing expense was $0.3 million for the year ended December 31, 2023 as compared to zero for the comparable period.

General and Administrative Expense

General and administrative expense increased approximately $1.3 million, or 30%, to approximately $5.7 million for the year ended December 31, 2023 as compared to approximately $4.4 million for the year ended December 31, 2022. This increase was primarily due to share-based compensation expense of $2.4 million and increased headcount related costs of approximately $0.6 million offset by a decrease of approximately $0.4 million for supporting our ongoing public company requirements and reduced legal and related costs of approximately $1.3 million relating to the completion of litigation for a wrongful death complaint and related matters more fully described in Note 9 to our consolidated financial statements.

Sublease Income

On January 5, 2022, the Company executed a four-month sublease agreement for certain laboratory and office space at its Holliston, Massachusetts facility. The Company further extended the sublease agreement to a month-to-month basis until August 31, 2022, when the other party vacated the premises. For the year ended December 31, 2022, the Company recorded sublease income of approximately $87,000 relating to this agreement. We had no sublease agreements generating sublease income for the year ended December 31, 2023.

Change in Fair Value of Warrant Liability

For the year ended December 31, 2022, the change in fair value of our warrant liability resulted in other income of approximately $2,000. These warrants expired unexercised in February of 2022.

Interest income

During the year ended December 31, 2023, we recorded interest income of approximately $64,000 earned from our money market account and certificate of deposit. During the year ended December 31, 2022, we received minimal interest income from cash accounts.

Interest expense

During the year ended December 31, 2023, we recorded interest expense of approximately $14,000 on insurance installment payments. During the year ended December 31, 2022, we recorded interest expense of approximately $9,000 on insurance installment payments.

Liquidity and Capital Resources

Sources of Liquidity. We have incurred operating losses since inception and as of December 31, 2023, we had an accumulated deficit of approximately $92.0 million. We are currently investing significant resources in the development and commercialization of our product candidates for use by clinicians and researchers in the field of regenerative medicine. As a result, we expect to incur operating losses and negative operating cash flows for the foreseeable future.

Operating Activities. Net cash used in operating activities of approximately $6.9 million for the year ended December 31, 2023 was due primarily to our net loss of approximately $8.9 million offset by adjustments for non-cash items of approximately $3.6 million due to non-cash expenses for share-based compensation, depreciation and amortization, and an approximately $1.6 million decrease to cash from changes in working capital due to the timing of payments for accounts receivable, inventory, prepaid expenses, deferred financing costs, long-term prepaid contracts, accounts payable and accrued expenses.

Net cash used in operating activities of approximately $5.1 million for the year ended December 31, 2022 was primarily a result of our net loss of approximately $6.1 million and $0.6 million for deferred financing costs, offset by approximately $1.1 million of non-cash items related to share-based compensation, depreciation and amortization, and an increase of approximately $0.5 million of cash provided from working capital due to the timing of prepaid expenses, accounts payable, and accrued and other current liabilities.

Investing Activities. Net cash used in investing activities for the years ended December 31, 2023 and 2022 totaled $11,000 and $5,000, respectively, and represented purchases of property, plant and equipment. During the year ended December 31, 2023, we invested in a certificate of deposit for $2.5 million. We withdrew $1.3 million from the certificate of deposit prior to the maturity date to pay clinical trial related deposits. The certificate of deposit matured in October 2023 with the remaining $1.2 million released from short-term investments into cash and cash equivalents.

Financing Activities. Net cash generated from financing activities was approximately $6.1 million during the year ended December 31, 2023 and consisted of net proceeds received from a private placement transaction for the issuance of common stock and stock option exercises. Net cash generated from financing activities was approximately $5.1 million during the year ended December 31, 2022 and consisted of net proceeds received from private placement transactions for the issuance of common stock and warrants to purchase common stock.

We continue to pursue our esophageal program, including advancing to operate as a clinical stage company. Given our current limited cash resources, we intend to closely monitor our cash expenses as such cash resources are expected to only allow us to meet our operating needs into the second quarter of 2024.

We have incurred substantial operating losses since our inception, and as of December 31, 2023 had an accumulated deficit of approximately $92.0 million and will require additional financing to fund future operations. We expect that our operating cash on-hand as of December 31, 2023 of approximately $0.4 million and debt financing of $0.5 million received in gross proceeds subsequent to December 31, 2023 will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2024. We expect to continue to incur operating losses and negative cash flows from operations in future years. Therefore, as disclosed in Note 1 to our Consolidated Financial Statements, these conditions raise substantial doubt about our ability to continue as a going concern.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable Securities and Exchange Commission rules.

Item 7A. ***Quantitative and Qualitative Disclosures about Market Risk.***

Not Applicable.

Item 8. ***Financial Statements and Supplementary Data.***

The information required by this item is contained in the consolidated financial statements filed as part of this Annual Report on Form 10-K listed under Item 15 of Part IV below.

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

None.

Item 9A. ***Controls and Procedures.***

This Annual Report on Form 10-K includes the certifications of our principal executive officer and principal financial officer required by Rule 13a-14 of the Securities Exchange Act of 1934, as amended, or the Exchange Act. See Exhibits 31.1 and 31.2. This Item 9A includes information concerning the controls and control evaluations referred to in those certifications.

(a) Evaluation of Disclosure Controls and Procedures

Disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) are designed to ensure that information required to be disclosed in reports filed or submitted under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in Securities and Exchange Commission's rules and forms and that such information is accumulated and communicated to management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosures. Based on the evaluation, our principal executive and principal financial officers concluded that, as of December 31, 2023, our disclosure controls and procedures were effective.

In connection with the preparation of this Annual Report on Form 10-K, our management, under the supervision and with the participation of our principal executive officer and principal financial officer, conducted an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as of December 31, 2023. Our disclosure controls and procedures are designed to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms, and our management necessarily was required to apply its judgment in evaluating and implementing our disclosure controls and procedures. Based upon the evaluation described above, our principal executive officer and principal financial officer have concluded that they believe that our disclosure controls and procedures were effective, as of the end of the period covered by this report, in providing reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosures, and is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms.

(b) Management's Annual Report on Internal Control Over Financial Reporting

Our management, under the supervision of the principal executive officer and the principal financial officer, is responsible for establishing and maintaining an adequate system of internal control over financial reporting. Internal control over financial reporting (as defined in Rules 13a-15(f) and 15d(f) under the Exchange Act) is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. GAAP.

A company's internal control over financial reporting includes those policies and procedures that: (a) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets; (b) provide reasonable assurance that transactions are recorded as necessary to permit preparation of consolidated financial statements in accordance with U.S. GAAP; (c) provide reasonable assurance that receipts and expenditures are being made only in accordance with appropriate authorization of management and the Board of Directors; and (d) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on the consolidated financial statements.

Due to its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, 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.

In connection with the preparation of this Annual Report on Form 10-K, our management conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2023 based on the criteria established in *Internal Control - Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO. As a result of that evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2023.

As a smaller reporting company, we are exempt from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002. As a result, Marcum LLP, our independent registered public accounting firm, has not audited or issued an attestation report with respect to the effectiveness of our internal control over financial reporting as of December 31, 2023.

(c) Changes in Internal Controls Over Financial Reporting

Our management, with the participation of the principal executive officer and the principal financial officer, has evaluated whether any change in our internal control over financial reporting occurred during the fourth quarter ended December 31, 2023. Except as noted above, management concluded that there were no changes in our internal controls over financial reporting during the quarter ended December 31, 2023 that materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

(d) Inherent Limitations on Effectiveness of Controls

The design of any system of control is based upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated objectives under all future events, no matter how remote, that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may not deteriorate. Because of their inherent limitations, systems of control may not prevent or detect all misstatements. Accordingly, even effective systems of control can provide only reasonable assurance of achieving their control objectives.

Item 9B. ***Other Information.***

None.

PART III

Item 10. ***Directors, Executive Officers and Corporate Governance.***

Incorporated by reference to our definitive Proxy Statement to be filed pursuant to Regulation 14A under the Exchange Act, in connection with our 2024 Annual Meeting of Stockholders. Information concerning executive officers of our company is included in Part I of this Annual Report on Form 10 K as Item 1. Business - Information about our Executive Officers and incorporated herein by reference.

Item 11. ***Executive Compensation.***

Incorporated by reference to our definitive Proxy Statement to be filed pursuant to Regulation 14A under the Exchange Act, in connection with our 2024 Annual Meeting of Stockholders.

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

Incorporated by reference to our definitive Proxy Statement to be filed pursuant to Regulation 14A under the Exchange Act, in connection with our 2024 Annual Meeting of Stockholders.

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

Incorporated by reference to our definitive Proxy Statement to be filed pursuant to Regulation 14A under the Exchange Act, in connection with our 2024 Annual Meeting of Stockholders.

Item 14. ***Principal Accounting Fees and Services.***

Our independent public accounting firm is Marcum LLP, Boston, Massachusetts, PCAOB Auditor ID 688.

Incorporated by reference to our definitive Proxy Statement to be filed pursuant to Regulation 14A under the Exchange Act, in connection with our 2024 Annual Meeting of Stockholders.

PART IV

Item 15. ***Exhibits, Financial Statement Schedules.***

(a) Documents Filed. The following documents are filed as part of this Annual Report on Form 10-K:

(1) Financial Statements. The consolidated financial statements of Harvard Apparatus Regenerative Technology, Inc. and its subsidiaries filed under this Item 15:

(2) Financial Statement Schedules: None. Financial statement schedules have been omitted since the required information is included in our consolidated financial statements contained elsewhere in this Annual Report on Form 10-K.

(3) Exhibits. The exhibits listed in the accompanying Exhibit Index are filed as a part of this Annual Report on Form 10-K.

(b) Exhibits: The exhibits listed in the accompanying Exhibit Index are filed as a part of this Annual Report on Form 10-K.

(c) Separate Financial Statements and Schedules: None. Financial statement schedules have been omitted since the required information is included in our consolidated financial statements contained elsewhere in this Annual Report on Form 10-K.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS
HARVARD APPARATUS REGENERATIVE TECHNOLOGY, INC.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and Board of Directors of
Harvard Apparatus Regenerative Technology, Inc. and Subsidiaries

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Harvard Apparatus Regenerative Technology, Inc. and Subsidiaries (the "Company") (formerly known as Biostage, Inc.) as of December 31, 2023 and 2022, the related consolidated statements of operations, changes in stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2023, 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, 2023 and 2022, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2023, in conformity with accounting principles generally accepted in the United States of America.

Explanatory Paragraph – Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As more fully described in Note 1, the Company has suffered recurring losses from operations, has an accumulated deficit, uses cash flows in its operations, and will require additional financing to continue to fund its operations. These conditions raise substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated 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 audits 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 Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Share-Based Compensation – Performance-Based Awards

Description of the Matter

As described in Note 14 to the consolidated financial statements, the Company has 773,195 unvested performance-based options outstanding for which there is unrecognized compensation expense of approximately $2.8 million at December 31, 2023. No expense has been recognized for these unvested awards as of December 31, 2023 given that the milestone achievements for these awards have not yet been deemed probable for accounting purposes. As described in Note 2 to the consolidated financial statements, the Company measures all stock options and restricted stock awards granted to employees, directors and non-employees based on the fair value on the date of the grant and recognizes compensation expense of those awards, net of estimated forfeitures, over the requisite vesting period. Expense on share-based awards for which vesting is performance or milestone based is recognized on a straight-line basis from the date when it is determined that the achievement of the milestone is probable to the vesting/milestone achievement date.

We identified the Company's expense recognition for share-based awards that contain performance-based vesting provisions as a critical audit matter. The principal considerations for our determination that the expense recognition for share-based awards that contain performance-based vesting provision awards is a critical audit matter are the assumptions and risk of bias related to the conclusion of the probability of achievement of the performance conditions impacting vesting of the awards, or more specifically, the achievement of the business milestones, as defined in the grant agreements. Auditing management's assumptions regarding the probability of achievement of the business milestones defined in the grant agreements was complex and required a high degree of auditor judgment and increased audit effort.

How We Addressed the Matter in Our Audit

Our audit procedures related to the expense recognition of share-based awards that contain performance-based vesting provisions included the following, among others, (i) obtaining and analyzing the grant agreements for outstanding share-based awards with performance-based vesting provisions, (ii) recalculated the total outstanding share-based awards with performance-based vesting provisions at year-end based upon cumulative grants, net of cumulative forfeitures, and (iii) discussed with management and evaluated their conclusions reached on the probability of achievement of the business milestones within the performance based awards by assessing the Company's liquidity requirements needed to fund the achievement of the milestones outlined in the grant agreements and reviewed the Company's public press releases through the issuance date of these financials.

Marcum LLP

We have served as the Company's auditor since 2022.

Boston, MA
March 28, 2024

(PCAOB ID # 688)

HARVARD APPARATUS REGENERATIVE TECHNOLOGY, INC. AND SUBSIDIARIES
CONSOLIDATED BALANCE SHEETS
(*In thousands, except share and par value data*)

	December 31, 2023	December 31, 2022
ASSETS		
Current assets:		
Cash and cash equivalents	$ 432	$ 1,241
Accounts receivable	4	—
Inventory	50	—
Prepaid research and development	210	274
Prepaid expenses and other current assets	87	79
Total current assets	783	1,594
Property, plant and equipment, net	25	49
Right-of-use assets, net	48	147
Deferred financing costs	544	610
Long-term prepaid contracts	1,214	—
Total assets	$ 2,614	$ 2,400
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 445	$ 682
Accrued and other current liabilities	475	582
Operating lease liability, current	48	99
Total current liabilities	968	1,363
Operating lease liability, net of current portion	—	48
Total liabilities	968	1,411
Commitments and contingencies (Note 9)		
Series E convertible preferred stock, par value $0.01 per share, 5,000 shares authorized; 0 and 4,180 shares issued and outstanding at December 31, 2023 and 2022, respectively	—	4,180
Stockholders' equity (deficit):		
Common stock, par value $0.01 per share, 60,000,000 shares authorized; 13,947,324 and 12,174,467 issued and outstanding at December 31, 2023 and 2022, respectively	139	122
Additional paid-in capital	93,463	79,698
Accumulated deficit	(91,956)	(83,011)
Total stockholders' equity (deficit)	1,646	(3,191)
Total liabilities and stockholders' equity (deficit)	$ 2,614	$ 2,400

See accompanying notes to consolidated financial statements.

HARVARD APPARATUS REGENERATIVE TECHNOLOGY, INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except share and per share data)

	Year Ended December 31,	
	2023	**2022**
Product revenue	$ 103	$ —
Operating expenses:		
Cost of sales	24	—
Research and development	3,062	1,742
Sales and marketing	294	—
General and administrative	5,713	4,411
Total operating expenses	9,093	6,153
Operating loss	(8,990)	(6,153)
Other income (expense), net:		
Sublease income	—	87
Change in fair value of warrant liability	—	2
Interest income	64	—
Interest expense	(14)	(9)
Other expense	(5)	—
Total other income, net	45	80
Net loss	(8,945)	(6,073)
Preferred stock dividends	(77)	(180)
Net loss attributable to common stockholders	$ (9,022)	$ (6,253)
Basic and diluted net loss per share attributable to common stockholders	$ (0.67)	$ (0.55)
Weighted average common shares outstanding, basic and diluted	13,455,666	11,349,610

See accompanying notes to consolidated financial statements.

HARVARD APPARATUS REGENERATIVE TECHNOLOGY, INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except share data)

	Series E Convertible Preferred Stock	Number of Common Shares Outstanding	Common Stock	Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance at January 1, 2022	$ —	10,760,871	$ 108	$ 73,801	$ (76,938)	$ (3,029)
Net loss	—	—	—	—	(6,073)	(6,073)
Share-based compensation	—	—	—	1,031	—	1,031
Issuance of series E convertible preferred stock	4,000	—	—	—	—	—
Preferred stock dividends	180	—	—	(180)	—	(180)
Issuance of common stock and warrants to purchase common stock	—	854,771	8	5,052	—	5,060
Issuance of common stock from exercise of warrants	—	558,825	6	(6)	—	—
Balance at December 31, 2022	4,180	12,174,467	122	79,698	(83,011)	(3,191)
Net loss	—	—	—	—	(8,945)	(8,945)
Share-based compensation	—	—	—	3,461	—	3,461
Conversion of preferred stock for common stock	(4,257)	706,626	7	4,250	—	4,257
Preferred stock dividends	77	—	—	(77)	—	(77)
Issuance of common stock	—	1,000,967	10	5,982	—	5,992
Issuance of common stock from exercise of options	—	65,264	—	149	—	149
Balance at December 31, 2023	$ —	13,947,324	$ 139	$ 93,463	$ (91,956)	$ 1,646

See accompanying notes to consolidated financial statements.

HARVARD APPARATUS REGENERATIVE TECHNOLOGY, INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year ended December 31,	
	2023	**2022**
OPERATING ACTIVITIES		
Net loss	$ (8,945)	$ (6,073)
Adjustments to reconcile net loss to net cash and cash equivalents used in operating activities:		
Share-based compensation expense	3,461	1,031
Depreciation	35	52
Amortization of operating right-of-use assets	99	22
Change in fair value of warrant liability	—	(2)
Changes in operating assets and liabilities:		
Accounts receivable	(4)	—
Inventory	(50)	—
Prepaid research and development	64	(274)
Prepaid expenses and other current assets	(8)	216
Deferred financing costs	66	(610)
Long-term prepaid contracts	(1,214)	—
Accounts payable	(237)	6
Operating lease liability	(99)	(22)
Accrued and other current liabilities	(107)	548
Net cash used in operating activities	(6,939)	(5,106)
INVESTING ACTIVITIES		
Purchases of short-term investments	(2,523)	—
Redemption of short-term investments	2,523	—
Purchases of property, plant and equipment	(11)	(5)
Net cash used in investing activities	(11)	(5)
FINANCING ACTIVITIES		
Proceeds from issuance of common stock	5,992	5,060
Proceeds from exercise of stock options	149	—
Net cash provided by financing activities	6,141	5,060
Net decrease in cash and cash equivalents	(809)	(51)
Cash and cash equivalents at the beginning of the year	1,241	1,292
Cash and cash equivalents at the end of the year	$ 432	$ 1,241
SUPPLEMENTAL INFORMATION		
Interest paid in cash	$ 14	$ 9
Supplemental disclosure of non-cash activities:		
Settlement of contingency matter	$ —	$ (3,250)
Settlement of due to Harvard Bioscience included in accrued and other current liabilities	$ —	$ (750)
Issuance of Series E convertible preferred stock	$ —	$ 4,000
Preferred stock dividends	$ 77	$ 180
Increase of right-of-use asset and liability due to lease extension	$ —	$ 63

See accompanying notes to consolidated financial statements.

1. Organization

Overview

Harvard Apparatus Regenerative Technology, Inc. (Harvard Apparatus Regenerative Technology or the Company) is a biotechnology company with a mission to cure patients of cancers, injuries, and birth defects of the gastro-intestinal tract and the airways. The Company believes its technology is likely to be used to treat esophageal cancer, esophageal injuries, and birth defects in the esophagus. The Company believes additional product candidates in its pipeline may treat intestinal cancer and colon cancer. Since inception, the Company has devoted substantially all of its efforts to business planning, research and development, recruiting management and technical staff, and acquiring operating assets.

On October 31, 2013, Harvard Bioscience, Inc., or Harvard Bioscience, contributed its regenerative medicine business assets, plus $15 million of cash, into Harvard Apparatus Regenerative Technology, or the Separation. On November 1, 2013, the spin-off of the Company from Harvard Bioscience was completed. On that date, the Company became an independent company that operates the regenerative medicine business previously owned by Harvard Bioscience. The spin-off was completed through the distribution to Harvard Bioscience stockholders of all the shares of common stock of Harvard Apparatus Regenerative Technology, or the Distribution.

Basis of Presentation

The consolidated financial statements reflect the Company's financial position, results of operations and cash flows in conformity with generally accepted accounting principles in the United States, or U.S. GAAP.

Going Concern

The Company has incurred substantial operating losses since its inception, and as of December 31, 2023 had an accumulated deficit of approximately $92.0 million and will require additional financing to fund future operations. The Company expects that its operating cash on-hand as of December 31, 2023 of approximately $0.4 million and debt financing of $0.5 million in gross proceeds received subsequent to December 31, 2023 will enable it to fund its operating expenses and capital expenditure requirements only into the second quarter of 2024. Therefore, these conditions raise substantial doubt about the Company's ability to continue as a going concern.

The Company will need to raise additional funds to fund its operations. In the event the Company does not raise additional capital from outside sources during the first quarter of 2024, it may be forced to curtail or cease its operations. Cash requirements and cash resource needs will vary significantly depending upon the timing of the financial and other resource needs that will be required to complete ongoing development, pre-clinical and clinical testing of product candidates, as well as regulatory efforts and collaborative arrangements necessary for the Company's product candidates that are currently under development. The Company is currently seeking and will continue to seek financings from other existing and/or new investors to raise necessary funds through a combination of public or private equity offerings. The Company may also pursue debt financings, other financing mechanisms, research grants, or strategic collaborations and licensing arrangements. The Company may not be able to obtain additional financing on favorable terms, if at all.

The Company's operations will be adversely affected if it is unable to raise or obtain needed funding and may materially affect the Company's ability to continue as a going concern. The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern and therefore, the consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amount and classifications of liabilities that may result from the outcome of this uncertainty.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The consolidated financial statements include the accounts of Harvard Apparatus Regenerative Technology, Inc. (Regenerative Biotech) and its three wholly-owned subsidiaries, Harvard Apparatus Regenerative Technology Limited (Hong Kong), Harvard Apparatus Regenerative Technology (Hangzhou) Limited (China) and Harvard Apparatus Regenerative Technology GmbH (Germany). All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The process of preparing consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Such estimates include, but are not limited to, share-based compensation, valuation of warrant liability, accrued expenses and the valuation allowance for deferred income taxes. Actual results could differ from those estimates.

Revenue

We recognize revenue in accordance with FASB ASC 606, *Revenue from Contracts with Customers*. We offer consumer products primarily through a third-party online store. Revenue is recognized at a point in time when control of the goods is transferred to the customer, which generally occurs upon the delivery to the customer. For any company direct sales to customers, revenue is recognized at a point in time upon shipment of product or hand-delivery to customer. Revenue also excludes any amounts collected on behalf of third parties, including sales and indirect taxes.

We identify a performance obligation as distinct if both the following criteria are true: the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer and the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract. Determining the standalone selling price ("SSP") and allocation of consideration from a contract to the individual performance obligations, and the appropriate timing of revenue recognition, is the result of significant qualitative and quantitative judgments. Management considers a variety of factors such as historical sales, usage rates, costs, and expected margin, which may vary over time depending upon the unique facts and circumstances related to each performance obligation in making these estimates. While changes in the allocation of the SSP between performance obligations will not affect the amount of total revenue recognized for a particular contract, any material changes could impact the timing of revenue recognition, which would have a material effect on our financial position and result of operations. This is because the contract consideration is allocated to each performance obligation, delivered or undelivered, at the inception of the contract based on the SSP of each distinct performance obligation.

Cost of Sales

Cost of sales primarily consists of the purchase price of consumer products, taxes, inbound and outbound shipping costs. Shipping costs to receive products from our suppliers are recognized as cost of sales when incurred. E-commerce processing and related transaction costs, including those associated with seller transactions, are classified in sales and marketing on our consolidated statements of operations.

Research and Development

Research and development costs are expensed as incurred.

Sales and Marketing

Sales and marketing costs include advertising and payroll and related expenses for personnel engaged in marketing and selling activities.

General and Administrative

General and administrative expenses primarily consist of costs for corporate functions, including payroll and related expenses; facilities and equipment expenses, such as depreciation and amortization expense and rent; and professional fees.

Segment Information

The Company manages its operations as two separate operating segments for the purposes of assessing performance and making operating decisions. The Company has one operating unit focused on the development and commercialization of therapies to cure patients of cancers, injuries, and birth defects of the gastro-intestinal tract and the airways. The other operating unit is focused on personal healthcare through longevity dietary supplements. We have determined that our chief executive officer is the chief operating decision maker (CODM). The CODM reviews financial information presented by operating unit. Resource allocation decisions are made by the CODM based on operating unit results.

Cash and Cash Equivalents

The Company considers all highly liquid investments with a maturity of three months or less at the date of purchase to be cash equivalents. The Company currently invests available cash in money market funds. As of December 31, 2023, the Company had approximately $111,000 of cash equivalents in a money market fund.

Accounts Receivable

Allowances are provided for estimated amounts of accounts receivable which may not be collected. At December 31, 2023, we determined that no allowance against accounts receivable was necessary.

Inventory

Inventory, consisting of products available for sale, are primarily accounted for using the first-in, first-out method, and are valued at the lower of cost or net realizable value.

We maintain ownership of our inventory at the third-party warehouse, regardless of whether fulfillment is provided by us or the third-party e-commerce seller, and therefore these products are included in our inventories.

Deferred Financing Costs

We capitalized costs relating to a registered offering that we postponed in 2023 but expect to resume in the near future. The costs include payments made to attorneys, accountants, regulators and consultants. Once we complete the registered offering, the deferred financing costs will be reclassified to stockholders' equity (deficit) on the consolidated balance sheets to offset the proceeds from the registered offering.

Long-term prepaid contracts

We have contracted with partners relating to our clinical trial activities. Upon execution of the contracts, we made initial payments of $1.2 million as deposits recorded as long-term assets and will be applied against final invoices which are more than a year away. The deposits will be recorded as expense when the clinical trial is substantially completed. Costs for the clinical trial activities throughout our clinical trial under these contracts are recognized as expense and payable based on costs incurred.

Property, Plant and Equipment

Property, plant and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the assets as follows:

Leasehold improvements	Shorter of expected useful life or lease term
Computer equipment and software	3 years
Furniture, machinery and equipment	5-7 years

Maintenance and repairs are charged to expense as incurred, while any additions or improvements are capitalized.

Impairment of Long-Lived Assets

Assessments of long-lived assets and the remaining useful lives of such long-lived assets are reviewed for impairment whenever a triggering event occurs or changes in circumstances indicate that the carrying amount of the assets may not be recoverable. An asset, or group of assets, are considered to be impaired when the undiscounted estimated net cash flows expected to be generated by the asset, or group of assets, are less than its carrying amount. The impairment recognized is the amount by which the carrying amount exceeds the fair market value of the impaired asset, or group of assets, based on the present value of the expected future cash flows associated with the use of the asset. Through December 31, 2023, no such impairment charges have been recorded.

Share-based Compensation

The Company measures all stock options and restricted stock awards granted to employees, directors and non-employees based on the fair value on the date of the grant and recognizes compensation expense of those awards, net of forfeitures, over the requisite vesting period, which is generally the service period of the respective award. Generally, the Company issues stock options and restricted stock awards with only service-based vesting conditions on a straight-line basis over the requisite service period for the entire award (that is, over the requisite service period of the last separately vesting portion of the award). Expense on share-based awards for which vesting is performance or milestone based is recognized on a straight-line basis from the date when it is determined that the achievement of the milestone is probable to the vesting/milestone achievement date.

The Company elected to use the Black-Scholes option-pricing model for the valuation of stock-based payment awards. The determination of the fair value of stock-based payment awards is determined on the date of grant using the Black-Scholes option-pricing model which is affected by the market price as well as assumptions regarding a number of subjective variables. These variables include, but are not limited to, its expected stock price volatility over the term of the awards and actual and projected employee stock option exercise behaviors. When performance-based grants are issued, the Company recognizes no expense until achievement of the performance requirement is deemed probable.

Share-based compensation expense is based on awards ultimately expected to vest and has been reduced for annualized estimated forfeiture where the minimum amount of expense recorded is at least equal to the percent of an award vested. Forfeitures are estimated based on historical experience and weighting of various employee classes under the respective plan at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Until December 31, 2022, we estimated forfeitures at the time of grant and would revise our estimate, if necessary, in subsequent periods. As of January 1, 2023, we account for forfeitures as they occur.

The fair value of Restricted Stock Units, or RSUs, is based on the number of shares granted and market price of the stock on the date of grant and is recorded as compensation expense ratably over the applicable service period, which is generally four years. Unvested restricted stock units and vested and unvested stock options are forfeited in the event of termination of employment.

Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, as well as for operating losses and tax credit carry-forwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to be applied to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. Deferred tax assets and liabilities are recorded net as long-term on the consolidated balance sheets.

Foreign Currency

Assets and liabilities of non-U.S. operations where the functional currency is other than the U.S. dollar are translated from the functional currency into U.S. dollars at year end exchange rates, and revenues and expenses are translated at average rates prevailing during the year. Resulting translation adjustments are accumulated as part of accumulated other comprehensive income. Transaction gains or losses are recognized in income or loss in the period in which they occur. The cumulative translation adjustment for the year ended December 31, 2023 was less than $1,000 and therefore not separately reported on the consolidated financial statements.

A valuation allowance is recorded when it is more likely than not that some or all of the net deferred tax assets will not be realized. Accordingly, the Company provides a valuation allowance, if necessary, to reduce net deferred tax assets to the amount that is expected to be realized.

Tax positions taken or expected to be taken in the course of preparing the Company's tax returns are required to be evaluated to determine whether the tax positions are "more-likely-than-not" of being sustained by the applicable tax authority. Tax positions not deemed to meet a "more-likely-than-not" threshold would be recorded as a tax expense in the current year.

When necessary, the Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss applicable to common stockholders by the weighted-average number of shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting the weighted-average number of shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the diluted net loss per share calculation, warrants to purchase common stock and stock options are considered to be common stock equivalents, but have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share applicable to common stockholders were the same for all periods presented.

Warrant Liability

The Company classifies warrants to purchase shares of its common stock as a liability on its consolidated balance sheets when the warrant is a free-standing financial instrument that may require the Company to transfer cash consideration upon exercise and that cash transfer event would be out of the Company's control. Such a "liability warrant" is initially recorded at fair value on date of grant using the Black-Scholes model and net of issuance costs, and it is subsequently re-measured to fair value at each subsequent balance sheet date. Changes in the fair value of the warrant are recognized as a component of other income (expense), net in the consolidated statements of operations. The Company will continue to adjust the liability for changes in fair value until the earlier of the exercise or expiration of the warrant.

For warrants that do not meet the criteria of a liability warrant and are classified on the Company's consolidated balance sheets as equity instruments, the Company uses the Black-Scholes model to measure the value of the warrants at issuance and then applies the relative fair-value of the equity transaction between common stock, preferred stock and warrants. Common stock and equity-classified warrants each are considered permanent equity.

Concentration of Credit Risk

Financial investments that potentially subject the Company to credit risk consist of cash. The Company has all cash at accredited financial institutions. Bank accounts in the United States are insured by the Federal Deposit Insurance Corporation (FDIC) up to $250,000. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies we adopt as of the specified effective date. Unless otherwise discussed below, we do not believe that the adoption of recently issued standards have or may have a material impact on our consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments (ASU 2016-12)*. The new standard requires that expected credit losses relating to financial assets measured on an amortized cost basis and available-for-sale debt securities be recorded through an allowance for credit losses. It also limits the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and also requires the reversal of previously recognized credit losses if fair value increases. The Company adopted this standard on January 1, 2023, and the adoption of ASU 2016-13 did not have a material impact on its consolidated financial statements.

3. Fair Value Measurements

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date.

The Company utilizes a valuation hierarchy for disclosure of the inputs to the valuations used to measure fair value. This hierarchy prioritizes the inputs into three broad levels as follows. Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities. Level 2 inputs are quoted prices for similar assets and liabilities in active markets or inputs that are observable for the asset or liability, either directly or indirectly through market corroboration, for substantially the full term of the financial instrument. Level 3 inputs are unobservable inputs based on the Company's own assumptions used to measure assets and liabilities at fair value. A financial asset or liability's classification within the hierarchy is determined based on the lowest level input that is significant to the fair value measurement.

The Company had no assets or liabilities classified as Level 2 or Level 3 as of December 31, 2023 and 2022. In 2023, the Company had a certificate of deposit which matured in October 2023 with the remaining $1.2 million released from short-term investments into cash and cash equivalents. The carrying value of financial instruments (consisting of cash, accounts payable, accrued compensation and accrued expenses) is considered to be representative of their respective fair values due to the short-term nature of those instruments.

Investment income is included as interest income in the accompanying consolidated statement of operations for the year ended December 31, 2023.

There were no transfers between Level 1, Level 2 and Level 3 in either of the years ended December 31, 2023 and December 31, 2022.

4. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following:

	December 31,	
	2023	2022
	(in thousands)	
Deposits	$ —	$ 20
Insurance	8	8
Prepaid contracts	79	51
Total prepaid expenses and other current assets	$ 87	$ 79

5. Property, Plant and Equipment, Net

Property, plant and equipment, net consist of the following:

	December 31,	
	2023	2022
	(in thousands)	
Leasehold improvements	$ 35	$ 35
Furniture, machinery and equipment	1,414	1,405
Computer equipment and software	38	36
Total property, plant and equipment	1,487	1,476
Less: accumulated depreciation	(1,462)	(1,427)
Property, plant and equipment, net	$ 25	$ 49

Depreciation expense amounted to approximately $35,000 and $52,000 for the years ended December 31, 2023 and 2022, respectively.

6. Long-term prepaid contracts

We have contracted with partners relating to our clinical trial activities. Upon execution of the contracts, we made initial payments of $1.2 million as deposits recorded as long-term assets and will be applied against final invoices which are more than a year away. The deposits will be recorded as expense when the clinical trial is substantially completed. Costs for the clinical trial activities throughout our clinical trial under these contracts are recognized as expense and payable based on costs incurred.

7. Accrued and Other Current Liabilities

Accrued and other current liabilities consist of the following:

	December 31,	
	2023	2022
	(in thousands)	
Advisory costs	$ 325	$ 300
Legal costs	—	135
Audit services	70	80
Payroll	79	55
Other liabilities	1	12
Total expenses	$ 475	$ 582

8. Warrant Liability

During 2016 and 2017, the Company closed a sale of shares of the Company's common stock, the issuance of warrants to purchase shares of common stock, and the issuance of warrants to the placement agent for each transaction. Due to a cash put provision within the warrant agreement, which could be enacted in certain change in control events, a liability associated with those 1,044,396 warrants were initially recorded at fair value and subsequently re-measured each reporting period. The changes in the fair value between issuance and the end of each reporting period is recorded as a component of other income (expense), net in the consolidated statements of operations.

During 2017, the holders of 952,184 warrants agreed to a modification of the term which removed the cash put provision. The remaining 92,212 warrants continued to be re-measured at each reporting period as long as they were outstanding and un-modified. In February 2022, the remaining 92,212 warrants expired unexercised.

The following table presents a reconciliation of the Company's warrant liabilities for the year ended December 31, 2022:

	Warrant Liability
	(in thousands)
Balance as of January 1, 2022	$ 2
Change in fair value upon re-measurement	(2)
Balance as of December 31, 2022	$ —

9. Commitments and Contingencies

On April 14, 2017, representatives for the estate of an individual plaintiff filed a wrongful death complaint with the Suffolk Superior Court, in the County of Suffolk, Massachusetts, against the Company and other defendants, including Harvard Bioscience, Inc., or HBIO, the former parent of the Company that spun off the Company in 2013, as well as another third party. The complaint sought payment for an unspecified amount of damages and alleged that the plaintiff sustained terminal injuries allegedly caused by products provided by certain of the named defendants and utilized in connection with surgeries performed by third parties in Europe in 2012 and 2013. This lawsuit related to the Company's first-generation trachea scaffold technology for which the Company discontinued development in 2014, and not to the Company's current HRGN Esophageal Implant.

On April 27, 2022, the Company and HBIO executed a settlement with the plaintiffs (the "Settlement"), which resolves all claims relating to the litigation. The Settlement resulted in the dismissal with prejudice of the wrongful death claim, and neither the Company nor HBIO admit any fault or liability in connection with the claim. The Settlement also resolved any and all claims by and between the parties and the Company's product liability insurance carriers, which resulted in the dismissal with prejudice of all claims asserted by or against those carriers, the Company and HBIO.

In relation to the litigation, the Company paid approximately $5.9 million of aggregate costs related to the lawsuit. As of December 31, 2022, all such lawsuit related costs had been paid or otherwise satisfied as provided below. This aggregate amount included the cost of legal and related costs incurred by the Company, which consisted of attorneys' fees and advisor and specialist costs as part of its defense in this matter. On March 3, 2022, the Company received a cash payment of approximately $0.1 million from Medmarc, the Company's insurance carrier. This amount represented a reimbursement of previously incurred legal costs and was recorded as a reduction to general and administrative expenses during the year ended December 31, 2022.

With respect to such $5.9 million of costs described above, the Company was required to either pay such costs directly or indemnify HBIO as to such amounts it incurs. Of such amounts, the Company anticipated that HBIO would pay an aggregate amount of $4.0 million by the end of the second quarter of 2022. With respect to the indemnification obligation of the Company to HBIO pertaining to such costs, the Company and HBIO entered into a Preferred Issuance Agreement dated as of April 27, 2022 (the PIA). In connection with the PIA, the Company and HBIO agreed that once HBIO had paid at least $4.0 million in such costs, to satisfy the Company's indemnification obligations with respect thereto, in lieu of paying cash, the Company would issue senior 8% convertible preferred stock to HBIO that will contain terms as described in the PIA, including the term sheet attached thereto. On June 10, 2022, following the execution of a subscription agreement and HBIO providing evidence of payment of the requisite $4.0 million amount, the Company issued HBIO 4,000 shares of Series E 8% Convertible Preferred Stock at a price of $1,000 per share to satisfy the Company's related indemnification obligations aggregating $4.0 million, which included the accrual for contingency of $3.3 million and approximately $0.8 million of legal and related costs paid on behalf of the Company by HBIO previously included in accrued expenses.

From time to time, the Company may be involved in various claims and legal proceedings arising in the ordinary course of business. Other than the above matter, there are no such matters pending that the Company expects to be material in relation to its business, financial condition, results of operations, or cash flows.

We currently have a co-development initiative with Yale University and the McGowan Institute for Regenerative Medicine at the University of Pittsburgh. We are required to make advance payments of approximately $130,000 and $61,000, respectively at inception of the contracts. We plan to make these advance payments in the second quarter of 2024. The universities started preparatory work in 2023 with substantial work to be done in 2024. Either party can terminate the contract with reasonable notice and any incurred costs will be reimbursed by us to the universities.

10. Leases

The Company leases laboratory and office space and certain equipment with remaining terms ranging from 1 year to 3 years.

The laboratory and office space arrangement is under a sublease that was renewed in December of 2022 and currently extends through May 31, 2024. This lease automatically renews annually for one-year periods unless the Company or the counterparty provides a notice of termination within one hundred and eighty days prior to May 31st of each year.

All of the Company's leases qualify as operating leases. The following table summarizes the presentation of the Company's operating leases in its consolidated balance sheets:

	Balance Sheet Classification	December 31, 2023	December 31, 2022
		(in thousands)	
Assets:			
Operating lease assets	Right-of-use asset, net	$ 48	$ 147
Liabilities:			
Current portion of operating lease liabilities	Current portion of operating lease liabilities	48	99
Operating lease liabilities, net of current portion	Operating lease liabilities, net of current portion	—	48
Total operating lease liabilities		$ 48	$ 147

Cash paid for leases during each of the years ended December 31, 2023 and 2022 amounted to approximately $127,000 and $121,000, respectively.

The weighted average remaining lease terms and weighted average discount rates as of December 31, 2023 and 2022 were as follows:

	Year ended December 31, 2023	Year ended December 31, 2022
Remaining lease term (in years)	0.48	1.43
Discount rate	14.66%	14.74%

The following table summarizes the effect of lease costs in the Company's consolidated statements of operations:

		For the Year Ended December 31, 2023	For the Year Ended December 31, 2022
		(in thousands)	
Operating lease expense	Research and development	$ 68	$ 77
	Sales and marketing	15	—
	General and administrative	44	44
	Total	$ 127	$ 121

The minimum lease payments for the next year is as follows:

	As of December 31, 2023
	(in thousands)
2024	$ 50
Total lease payments	50
Less: imputed interest	(2)
Present value of operating lease liabilities	$ 48

11. Income Taxes

A reconciliation of taxes utilizing the expected federal tax rate of 21% and the effective tax rate is as follows:

	Years ended December 31,	
	2023	**2022**
Computed "expected" income tax benefit	21.0%	21.0%
State income tax benefit, net of federal income tax benefit	6.3%	6.3%
Tax credits	0.6%	0.8%
Change in valuation allowance	(27.9)%	(28.1)%
Total income taxes	—%	—%

The components of the Company's deferred tax assets and liabilities are as follows:

	Years ended December 31,	
	2023	**2022**
	(in thousands)	
Deferred tax assets:		
Operating loss and credit carryforwards	$ 19,167	$ 20,487
Capitalized research and development	1,288	1,083
Stock-based compensation	2,504	1,566
Lease liabilities	13	40
Total deferred tax assets	22,972	23,176
Less: valuation allowance	(22,959)	(23,136)
Deferred tax assets	13	40
Deferred tax liability:		
Operating lease assets	(13)	(40)
Total deferred tax liability	(13)	(40)
	$ —	$ —

The Company has recorded a valuation allowance against its deferred tax assets for the years ended December 31, 2023 and 2022, because the Company's management believes that it is more likely than not that these assets will not be realized. The valuation allowance decreased by approximately $0.2 million for the year ended December 31, 2023 and increased by approximately $2.9 million for the year ended December 31, 2022, respectively, primarily as a result of operating losses generated with no corresponding financial statement benefit.

As of December 31, 2023, the Company had federal net operating loss carryforwards, or NOLs, of approximately $68.7 million to offset future federal taxable income and state NOLs of approximately $68.1 million to offset future state taxable income. The federal and state NOLs generated for annual periods prior to January 1, 2018 begin to expire in 2033. The Company's federal NOL generated for the years ended December 31, 2018 through December 31, 2023, which amount to $42.3 million, can be carried forward indefinitely, however, are limited to be utilized to offset 80% of taxable income in each successive year. As of December 31, 2023, the Company also has federal and state tax research and development credit carryforwards of approximately $1.5 million and $1.0 million, respectively, to offset future income taxes. The federal and state research and development tax credit carryforwards begin to expire in 2033 and 2029, respectively.

Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has recently completed several equity financings transactions which have either individually or cumulatively resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code or could result in a change in control in the future. The Company does not believe the impact of any limitation on the use of its net operating loss or credit carryforwards will have a material impact on the Company's consolidated financial statements since the Company has a full valuation allowance against its net deferred tax assets due to the uncertainty regarding future taxable income for the foreseeable future.

For all years through December 31, 2023, the Company generated research 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 credit carryforwards; however, until a study is completed, and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

Harvard Bioscience received a Supplemental Ruling to the Private Letter Ruling dated March 22, 2013 from the IRS to the effect that, among other things, the Separation and Distribution by Harvard Bioscience will qualify as a transaction that is tax-free for U.S. federal income tax purposes under Section 355 and 368(a)(1)(D) of the Internal Revenue Code continuing in effect. The private letter and supplemental rulings and the tax opinion that Harvard Bioscience received from legal counsel to Harvard Bioscience rely on certain representations, assumptions and undertakings, including those relating to the past and future conduct of the Harvard Apparatus Regenerative Technology business, and neither the private letter and supplemental rulings nor the opinion would be valid if such representations, assumptions and undertakings were incorrect. Moreover, the private letter and supplemental rulings do not address all the issues that are relevant to determining whether the Distribution will qualify for tax-free treatment. Notwithstanding the private letter and supplemental rulings and opinion, the IRS could determine the Distribution should be treated as a taxable transaction for U.S. federal income tax purposes if, among other reasons, it determines any of the representations, assumptions or undertakings that were included in the request for the private letter and supplemental rulings are false or have been violated or if it disagrees with the conclusions in the opinion that are not covered by the IRS ruling.

To preserve the tax-free treatment to Harvard Bioscience of the Separation and Distribution, for the two-year period following the Distribution, which such period ended November 1, 2015, the Company was limited, except in specified circumstances, from entering into certain transactions pursuant to which all or a portion of the Company's stock would be acquired, whether by merger or otherwise; issuing equity securities beyond certain thresholds; repurchasing the Company's common stock; and ceasing to actively conduct the Company's regenerative medicine business. In addition, at all times, including during and following such two-year period, the Company may not take or fail to take any other action that prevents the Separation and Distribution and related transactions from being tax-free.

If the Distribution fails to qualify for tax-free treatment, in general, Harvard Bioscience would be subject to tax as if it had sold the Company's common stock in a taxable sale for its fair market value, and Harvard Bioscience stockholders who received shares of Harvard Apparatus Regenerative Technology common stock in the Distribution would be subject to tax as if they had received a taxable Distribution equal to the fair market value of such shares.

Under the tax sharing agreement between Harvard Bioscience and the Company, the Company would generally be required to indemnify Harvard Bioscience against any tax resulting from the Distribution to the extent that such tax resulted from (i) an acquisition of all or a portion of the Company's stock or assets, whether by merger or otherwise, (ii) other actions or failures to act by the Company, or (iii) any of the Company's representations or undertakings being incorrect or violated. The Company's indemnification obligations to Harvard Bioscience and its subsidiaries, officers and directors are not limited by any maximum amount. If the Company is required to indemnify Harvard Bioscience or such other persons under the circumstances set forth in the tax sharing agreement, the Company may be subject to substantial liabilities.

All deferred tax assets prior to the Separation remained with Harvard Bioscience.

The Company has determined that any uncertain tax positions would have no material impact on the consolidated financial statements of the Company and there are no unrecognized tax benefits or related interest and penalties accrued for the period for the years ended December 31, 2023 and 2022.

The Company is subject to U.S. federal income tax and Massachusetts state income tax. The statute of limitations for assessment by the IRS and state tax authorities is open for all periods from inception through December 31, 2022; currently, no federal or state income tax returns are under examination by the respective taxing authorities.

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security, or CARES, Act was signed into law making several changes to the Internal Revenue Code. The changes include but are not limited to increasing the limitation on the amount of deductible interest expense, allowing companies to carryback certain net operating losses, and increasing the amount of net operating loss carryforwards that corporations can use to offset taxable income. The tax law changes in the CARES Act did not have a material impact on the Company's income tax provision.

12. Employee Benefit Plan

The Company sponsors a retirement plan for its U.S. employees, which includes an employee savings plan established under Section 401(k) of the U.S. Internal Revenue Code, or the 401(k) Plan. The 401(k) Plan covers substantially all full-time employees who meet certain eligibility requirements. Contributions to the retirement plan are at the discretion of management. The Company's matching contributions to the plan were approximately $66,000 and $35,000 for the years ended December 31, 2023 and 2022, respectively.

13. Series E Convertible Preferred Stock

On April 28, 2022, the Company entered into a Preferred Issuance Agreement, or PIA, with Harvard Bioscience, Inc., or HBIO, dated as of April 27, 2022. Pursuant to the PIA, the Company and HBIO agreed that once HBIO has paid at least $4.0 million in certain settlement and related legal expenses, to satisfy the Company's indemnification obligations with respect thereto, in lieu of paying cash, the Company would issue senior convertible preferred stock to HBIO that will contain terms as described in the PIA.

On June 10, 2022, following the execution of a subscription agreement and HBIO providing evidence of payment of the requisite $4.0 million amount, the Company issued HBIO 4,000 shares of Series E Convertible Preferred Stock, or Series E Preferred, at a price of $1,000 per share to satisfy the Company's related indemnification obligations pertaining to the $4.0 million, in lieu of paying cash.

On January 18, 2023, HBIO converted 200 Series E Preferred Shares with accrued dividends of $9,545 into 31,933 shares of common stock.

In connection with the private placement, as of April 12, 2023, the Company had received $6.0 million in aggregate proceeds in such private placement. The private placement resulted in gross proceeds of at least $4.0 million which triggered the mandatory conversion of all the Company's outstanding Series E Preferred Stock and related accrued dividends into shares of common stock at a conversion price of $6.00 per share. The conversion resulted in 674,693 shares of common stock being issued to the holder of the Series E Preferred Stock. Following such conversion, there are no shares of Series E Preferred Stock outstanding.

There were no shares of any of the classes of preferred stock outstanding as of December 31, 2023. There were no changes to authorized shares for the years ending December 31, 2022 and 2023. Authorized shares for each preferred stock class are as follows:

	Authorized
Undesignated Preferred Stock	979,000
Series B Convertible Preferred Stock	1,000,000
Series C Convertible Preferred Stock	4,000
Series D Convertible Preferred Stock	12,000
Series E Convertible Preferred Stock	5,000

14. Common Stock

The Company has 60,000,000 shares authorized as of December 31, 2023 and 40,961,765 shares of common stock available for issuance.

The following represent the Company's common stock transactions during December 31, 2023 and 2022:

2023 Capital Transactions

On April 12, 2023 and on March 31, 2023, the Company entered into Securities Purchase Agreements, each a Purchase Agreement, with new and existing investors, the Investors, pursuant to which the Investors agreed to purchase in a private placement an aggregate of 1,000,967 shares of common stock for the aggregate purchase price of approximately $6 million with a purchase price per unit of $6.00.

2022 Capital Transactions

On May 12, 2022, the Company entered into Securities Purchase Agreements, each a Purchase Agreement, with new and existing investors, the Investors, pursuant to which the Investors agreed to purchase in a private placement an aggregate of 854,771 shares of common stock and warrants to purchase 427,390 shares of common stock, subject to adjustment as provided in the warrant agreement, the Warrants, for the aggregate purchase price of approximately $5.1 million with a purchase price per unit of $5.92, the Private Placement. Each unit consisted of one share of common stock and a warrant to purchase one half of one share of common stock, subject to adjustment, as provided in the Warrants. The Company received an aggregate of $5.1 million gross and net proceeds from the Private Placement by May 16, 2022.

The $5.1 million of gross and net proceeds were allocated $3.6 million and $1.5 million to the common stock and warrants, respectively. The Company classified these warrants on its consolidated balance sheets as equity as the warrants do not have any redemption features nor a right to put for cash that is outside the control of the Company, and valued using the Black-Scholes model based on the following weighted average assumptions:

Risk-free interest rate		2.81%
Expected volatility		127.36%
Expected term		5 years
Expected dividend yield		—
Exercise price	$	8.88
Market value of common stock	$	5.50

In June 2022, the Company issued 4,000 shares of Series E Convertible Preferred Stock at a price of $1,000 per share to satisfy certain indemnification obligations in the amount of $4.0 million, in lieu of paying cash. The Company issued an aggregate of 180 shares of Series E Convertible Preferred Stock relating to accrued dividends during the year ended December 31, 2022.

Warrant to purchase common stock activity for the year ended December 31, 2022 was as follows:

	Amount	Weighted-average exercise price
Outstanding at January 1, 2022	2,501,419	$ 4.35
Issued	427,390	8.88
Exercised	(775,000)	7.17
Expired	(1,040,187)	7.59
Outstanding at December 31, 2022	1,113,622	4.69
Outstanding at December 31, 2023	1,113,622	4.69

There was no warrant activity during the year ended December 31, 2023.

Employee Stock Purchase Plan

The Company maintains the 2013 Employee Stock Purchase Plan, or the ESPP Plan, whereas participating employees can authorize the Company to withhold a portion of their base pay during consecutive six-month payment periods for the purchase of shares of the Company's common stock. At the conclusion of the period, participating employees can purchase shares of the Company's common stock at 85% of the lower of the fair market value of the Company's common stock at the beginning or end of the period. Shares are issued under the plan for the six-month periods ending June 30 and December 31. Under this plan, 7,500 shares of common stock are authorized for issuance of which 4,534 shares have been issued as of December 31, 2023. There are 2,966 shares available for issuance as of December 31, 2023 and December 31, 2022. There was no ESPP Plan activity in 2023 or 2022.

15. Share-based Compensation

Harvard Apparatus Regenerative Technology Amended and Restated Equity Incentive Plan

The Company maintains the Amended and Restated Equity Incentive Plan, or the Plan, for the benefit of certain officers, employees, non-employee directors, and other key persons (including consultants and advisory board members). All options and awards granted under the Plan consist of the Company's shares of common stock. The Company's policy is to issue stock available from its registered but unissued stock pool through its transfer agent to satisfy stock option exercises and the vesting of restricted stock units. The vesting period for awards is generally four years and the contractual life is ten years. Canceled and forfeited options and awards are available to be reissued under the Plan.

As of December 31, 2023, the Company's Plan has 9,098,000 authorized shares to be issued under the Plan. There are 5,034,760 shares available for issuance under the Plan as of December 31, 2023.

Stock option activity under the Plan for the years ended December 31, 2022 and 2023 was as follows:

	Amount	Weighted-average exercise price	Weighted-average contractual life (years)	Aggregate intrinsic value (in thousands)
Outstanding at January 1, 2022	2,332,603	$ 3.93	8.30	$ 294
Granted	334,418	4.84		
Canceled / forfeited	(150,097)	3.39		
Outstanding at December 31, 2022	2,516,924	3.95	7.68	6,917
Granted	2,130,007	5.81		
Exercised	(65,264)	2.29		
Canceled / forfeited	(604,378)	6.13		
Outstanding at December 31, 2023	3,977,289	$ 4.64	7.7	$ 5,728
Options exercisable at December 31, 2023	2,281,655	$ 4.64	7.24	$ 4,209
Options vested or expected to vest at December 31, 2023	3,877,871	$ 4.69	7.7	$ 5,522

The Company's outstanding stock options include 773,195 performance-based awards that have vesting provisions subject to the achievement of certain business milestones. Total unrecognized compensation expense for the remaining performance-based awards is approximately $2.8 million. No expense has been recognized for these awards as of December 31, 2023 given that the milestone achievements for these awards have not yet been deemed probable for accounting purposes.

Aggregate intrinsic value for outstanding options for the year ended December 31, 2023 was approximately $5.7 million and calculated as the difference between the Company's closing stock price of $4.99 per share as of December 29, 2023 and the weighted average exercise price of $4.64. As of December 31, 2023, unrecognized compensation cost related to unvested non-performance-based awards amounted to $3.9 million, which will be recognized over a weighted-average period of 2.2 years.

The weighted average assumptions for valuing the Company's stock options granted were as follows:

	Year Ended December 31,	
	2023	2022
Risk-free interest rate	3.82%	2.74%
Expected volatility	125.35%	123.61%
Expected term (in years)	5.8 years	5.8 years
Expected dividend yield	—%	—%

The grant date fair value of stock options is estimated using the Black-Scholes option pricing model that takes into account the fair value of its common stock, the exercise price, the expected life of the option, the expected volatility of its common stock, expected dividends on its common stock, and the risk-free interest rate over the expected life of the option. The risk-free interest rate assumption is based upon observed treasury bill interest rates (risk-free) appropriate for the expected term of the Company's employee stock options. The computation of expected volatility is based on the historical volatility of the Company's common stock. The simplified method of estimating expected term was used. The Company has not paid and do not anticipate paying cash dividends on the Company's shares of common stock; therefore, the expected dividend yield is assumed to be zero.

The weighted average estimated fair value of stock options granted using the Black-Scholes model was $5.12 and $4.23 per share for the years ended December 31, 2023 and 2022, respectively.

The Company also estimated the fair value of non-employee share options using the Black-Scholes option pricing model reflecting the same assumptions as applied to employee and director options in each of the reporting periods, other than the expected life, which is assumed to be the remaining contractual life of the options.

Share-based compensation expense related to the Plan for the years ended December 31, 2023 and 2022 was allocated as follows:

	Years Ended December 31,	
	2023	2022
	(in thousands)	
Research and development	$ 327	$ 284
Selling, general and administrative	3,134	747
Total stock-based compensation	$ 3,461	$ 1,031

16. Net Loss per Share

Basic and diluted net loss per share was calculated as follows:

	Years Ended December 31,	
	2023	2022
	(in thousands, except shares and per share data)	
Net loss	$ (8,945)	$ (6,073)
Preferred stock dividends	(77)	(180)
Net loss attributable to common stockholders	(9,022)	(6,253)
Basic and diluted weighted average common shares outstanding	13,455,666	11,349,610
Basic and diluted net loss per share attributable to common stockholders	$ (0.67)	$ (0.55)

The Company's potentially dilutive securities, which include stock options, unvested restricted common stock units and warrants, have been excluded from the computation of diluted net loss per share whenever the effect of including them would be to reduce the net loss per share. In periods where there is a net loss, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same.

The following potential common shares were excluded from the calculation of diluted net loss per share attributable to common stockholders for the years ended December 31, 2023 and 2022 because including them would have had an anti-dilutive effect:

	Years Ended December 31,	
	2023	2022
Warrants to purchase common stock	1,113,622	1,113,622
Options to purchase common stock	3,977,289	2,516,924
Series E convertible preferred stock	—	619,259
Total	5,090,911	4,249,805

17. Segments and Geographical Information

The Company's chief operating decision maker is its Chief Executive Officer. The Company's chief operating decision maker evaluates the operating results of the Company's reportable segments based on revenues and net income (loss).

The Company has two operating and reportable segments: i) Regenerative Biotech focused on the development of regenerative medicine treatments with operations currently in the United States and ii) Longevity Products relating to longevity products with operations currently in Asia. The following table presents the Company's reportable segment results for the year ended 2023:

	Regenerative Biotech	Longevity Products	Total
2023			
Revenues	$ —	$ 103	$ 103
Net loss	(8,677)	(268)	(8,945)
Total assets	2,426	188	2,614

18. Subsequent Events

In March 2024, the Company received cash deposits in escrow of approximately $0.3 million from a group of prospective investors pertaining to a potential private placement transaction. These funds remain the respective investor's property and are being held by the Company in its bank account with Bank of America until the execution of a common stock purchase agreement.

On February 1, 2024, the Company entered into a loan arrangement with Junli He, the Chairman and Chief Executive Officer of the Company (the "Lender"), pursuant to which the Lender has agreed to loan the Company an aggregate amount of $500,000 as evidenced by a Bridge Note executed by the Company in favor of, and accepted by, the Lender (the "Bridge Note").

The Bridge Note accrues interest at an annual fixed rate of 8%, and the principal amount thereof will be due and payable in full, together with all accrued and unpaid interest thereon, on the earlier to occur of a) the closing date (or later date of capital being provided pertaining to such continued offering that the following threshold is tripped) of the Company's next capital raise that includes gross proceeds of at least $5,000,000 or b) February 1, 2025. The Bridge Note provides for optional conversion at the discretion of the Lender, contains covenants, and provides for certain events of default including if the Company fails to pay when due any amount owed thereunder, fails to comply with any agreement, covenant, condition, provision or term contained therein and other customary events of default.

Item 16. ***Form 10-K Summary.***

None.

EXHIBIT INDEX

The following exhibits are filed as part of this Annual Report on Form 10-K. Where such filing is made by incorporation by reference to a previously filed document, such document is identified.

Exhibit Number	Description of Exhibit
2.1§	Separation and Distribution Agreement between Harvard Apparatus Regenerative Technology, Inc. and Harvard Bioscience, Inc. dated as of October 31, 2013 (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on November 6, 2013, and incorporated by reference thereto).
3.1	Amended and Restated Certificate of Incorporation of Harvard Apparatus Regenerative Technology, Inc. (previously filed as an exhibit to the Company's Registration Statement on Form 10-12B, filed July 31, 2013, and incorporated by reference thereto).
3.2	Certificate of Amendment to Amended and Restated Certificate of Incorporation of Harvard Apparatus Regenerative Technology, Inc. dated March 30, 2016 (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on March 31, 2016, and incorporated by reference thereto).
3.3	Certificate of Amendment to Amended and Restated Certificate of Incorporation of Harvard Apparatus Regenerative Technology, Inc. dated May 26, 2016 (previously filed as an exhibit to the Company's Annual Report on Form 10-K, filed on March 17, 2017, and incorporated by reference thereto).
3.4	Certificate of Designations, Preferences and Rights of Series A Preferred Stock of Harvard Apparatus Regenerative Technology, Inc. classifying and designating the Series A Junior Participating Cumulative Preferred Stock (previously filed as an exhibit to the Company's Registration Statement on Form 8-A, filed October 31, 2013, and incorporated by reference thereto).
3.5	Certificate of Designation of Series B Convertible Preferred Stock of Harvard Apparatus Regenerative Technology, Inc. classifying and designating the Series B Convertible Preferred Stock (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on February 12, 2015, and incorporated by reference thereto).
3.6	Certificate of Amendment to Amended and Restated Certificate of Incorporation of Harvard Apparatus Regenerative Technology, Inc. dated April 26, 2017 (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on April 27, 2017, and incorporated by reference thereto).
3.7	Certificate of Designations, Preferences, Rights and Limitations of Series C Convertible Preferred Stock of Harvard Apparatus Regenerative Technology, Inc. classifying and designating the Series C Convertible Preferred Stock (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on August 17, 2017, and incorporated by reference thereto).
3.8	Certificate of Elimination of Series A Junior Participating Cumulative Preferred Stock (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on August 17, 2017, and incorporated by reference thereto).
3.9	Certificate of Amendment to Amended and Restated Certificate of Incorporation of Harvard Apparatus Regenerative Technology, Inc. dated December 22, 2017 (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on December 22, 2017, and incorporated by reference thereto).
3.10	Certificate of Designations, Preferences, Rights and Limitations of Series D Convertible Preferred Stock of Harvard Apparatus Regenerative Technology, Inc. classifying and designating the Series D Convertible Preferred Stock (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on January 3, 2018, and incorporated by reference thereto).
3.11	Certificate of Amendment to Amended and Restated Certificate of Incorporation of Harvard Apparatus Regenerative Technology, Inc. dated May 24, 2019 (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on May 28, 2019, and incorporated by reference thereto).
3.12	Amended and Restated By-laws of the Harvard Apparatus Regenerative Technology, Inc. (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on March 31, 2016, and incorporated by reference thereto).
3.13	Certificate of Amendment to Amended and Restated Certificate of Incorporation (previously filed as an exhibit to the Current Report on Form 8-K, filed on July 20, 2023, and incorporated herein by reference).
3.14	Third Amended and Restated Bylaws (previously filed as an exhibit to the Current Report on Form 8-K, filed on July 20, 2023, and incorporated herein by reference).
4.1	Specimen Stock Certificate evidencing shares of common stock (previously filed as an exhibit to the Company's Registration Statement on Form 10-12B, filed July 31, 2013, and incorporated by reference thereto).
4.2	Specimen Series B Convertible Preferred Stock Certificate (previously filed as an exhibit to the Company's Annual Report on Form 10-K, filed on March 27, 2015, and incorporated by reference thereto).
4.3	Form of Common Stock Purchase Warrant (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on January 3, 2018, and incorporated by reference thereto).
4.4	Form of Amendment to Common Stock Purchase Warrant (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on December 18, 2019, and incorporated by reference thereto).

4.5	Form of Common Stock Purchase Warrant (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on January 2, 2020, and incorporated by reference thereto).
4.6	Form of Common Stock Purchase Warrant (previously filed as an exhibit to the Company's Current Report on Form 8 K, filed on June 22, 2021, and incorporated by reference thereto).
4.7	Form of Common Stock Purchase Warrant (previously filed as an exhibit to the Company's Current Report on Form 8 K, filed on September 8, 2021, and incorporated by reference thereto).
4.8	Form of Common Stock Purchase Warrant (previously filed as an exhibit to the Company's Current Report on Form 8 K, filed on November 30, 2021, and incorporated by reference thereto).
4.9	Description of Securities (previously filed as an exhibit to the Company's Annual Report on Form 10 K, filed on March 27, 2020, and incorporated by reference thereto).
4.10	Form of Common Stock Purchase Warrant (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on May 13, 2022, and incorporated by reference thereto).
10.1	Intellectual Property Matters Agreement between Harvard Apparatus Regenerative Technology, Inc. and Harvard Bioscience, Inc. dated as of October 31, 2013 (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on November 6, 2013, and incorporated by reference thereto).
10.2	Product Distribution Agreement between Harvard Apparatus Regenerative Technology, Inc. and Harvard Bioscience, Inc. dated as of October 31, 2013 (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on November 6, 2013, and incorporated by reference thereto).
10.3	Tax Sharing Agreement between Harvard Apparatus Regenerative Technology, Inc. and Harvard Bioscience, Inc. dated as of October 31, 2013 (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on November 6, 2013, and incorporated by reference thereto).
10.4	Sublease by and between Harvard Apparatus Regenerative Technology, Inc. and Harvard Bioscience, Inc. dated as of October 31, 2013 (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on November 6, 2013, and incorporated by reference thereto).
10.5	Form of Indemnification Agreement for Officers and Directors (previously filed as an exhibit to the Company's Registration Statement on Form 10-12B, filed July 31, 2013, and incorporated by reference thereto).
10.6#	Third Amended and Restated Equity Incentive Plan, as amended (previously filed as exhibit to the Company's Quarterly Report on Form 10-Q, filed on November 13, 2023, and incorporated by reference thereto).
10.7	Employee Stock Purchase Plan (previously filed as an exhibit to the Company's Registration Statement on Form 10-12B, filed July 31, 2013, and incorporated by reference thereto).
10.8#	Form of Incentive Stock Option Agreement (previously filed as an exhibit to the Company's Registration Statement on Form 10-12B, filed July 31, 2013, and incorporated by reference thereto).
10.9#	Form of Non-Qualified Stock Option Agreement for executive officers (previously filed as an exhibit to the Company's Registration Statement on Form 10-12B, filed July 31, 2013, and incorporated by reference thereto).
10.10#	Form of Non-Qualified Stock Option Agreement for directors (previously filed as an exhibit to the Company's Registration Statement on Form 10-12B, filed July 31, 2013, and incorporated by reference thereto).
10.11#	Form of Deferred Stock Award Agreement (previously filed as an exhibit to the Company's Registration Statement on Form 10-12B, filed July 31, 2013, and incorporated by reference thereto).
10.12†	Sublicense Agreement dated as of December 7, 2012 between Harvard Apparatus Regenerative Technology, Inc. and Harvard Bioscience, Inc., and related Trademark License Agreement, dated December 19, 2002, by and between Harvard Bioscience, Inc. and President and Fellows of Harvard College (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on March 7, 2023, and incorporated by reference thereto).
10.13	Patent Rights Assignment dated December 21, 2012 between Harvard Apparatus Regenerative Technology, Inc. and Dr. Paolo Macchiarini (previously filed as an exhibit to the Company's Registration Statement on Form 10-12B, filed July 31, 2013, and incorporated by reference thereto).

10.14#	Offer Letter, dated June 4, 2018, between Harvard Apparatus Regenerative Technology, Inc. and William Fodor, PhD (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on July 10, 2018, and incorporated by reference thereto).
10.15	Form of Securities Purchase Agreement (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on April 6, 2023 and incorporated herein by reference).
10.16#	Employment Agreement, dated August 8, 2022, between Harvard Apparatus Regenerative Technology, Inc. and Joseph L. Damasio, Jr. (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on August 9, 2022 and incorporated by reference thereto).
10.17#	Amended and Restated Employment Agreement, dated January 11, 2023, between Harvard Apparatus Regenerative Technology, Inc. and David Green (previously filed as an exhibit to the Company's Current Report on Form 8-K, filed on January 12, 2023 and incorporated by reference thereto).
10.18#	Employment Agreement, effective as of March 1, 2023, by and between Harvard Apparatus Regenerative Technology, Inc. and Junli He (previously filed as an exhibit to the Current Report on Form 8-K, filed on March 14, 2023, and incorporated herein by reference).
10.19#	Amendment to Employment Agreement, dated as of July 10, 2023, by and between Harvard Apparatus Regenerative Technology, Inc. and Junli He (previously filed as an exhibit to the Current Report on Form 8-K, filed on July 10, 2023, and incorporated herein by reference).
21.1*	Subsidiaries of Harvard Apparatus Regenerative Technology, Inc.
23.1*	Consent of Marcum LLP.
31.1*	Certification of Chief Executive Officer of Harvard Apparatus Regenerative Technology, Inc., pursuant to Rules 13a-15(e) and 15d-15(e), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Chief Financial Officer of Harvard Apparatus Regenerative Technology, Inc., pursuant to Rules 13a-15(e) and 15d-15(e), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Chief Executive Officer of Harvard Apparatus Regenerative Technology, Inc., 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 Chief Financial Officer of Harvard Apparatus Regenerative Technology, Inc., 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 in iXBRL and contained in Exhibit 101)

* Filed herewith.

** This certification shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, or otherwise subject to the liability of that section, nor shall it be deemed to be incorporated by reference into any filing under the Securities Act of 1933 or the Securities Exchange Act of 1934.

Management contract or compensatory plan or arrangement.

§ The schedules and exhibits to the Separation and Distribution Agreement have been omitted. A copy of any omitted schedule or exhibit will be furnished to the SEC supplementally upon request. The Company will furnish to stockholders a copy of any exhibit without charge upon written request.

† Certain identified information has been excluded from the exhibit because it is both not material and is of the type that the registrant treats as private or confidential.

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 28, 2024

Harvard Apparatus Regenerative Technology, Inc.

By: */s/ Junli (Jerry) He*
Junli (Jerry) He
Chief Executive Officer

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/ Junli (Jerry) He **Junli (Jerry) He**	Chief Executive Officer, Director, and Chairman (principal executive officer)	March 28, 2024
/s/ Joseph Damasio Jr. **Joseph Damasio Jr.**	Chief Financial Officer (principal financial officer and principal accounting officer)	March 28, 2024
/s/ Jason Jing Chen **Jason Jing Chen**	Vice Chairman	March 28, 2024
/s/ David Green **David Green**	Director	March 28, 2024
/s/ Ting Li **Ting Li**	Director	March 28, 2024
/s/ Ronald Packard **Ronald Packard**	Director	March 28, 2024
/s/ Herman Sanchez **Herman Sanchez**	Director	March 28, 2024
/s/ James Shmerling **James Shmerling**	Director	March 28, 2024

Exhibit 21.1

Subsidiaries of the Registrant

Harvard Apparatus Regenerative Technology Limited	**(China)**
Harvard Apparatus Regenerative Technology GmbH	**(Germany)**
Harvard Apparatus Regenerative Technology Limited	**(Hong Kong)**

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement of Harvard Apparatus Regenerative Technology, Inc. (formerly known as Biostage, Inc.) on Forms S-8 (No. 333-192026, 333-192027, 333-203105, 333-212993, 333-219988, 333-225336, 333-239346, and 333-275592) of our report dated March 28, 2024, which includes an explanatory paragraph as to the Company's ability to continue as a going concern, with respect to our audits of the consolidated financial statements of Harvard Apparatus Regenerative Technology, Inc. as of December 31, 2023 and 2022 and for the years then ended, which report is included in this Annual Report on Form 10-K of Harvard Apparatus Regenerative Technology, Inc. for the year ended December 31, 2023.

/s/ Marcum LLP

Marcum LLP
Boston, Massachusetts
March 28, 2024

EXHIBIT 31.1

Certification

I, Junli He, certify that:

1. I have reviewed this Annual Report on Form 10-K of Harvard Apparatus Regenerative Technology, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)), and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 28, 2024

/s/ Junli (Jerry) He
Junli (Jerry) He
Chief Executive Officer, Director, and Chairman

EXHIBIT 31.2

Certification

I, Joseph Damasio Jr., certify that:

1. I have reviewed this Annual Report on Form 10-K of Harvard Apparatus Regenerative Technology, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)), and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 28, 2024

/s/ Joseph Damasio Jr.
Joseph Damasio Jr.
Chief Financial Officer

EXHIBIT 32.1

CERTIFICATION OF PERIODIC FINANCIAL REPORT
PURSUANT TO 18 U.S.C. SECTION 1350

The undersigned officer of Harvard Apparatus Regenerative Technology, Inc. (the Company) hereby certifies to his knowledge that the Company's Annual Report on Form 10-K for the year ended December 31, 2023 (the Report) to which this certification is being furnished as an exhibit, as filed with the Securities and Exchange Commission on the date hereof, fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended (the Exchange Act), and that the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company. This certification is provided solely pursuant to 18 U.S.C. Section 1350 and Item 601(b)(32) of Regulation S-K (Item 601(b)(32)) promulgated under the Securities Act of 1933, as amended (the Securities Act), and the Exchange Act. In accordance with clause (ii) of Item 601(b)(32), this certification (A) shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, and (B) shall not be deemed to be incorporated by reference into any filing under the Securities Act or the Exchange Act, except to the extent that the Company specifically incorporates it by reference.

Date: March 28, 2024

/s/ Junli (Jerry) He
Name: Junli (Jerry) He
Title: Chief Executive Officer, Director, and Chairman

EXHIBIT 32.2

CERTIFICATION OF PERIODIC FINANCIAL REPORT
PURSUANT TO 18 U.S.C. SECTION 1350

The undersigned officer of Harvard Apparatus Regenerative Technology, Inc. (the Company) hereby certifies to his knowledge that the Company's Annual Report on Form 10-K for the year ended December 31, 2023 (the Report) to which this certification is being furnished as an exhibit, as filed with the Securities and Exchange Commission on the date hereof, fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended (the Exchange Act), and that the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company. This certification is provided solely pursuant to 18 U.S.C. Section 1350 and Item 601(b)(32) of Regulation S-K (Item 601(b)(32)) promulgated under the Securities Act of 1933, as amended (the Securities Act), and the Exchange Act. In accordance with clause (ii) of Item 601(b)(32), this certification (A) shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, and (B) shall not be deemed to be incorporated by reference into any filing under the Securities Act or the Exchange Act, except to the extent that the Company specifically incorporates it by reference.

Date: March 28, 2024

/s/ Joseph Damasio Jr.
Name: Joseph Damasio Jr.
Title: Chief Financial Officer